# Smith's Textbook of Endourology

# Smith's Textbook of Endourology

## Fourth Edition

## VOLUME 1

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## Foreword

"Endourology" was the 1978 branding brainchild of Elwin Fraley, Arthur Smith, and Paul Lange.[1] Most felt that the Minnesota cold had finally gone beyond their woolen headgear to create a "brain freeze" of monumental proportions. Fast forward nearly 40 years and, today, endourology has become urology. Diagnostically, from the urethral meatus to the uppermost renal calyx, the entire urogenital tract can be revealed in great detail using both endoscopic and sophisticated imaging technologies. Therapeutically, urologists of talent, innovation, and persistence have supplanted standard incisional access with an endoscopic, image-guided, or combined approach.

If you are reading this Foreword then you are reading a book that contains every aspect of urology and how it is benefited by a minimally invasive (i.e. percutaneous, ureteroscopic, laparoscopic, robotic) or noninvasive image-guided (i.e. shock-wave lithotripsy, focal therapy) approach. The authors are an international *Who's Who* of experts in endourology. The content ranges from basic to futuristic endourology. In 166 chapters, the latest advances in antegrade and retrograde endoscopic nephrostomy, laparoendoscopic single-site surgery, and robotic procedures as well the newest image-guided therapies are clearly detailed and illustrated both in photographs and often by instructional video demonstrations.

A wise mentor[2] once advised me: "You are only as good as tomorrow." That single sentence should haunt each of us as we arise every morning to provide relief to those who suffer. To that end, we must seek methods to relieve suffering rather than cause it, to heal without harming, to cure without substituting one malady for another. Endourology empowers each of us to provide all individuals seeking our care with a kinder, gentler solution to their urological problems. In the first part of the twentieth century, Sir William Osler opined: "Diseases that harm require treatments that harm less."[3] A century later, his dictum has been largely realized in the practice of endourology.

My heartfelt congratulations go out to Drs Smith, Badlani, Kavoussi, Preminger, and Rastinehad, who have provided a comprehensive guide of immense value to me, to you, and to all of our patients. Read *Smith's Textbook of Endourology* well, apply its principles earnestly, and, if opportunity presents, seek to further innovate and build on its contents. The text is not an end in and of itself; rather, it is another paver in the surgical journey in which each of us plays a role — using techniques borne of today's technology to proceed to further reduce the burden of the "surgical" cure we are obligated to apply.

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## Notes

1 Smith AD, Lange PH, and Fraley EE. Letter to the Editor: applications of percutaneous nephrostomy. New challenges and opportunities in endo-urology. *J Urol* 1979;121:382.

2 Arthur D. Smith.

3 Attributed to Sir William Osler (1849–1919).

# Preface

The cover of this textbook synthesizes the concepts of endourology. In order to perform endoscopic surgery one needs access to the organ and various forms of energy to facilitate access, control bleeding, and obliterate tissues. These goals can only be accomplished with appropriate devices. Fortunately, evolving technology allows the manufacture of improved devices. It is essential for endourologists to keep abreast of these advances. The fourth edition of this book accomplishes this with an update of the existing chapters by the original authors or complete revision by new authors.

In 1978 the concept of endourology was launched. It was defined as closed, controlled manipulation within the urinary tract. The word "closed" was used to indicate either a minimal incision or no incision at all and the control was achieved either endoscopically or by noninvasive imaging. Until then, residents had been taught that the only way to have good exposure was through a large incision. Now the ultimate goal is good exposure with no incision at all. This is achieved by utilizing a combination of endoscopy and the new modalities of imaging. There are now relatively few accepted open urological procedures and this has had the gratifying result of a dramatic decrease in the morbidity of our patients undergoing treatment.

In this era of fewer working hours for residents, the amount of time that the residents spend in the operating room has decreased dramatically and the necessary skills have to be taught using a combination of additional educational modalities. In addition to books and journals, there are an abundance of videos on surgical techniques, animal laboratories, teaching models, and virtual reality simulators. Fortunately, endourologic techniques are uniquely suited to these modalities and the student can become quite adept by using them before being instructed in the operating room.

As the technology has evolved, courses have been organized by the Endourology Society to train not only the residents and fellows, but also the practicing urologist so that their "learning curve" can be accelerated, and they can then use these techniques with the required expertise. In addition, the Endourology Society has developed the *Journal of Endourology* and the *Journal of Endourology Case Reports* to update urologists on the latest technology. The *Journal of Endourology* allows the members access the *Journal of Videourology* which features videos of new and established techniques on the computer or tablet.

This textbook consists of two volumes. Volume 1 is on stones of the upper tract. Volume 2 is on robotic and laparoscopic surgery and image-guided diagnostic and therapeutic techniques together with minimally invasive therapy of the lower urinary tract. Volume 1 consists of five sections. Section 1 discusses the basic principles. Section 2 is devoted to percutaneous renal surgery. Section 3 discusses the intricacies of ureteroscopy. Section 4 is on shock-wave lithotripsy. We are cognizant of the fact that there is no single modality for the treatment of stones and hence Section 5 describes the management of the patient with various stone-related problems in a composite format.

Volume 2 covers robotic and laparoscopic surgery. At present, there is very little difference between the techniques and that which there is is primarily related to technical experience, availability of the robot, and financial considerations. Sections 6 and 7 discuss image-guided diagnostics and therapeutics. This is an important addition to our *Textbook of Endourology*, as it is an essential component of the armamentarium of the practicing urologist, particularly as we move into the era of "no incision." If the procedures described in this section are not performed by urologists, then they will be taken over by radiologists. This in turn will result in the loss of continuity of care of our patients.

I would like to thank each of the contributors for the many hours they have devoted to writing, illustrating, and creating videos for their chapters. Hopefully, they will be as delighted with the results as the editors and publishers of this textbook. I am also deeply indebted to my co-editors, who have reviewed, edited, and re-reviewed chapters countless times. Thanks to their families as well, as the time spent on the book could have been devoted to them. The staff at Wiley Blackwell and the project manager Mirjana Misina have been highly professional and encouraging. When one deals with a large organization, it is reassuring to know that as a book bounces from one stage to the next there has been a "continuity of care throughout the operation." They are a great team and we appreciate all the help we received from them.

Finally, I would like to thank my wife, Kay, who inspired me to edit this fourth edition and has repeatedly helped me with this and countless other projects throughout my academic career. If I am regarded as the "father" of endourology, she is unquestionably the "mother" who has helped to nurture this field of urology.

June 2018 *Arthur D. Smith*

## About the Companion Website

This book is accompanied by a companion website:

**www.wiley.com/go/smith/textbookofendourology**

The website includes:

- Over 100 videos showing procedures as described in the book
- PowerPoints of all figures from the book for downloading

All videos are referenced in the text where you see this icon: 👁

# SECTION 1

# Basic Principles

# 1

# Care and Sterilization of Instruments

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## History of sterilization

The creation and use of surgical instruments has occurred since prehistoric times. The effects of using instruments that were neither clean nor sterile were not a major concern in past eras. The methods for the care and sterilization of instruments have gone through a huge change and have greatly improved over the last few centuries. It was not until the nineteenth century that the development and recognition of a process for instrument sterilization occurred. During this time the focus on the need to sterilize instruments prior to a surgical procedure developed from the effects of post-surgery wound management and the need to eliminate the increased infections of these wounds. This recognition led to the evolution and development of the current standard practice of instrument sterilization.

Noted in the nineteenth century, surgeons performed operations in their street clothes, which were often dirty, and they also reused instruments without a standard cleaning process. In 1864, Joseph Lister introduced the use of phenol, or carbolic acid, on inanimate objects and surfaces as well as human tissue, in hospital wards and operating rooms which resulted in a dramatic decrease in the incidence of wound infections. The carbolic acid was used in conjunction with other components to dress wounds in an antiseptic manner which prevented bacteria from entering the wound. This led Lister to introduce other methods of asepsis, such as sterilization of surgical instruments by applying heat and carbolic acid and the frequent cleaning of the surgeon's hands during an operation. After publication of these findings, in the *The Lancet* in 1867 the "era of antiseptic surgery" was introduced into the field of medicine and surgery. By the year 1875 Lister's principles of antiseptic surgery were accepted worldwide [1].

The steam autoclave was derived from a steam digester currently known as a pressure cooker invented by a physicist named Denis Papin in the late 1600s. By 1879, Charles Chamberland, a colleague of Louis Pasteur, made improvements to Papin's invention and invented a porcelain dish with tiny holes that was able to filter microorganisms from liquid that was poured through this dish. This is known as the Chamberland filter or the Chamberland–Pasteur filter and with his further research in 1884 the autoclave was invented. The use of pressurized steam sterilization of instruments with an autoclave was introduced by Ernst von Bergmann in 1886.

Ethylene oxide (ETO) was first used in 1938 to preserve spices. In the 1950s, ETO was accepted by the medical device industry as a sterilant after a US army researcher investigated the microbicidal effect of ETO and published his findings [2]. This method of sterilization has been used for heat-sensitive instruments, such as flexible scopes and lenses. In the early 1900s, urological instruments were sterilized in a formalin sterilizer and disinfected with a carbolic acid solution. The formalin sterilizer exposed instruments to heated formalin vapors for 2 hours and remained in the sterilizer until use [3].

Since the late 1980s other methods of sterilization were developed that were less caustic to instruments, required less process time, are noncarcinogenic, and allowed for sterile instrument availability. These methods have replaced some of the older sterilization methods.

## Instrument processing

Any item, such as an instrument or medical device that is intended to be reused in a sterile procedure, must be processed in a specific manner, beginning with cleaning and ending with sterilization or high-level disinfection (HLD).

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

In order for sterilization or HLD of an item to be effective, the following steps must occur in a proper and adequate manner: precleaning, cleaning, decontamination, rinsing, drying, disinfection (includes HLD immersion and rinsing with sterile water) or sterilization, and storage. The necessary type of package or container preparation the item will be placed in is determined by the method of sterilization, such as a paper peel package or metal container. In some instances the item may be placed in storage until reuse, such as those that require, at the minimum, HLD.

Urologic instruments consist of reusable flexible cystoscopes, flexible ureteroscopes, flexing instruments for endoscopes, rigid cystoscopes, semi-rigid ureteroscopes, transurethral resection instruments, rigid nephroscopes, laparoscopic instruments, metal dilators, various metal surgical instruments, and ultrasound probes, both external and internal (intracavity, endorectal, or prostate biopsy probes).

First the item should be categorized to determine which type of disinfection or sterilization method is recommended for processing. In 1968 Earl H. Spaulding categorized medical instruments and items used for patient care as critical, semicritical, and noncritical based on the degree of risk for infection with the processing and reuse of each item. These categories make up the Spaulding scheme or Spaulding classification system, which is a recognized resource when describing the appropriate disinfection and sterilization process for medical instruments and devices [4, 5]. Critical items are instruments which will come in direct contact with sterile tissue, enter the vascular system, or penetrate the skin. They require sterilization by such methods as steam, ETO, hydrogen peroxide gas plasma, or a liquid chemical sterilant such as peracetic acid [6]. Semicritical items are instruments which will come in contact with mucous membranes and require sterilization or at a minimum HLD. These items have been identified as high risk for transmitting infection [7]. Noncritical items are instruments or medical devices, such as a stethoscope or blood pressure cuff, which will come into contact with intact skin only and require intermediate to low-level disinfection, such as an impregnated antimicrobial wipe. Neglect of low-level disinfection can lead to cross-contamination to the healthcare worker's hands; reuse of the instrument or medical device with another patient also causes cross-contamination [5, 8–10].

Utilization of a reusable instrument or medical device is a major risk due to the potential introduction of pathogenic microorganisms, which can lead to infection. Therefore, adequate cleaning is imperative to successfully eliminate the bioburden or microbes present on an instrument. Cleaning and decontamination of any level of item used in any type of healthcare facility is a mandatory requirement prior to reuse. Each facility must have a policy and procedure manual in place which identifies the process of cleaning or decontamination, followed by the process for disinfection or sterilization of these items when indicated.

Cleaning is the most important step in the process leading to sterilization or HLD and begins with physically removing microbes in preparation for the next step, which is decontamination [8]. There are different accepted methods for cleaning instruments prior to disinfection or sterilization. These are either manual or automated, which can include a washer/sterilizer, ultrasonic cleaner, or washer/decontaminator [11].

Prior to the cleaning process, any healthcare personnel must don personal protective equipment (PPE) to protect their eyes, skin, and clothing from splashing or droplet contact from any angle [12]. PPE includes eye protection (goggles or mask with shield), mask, impervious gown with long sleeves, gloves, hair bonnet or cap, and shoe covers to avoid exposure to microorganisms and for personal safety protection [6, 11]. After the cleaning and decontamination process, the PPE must be removed or doffed followed by hand hygiene practice [12].

Manual cleaning involves three components: a low-sudsing detergent or enzymatic cleaner, a brush or sponge, and friction [13]. These components will ensure the removal of tissue and debris from an instrument. Manual cleaning of an item begins with immersion in a receptacle or deep sink filled with detergent or enzyme cleaner and warm water solution. Preparation of the detergent or enzymatic cleaner must follow the manufacturer's instructions to ensure the solution is the correct concentration and temperature to maintain its effectiveness. Many cleaners are designed with a premeasuring pump mechanism; healthcare personnel must make certain a full depression of the pump occurs to ensure appropriate solution concentration. A weak solution may fail to break down proteinaceous tissue or a strong solution may create sudsy bubbles which form air pockets and can prevent surface contact by the cleaner. To accurately fill the receptacle or sink with the correct amount of water, a fluid depth indicator or line should be placed for guidance of accuracy [13, 14]. An example is shown in Figure 1.1. A visible instruction guide should indicate the correct solution amount to be added to the correct measurement of water; for example 1 ounce of detergent to 1 gallon of water (Figure 1.2). To prevent aerosol formation by microorganisms, the item being cleaned should be kept immersed below the solution level [8].

Prior to immersion, if the item has numerous parts it must be disassembled, and hinged instruments must be kept in the open, unlocked position. Gentle scrubbing of the item with a soft-bristle brush or sponge will assist in

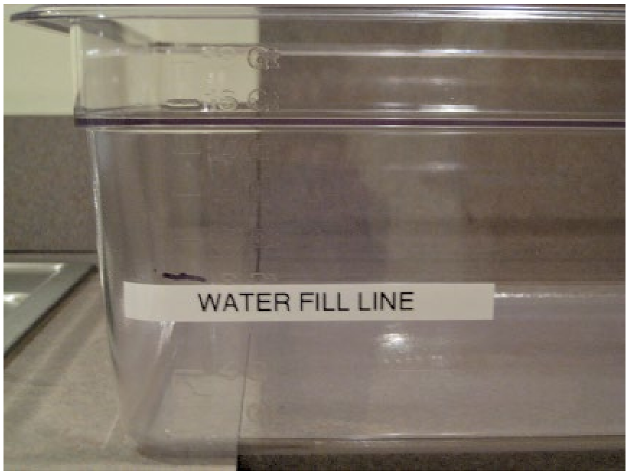
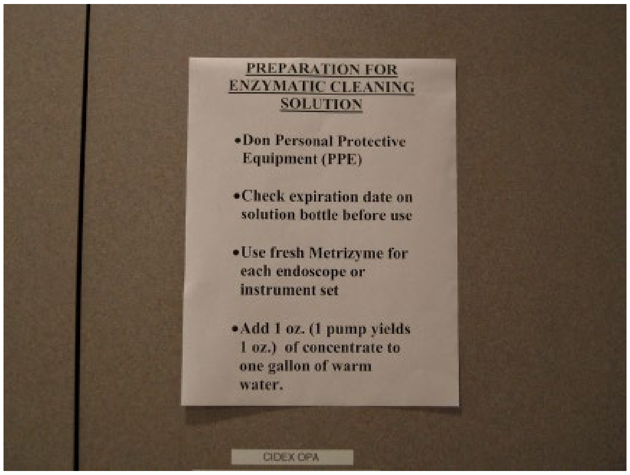


**Figure 1.1** Example of the fill line of a cleaning receptacle.



PREPARATION FOR ENZYMATIC CLEANING SOLUTION

- Don Personal Protective Equipment (PPE)
- Check expiration date on solution bottle before use
- Use fresh Metrizyme for each endoscope or instrument set
- Add 1 oz. (1 pump yields 1 oz.) of concentrate to one gallon of warm water.

**Figure 1.2** Visible instructions for preparing an enzymatic cleaner.

removal of bioburden and preservation of the instrument's functions and effectiveness [11]. The most recent recommendation is to use a disposable, single-use brush or sponge. The use of disposable brushes or sponges during the cleaning process will help to prevent cross-contamination to instruments, endoscopes, and medical devices. If a reusable brush is to be used due to cost issues then it must follow undergo HLD between each use [6]. Endoscope manufacturers each have their own select line of various styles and sizes of single-use brushes, with instructions for use (IFU) guidelines for their specific endoscope models. The correct brush should be used for each instrument; the important components of the brush when selecting which one to use are its length, diameter, design, and material [15]. For example, the proper brush used for a flexible cystoscope should be longer than the scope itself, be the right diameter to easily fit through the internal working channels, be kink-resistant, and have a plastic tip on the end to protect the scope internal channel(s).

The next step in manual cleaning is to thoroughly rinse the item with cool tap water in a deep sink to allow for ample movement. Following rinsing, sufficient drying time is needed before the item is to be prepared for sterilization or HLD.

In urology, endoscopes, both flexible and rigid, are a frequently used. They are valuable diagnostic tools that are reusable and require healthcare personnel to follow the guidelines for reprocessing to prevent an outbreak of infection due to improper cleaning. These scopes are introduced into the bladder to examine its appearance and anatomy, as well as the lower urinary tract and prostate gland. Other uses are for urine specimen collection, bladder biopsies, removal of small stones, small foreign objects, or an indwelling ureteral stent. An estimated 4 million or more cystoscopies are performed in the United States each year [16].

When indicated by the manufacturer a leak test should be performed on flexible endoscopes after precleaning and prior to full immersion of the scope in the cleaning solution. This test is done to check the integrity of the outer covering and the internal lining of the scope shaft for any leaks. Before the shaft of the scope is submerged in water, the scope manufacturer leak testing device (which may be manual/hand-operated or automated) is connected to the flexible scope to allow pressurized air to fill the internal channel. The purpose of this test is to determine if there are any microscopic holes from continued use and reprocessing, which would be a source of contamination due to fluid accumulation. The presence of a leak will be identified if the pressurized scope produces a flow of bubbles when inserted in water. Careful inspection of the flexible endoscope for any visible cracks, tears in the sheath material, or malfunctions of its performance is another vital step in reprocessing [6, 7].

External surfaces should be washed with a soft brush or sponge to remove any visible debris. Careful attention should be focused on the lumens and working channels of all endoscopes. Lumens and working channels should be irrigated with a large syringe or a manufacturer-specific irrigating device. This is done first with detergent or enzymatic solution to help remove any residue, followed by a water rinse until it appears clear. Using the appropriate-size flexible brush will allow for proper cleaning of the lumens and working channels. Once the brush exits the tip of the scope, the bristles should be cleaned before pulling the brush back into the internal channel [6]. Brushes are available in a variety of sizes and shapes to accommodate any manufacturer's endoscopes, and proper selection is essential for prevention of damage to the endoscope (Figure 1.3). Use of newly prepared cleaning

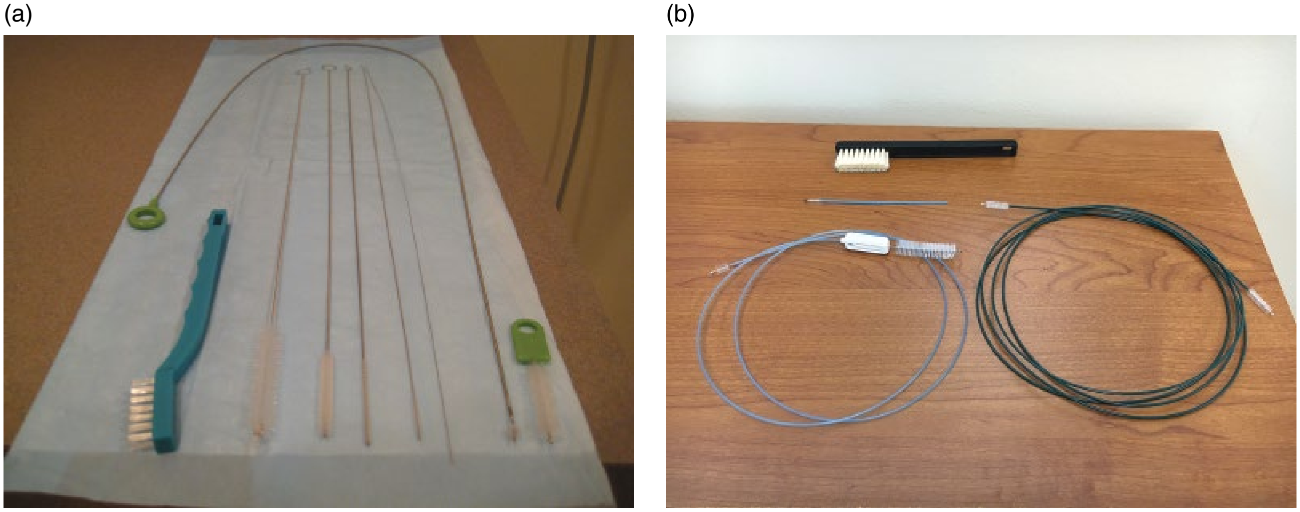


**Figure 1.3** (a) Examples of various cleaning brushes. (b) Examples of brushes and their tips.

solution prior to cleaning of each endoscope is most effective and helps prevent cross-contamination [13, 14].

A washer/sterilizer is designed to have several cycles, starting with a cold water pre-rinse, followed by a high-temperature wash cycle with an alkaline low-sudsing detergent, a neutralizing cycle, and then by a final rinse, steam sterilization, and a drying cycle [9, 11]. An ultrasonic cleaner functions by cavitation. Ultrasonic energy is passed through a water bath, creating microscopic bubbles that implode. The implosion process creates a suction action that pulls soil and foreign body matter away from instrument surfaces [9, 11]. Instruments that contain plastic or rubber should not be placed in an ultrasonic cleaner. The washer/decontaminator is a single or multi-chamber unit that cleans using an alkaline low-sudsing detergent with a spray force action and heat during the drying cycle. Multi-chamber units allow multiple single tasks to be performed simultaneously including a cool-water rinse, pre-wash with an enzymatic cleaner, wash cycle with detergent, ultrasonic cleaning, pure hot water rinse, and high-temperature drying [9, 11].

## Protection, handling, and maintenance of instruments

Protection, proper handling, and maintenance of instruments are vital in maintaining the efficacy of instruments as well as keeping instrument replacement costs down [17]. During and immediately following a procedure, heavily soiled instruments should be immersed in warm water to prevent the onset of corrosion, pitting, and rusting [11, 17]. Precleaning helps to remove debris or bioburden and prevent it from drying on the instrument. If not removed completely debris could cause an obstacle in the next steps of reprocessing and be a potential source of cross-contamination. When using flexible or rigid endoscopes, the working channel should be flushed immediately after use to prevent bioburden from drying inside and the external part should be wiped down to remove visible debris [6].

Proper handling of instruments is a crucial part of maintaining an instrument's function, especially when setting up a procedure and during reprocessing. This step is often overlooked in a careless manner due to one's haste in preparing for the next procedure. Any delicate instruments such as telescopes, flexible scopes, light cables, and fine instruments such as microinstruments must be handled in a specific manner. During a procedure these instruments should be kept in a separate location on the sterile field/setup to avoid other instruments from being placed on top of them and causing potential damage. When transporting delicate instruments to the soiled processing room they should be placed in a specific labeled biohazard container designed for instrument transport [12]. Flexible scopes and light cables must not be over-coiled while on the sterile field/setup or during transport; this will help prevent the internal fiber optics from becoming cracked or broken.

After cleaning, instruments should be checked for their function and lubricated when recommended by the manufacturer with a water-soluble lubricant [4]. Lubrication also helps prevent rusting and maintains the function of any movable piece, such as a Leur Lock part.

## Methods of sterilization

Sterilization can be achieved by way of several approved methods. These methods include using steam, ETO gas, peracetic acid, or hydrogen peroxide gas plasma.

Each method has its advantages and disadvantages along with specific indications for use. The manufacturer's guidelines and IFU for any instrument must be followed when selecting which method to use to ensure instrument viability and appropriate sterilization [18]. The healthcare setting will determine which method is suitable for the facility's operational workflow. Monitoring and documentation of the effectiveness of any sterilization method is a mandatory requirement and must be followed according to your facility's policy and procedure guidelines.

### Steam sterilization

The process of steam sterilization occurs in a steam autoclave unit designed to produce boiling water at 121 and 132 °C. A pressure of 103.42 kPa further produces steam to penetrate packaged or wrapped instruments or instruments in sterilization containers to kill any microorganisms present, including spores [19]. In order for steam sterilization to be successful the following standards are required: direct exposure to pressurized steam, a specific temperature, and a specific length of time [4].

There are types of cycle in a steam autoclave. One is the gravity-displacement cycle which removes air by the force of gravity from the top downward. Another method is the prevacuum cycle, in which the air is removed via a vacuum pump; this is also referred to as dynamic air removal [4]. The temperature and exposure time vary depending on the type of autoclave unit and the contents of the load.

A common cycle consists of 15 minutes of preheat, 15 minutes of pressurized steam, and 5–15 minutes of cooling [19]. Steam sterilization has been in existence for a long time and it is recognized to be one of the most effective, safe, and economical sterilization techniques [20].

One major disadvantage of steam sterilization is the inability to sterilize heat-sensitive materials, such as plastic or some rubber materials. Some advantages are that it is a short process, allowing a quick turnaround of packaged items, and it can be used in any healthcare setting due to the availability of various sizes of autoclave, including a table-top version which can be used in an office setting. However, some healthcare systems are moving away from table-top steam autoclaves due to the age of the technology, and the lack of quality control and biological indicator monitoring. Hence, critical items that need to be sterilized are transported to a hospital facility or a designated outsourced instrument processing facility with free-standing steam autoclaves. Depending on the cost, outpatient office settings can purchase various disposable, one-time-use, single instruments or use reusable instruments.

### ETO

ETO has the ability to sterilize heat- and moisture-sensitive instruments and medical devices, such as ones made of plastic or rubber, flexible scopes, and other instruments with lenses. ETO sterilization is a lengthy process, lasting 12 hours or more, which decreases the availability of a center's instruments. The process must be carried out in an area with proper ventilation, vent-failure alarms, and a special sterilization chamber. Careful monitoring of ETO concentration must be maintained in work areas to prevent potential injury to healthcare personnel. Due to ETO's high flammability it is mixed with inert gases, such as carbon dioxide or a fluorinated hydrocarbon, to decrease the risk of fire. In recent years hydrocarbons such as Freon 12, which used to be mixed with ETO for sterilization, have been found to contribute to destruction of the Earth's ozone layer. Therefore, since 1998 there has been a significant decrease in the use of ETO for sterilization, since other methods have been introduced [20]. Other disadvantages of ETO are it has the potential to cause harm to healthcare personnel if there is exposure, either acute or chronic. Irritation to the eyes or skin may occur from acute exposure. Chronic exposure may lead to hematologic changes, increased risk of spontaneous abortion, and some forms of cancer [4].

### Peracetic acid

In 1988 a low-temperature sterilization method using a peracetic acid compound was introduced for medical and surgical instruments, including endoscopes and instruments with lumens. Peracetic acid is an oxidizing agent composed of acetic acid, hydrogen peroxide, and water but has the disadvantage of being corrosive [21]. To allow for sterilization with peracetic acid, the STERIS Corporation in Mentor, Ohio, USA manufactured a sterilant of 35% peracetic acid and a noncorrosive chemical. This sterilant was packaged in a sealed, single-dose container and was designed to be used in the manufacturer's table-top sterilizer. This system was for "just in time" use, and so it did not require instruments to be wrapped or packaged. The table-top system was equipped with covered tray inserts to accommodate various sizes of flexible endoscopes, rigid endoscopes, and other instruments. To circulate the sterilant and rinse water through the lumens and working channels of endoscopes, specific connecting tubes were designed to attach to the different styles of scopes.

This sterilization process required filtered water of 50 °C to dilute the sterilant to a 2% concentration and the system was designed to empty the liquid concentrated sterilant via a drainage system that had to be connected to the facility's waste management line. The final phase removed excess water by passing clean filtered air through the machine's chamber, including the tubing connected to the lumens and working channels of the scopes. This table-top unit was equipped with a computer controlling the cycle's temperature, duration, and verification of completion status. Another feature of this unit was it allowed a diagnostic cycle to be run before daily use to ensure the unit had full functionality. An internal sensor would stop the unit and abort the procedure if an error in the process was detected [4, 21].

In December 2009 the US Food and Drug Administration (FDA) ceased to allow the use of the original STERIS I system due to it being unable to sterilize instruments as originally intended. The system may not have performed appropriately and therefore caused possible transmission of microorganisms to patients and healthcare workers and improper instrument function [22].

But in April 2010 the FDA approved a newly designed liquid chemical sterilization system known as the Steris System 1E Liquid Chemical Sterilant (SS1E), which uses a peracetic acid-based germicide to sterilize medical instruments such as flexible endoscopes. The system uses filtered tap water that is exposed to ultraviolet rays to eliminate microorganisms such as fungi, protozoa, and bacteria in the water. Once the process is completed the instrument or device is ready for use or can be placed in storage if not needed. Since this system uses filtered tap water, which is not sterile, critical items are contraindicated for this method [22–24].

## Gas plasma

The newest method of sterilization is hydrogen peroxide gas plasma sterilization, which has been available in the United States since 1993. This low-temperature system allows for sterilization of instruments, especially heat-sensitive or delicate ones, in just 60–75 minutes, depending on the model [20].

This technology is based on gas plasma, which has been referred to as the fourth state of matter (i.e. liquids, solids, gases, and gas plasmas) [4]. There are five phases of this process: the vacuum phase, injection phase, diffusion phase, plasma phase, and vent phase. Terminal sterilization occurs after these five phases have been completed.

The positive aspects of this system are there are no toxic fumes, no plumbing, no aeration time, and no ventilation system required. The compact, free-standing system requires a small area and an electrical source [21].

## Immediate-use sterilization

Flash sterilization, or immediate-use steam sterilization (IUSS) [10], is a high-temperature, high-moisture process used to sterilize wrapped or unwrapped instruments rapidly for just-in-time use. This method is most useful in an emergency situation when an instrument becomes contaminated during a procedure and there is no sterile replacement. Other reasons for using this method may include a low-volume inventory of specialty instruments that are needed for back-to-back procedures, or that a surgeon brings a specialty instrument required for a procedure that is not available in the healthcare facility. However, these reasons should be resolved by purchasing the appropriate amount of instruments based on the volume of cases and improved communication with surgeons in advance if any specialty instruments are needed for the case. These instruments can be brought to the healthcare facility and processed according to the manufacturer's guidelines in a timely manner with the proper communication and planning.

During the last 10 years, immediate-use sterilization in healthcare facilities has come under close scrutiny due to an increase in surgical site infections (SSI) in patients who had an immediate-use-sterilized item used or implanted during their procedure [4]. Although it is an approved method of sterilization for immediate use, excluding heat-and moisture-sensitive items such as flexible endoscopes or implants, it has become a controversial method.

IUSS is not effective if the instrument or device has not been appropriately cleaned, decontaminated, and rinsed according to the manufacturer's instructions. The cleaned item to be sterilized is placed in an open mesh pan or a specially designed rigid container with a lid that allows for rapid penetration of steam [4]. Once the sterilization cycle has been completed the covered, sterile item is transported to the point of use. Ineffective cleaning and sterilization can result in a SSI, increased length of hospital stay, increased hospital costs, and liability. As of 2014, the Joint Commission has included in their National Patient Safety Goals a focus on prevention of SSIs, which can be caused by instruments being improperly cleaned and processed by IUSS [25].

Multiple issues need to be considered when approving this method of sterilization in your healthcare facility. A most crucial issue is the location where the instrument will be cleaned prior to sterilization. It is ideal for the instrument to be processed in a designated soiled utility room with negative pressure and 10 air exchanges per hour [26]. If there is no designated soiled utility room within the operating environment then the instrument should be brought to the central sterile processing department for adequate processing. Location of the immediate-use sterilizer will determine whether pan or container method should be utilized, such as an open pan or a steam-penetratable container with a lid. With the implementation of IUSS, healthcare facilities are placing intended sterilizers for immediate use in close proximity to specific operating or procedure rooms to assist in aseptic transport to the sterile field. Healthcare personnel retrieving containers from the sterilizer and transporting sterilized devices must don heat-sensitive gloves to avoid the potential risk of burning. Once the item is accepted into the sterile field it must be cool before use to prevent a patient burn injury. If necessary the immediate-use-sterilized item should be placed in sterile saline to cool before use.

Depending on the type of sterilizer and the composition of the item to be sterilized for immediate use there are specific guidelines from the American National Standards Institute/Association for the Advancement of Medical Instrumentation (ANSI/AAMI) [24]. The temperature regardless of the sterilizer should always be 132–135 °C. The recommended sterilization exposure time ranges from 3 to 10 minutes and depends on the type of sterilizer and the contents of the load. Drying times of 0–1 minute are recommended for gravity-displaced sterilizers and will also depend on the item and the sterilizer manufacturers' instructions [4, 27].

Quality monitoring of the sterilizer's daily function and each cycle along with documentation is a vital part of the sterilization process. The types of monitoring for include physical, efficacy, chemical, and biological rapid readouts. Any breakdown in the process, such as an incorrect temperature or a positive biological indicator, must be reported immediately to management and the physician for further follow-up and corrective action.

Education of staff and documentation of competence of the procedure for immediate-use sterilization are other important requirements. Initial and annual training should be provided to all involved healthcare personnel, along with return demonstration by the staff to validate their competency in immediate-use sterilization [27, 28].

To avoid overuse of immediate-use sterilization, it is recommended to increase the inventory of high-volume items that are being sterilized for immediate use, to review the schedule the day before to anticipate instrumentation needs, to expedite immediate sterilization after use of surgeon or procedural specialty items to allow for availability of sterile equipment, and to take receipt of implants in a timely manner to allow for a full sterilization process to take place prior to the procedure's start time [28, 29].

## Other alternatives

HLD is the other alternative to sterilization in specific healthcare environments. HLD can be expected to kill all microorganisms, with the exception of a few bacterial spores when a high number is present [4, 6, 19]. The steps of this process are similar to sterilization but do not include packaging or placement of an item in a sterilization container. The steps of this process are precleaning, cleaning, rinsing, drying, immersion in disinfectant solution, sterile-water rinsing, drying, and immediate use or storage. As of March 2015, the FDA approved various agents for HLD: ≥2.4% glutaraldehyde, stabilized hydrogen peroxide, peracetic acid, and ≥0.575% *ortho*-phthalaldehyde (OPA) [5, 30]. Some of these agents may be mixed together at certain strengths to make one disinfectant solution. The required soak time and temperature of the solution differs based on the disinfectant used. Aldehyde agents are most commonly used for HLD, especially for the manual process. Glutaraldehyde, which is the most commonly used solution, has an alkaline pH and can be used for 2–4 weeks or 30 days depending on the formula, but must be checked daily for potency [19, 30]. The disinfectant solution to be used for the instrument or medical device must be approved by the instrument or device manufacturer and be stated in the IFU guidelines. Prior to use, healthcare personnel must don a new set of PPE, including a full face shield, impervious gown with sleeves, and nitrile gloves. The chemical disinfectant must be prepared in a well-ventilated area with a low traffic pattern.

Depending on the IFU, some flexible endoscopes can be processed in an automatic endoscope reprocessor. This is a closed system that allows the scope's external surface to be fully exposed to the disinfectant solution. Connection tubing is attached to the lumens, allowing internal channels to be purged with the solution as well. The benefit of this closed system is it lessens the chance for exposure to the chemical disinfectant solution [6].

With a shift of hospital procedures to outpatient healthcare facilities, there is an ever-present concern about HLD and sterilization of semicritical and critical instruments and medical devices. Nationwide in the United States there is an awareness of neglect in the required guidelines for processing of semicritical items by HLD, especially all flexible endoscopes, including cystoscopes. Healthcare-associated infections are on the rise and connected to contaminated endoscopes due to improper reprocessing [10, 31]. In September 2015 major regulatory organizations of the Department of Health and Human Services – the Centers for Disease Control (CDC) and the FDA – communicated an alert to healthcare staff regarding the importance of properly processing (cleaning, disinfecting, decontamination, and sterilization) semicritical and critical medical instruments and devices. The FDA recommended that any instrument or medical device that passes through an endoscope and comes into contact with sterile tissue, such as a biopsy forceps, must be sterilized prior to use [7, 31].

There are two factors that must be in place to ensure the proper process for cleaning and disinfecting instruments or medical devices prior to HLD or sterilization. One is the physical area or layout and the second is training and education of the staff preparing instruments for HDL or sterilization. The physical layout should consist of two separate work areas regardless of the healthcare setting, allowing a dirty-to-clean flow from one room to the other. An instrument processing room (dirty) receives the soiled instruments for cleaning and decontamination. A HLD system can be found in this room as well. The purpose of the adjacent room (clean) is for instrument preparation, sterilization, and storage of disinfected flexible scopes when necessary. Instruments stored in this room must be either sterile or HLD, and ready for use. Ideally, a third room for instrument storage would be beneficial to allow the clean room to be utilized just for instrument processing and sterilization. In some outpatient healthcare facilities there can be a substerile room adjacent to the procedure room that accommodates a free-standing steam sterilizer. This is for any instruments that can be sterilized as per the manufacturer's IFU, such as flexible instruments, vasectomy trays, or rigid cystoscopes. In the instrument processing room there should a designated dirty sink, a clean sink, and a hand-washing sink. A double sink should be designated as either dirty or clean and therefore there must be yet another two sinks, one for dirty or clean and the other for hand washing. The latter should have an eyewash station attached, in case there is exposure of the eyes to bodily fluids or any chemicals used in this area.

Designating a clean and dirty sink is to help prevent the possibility of cross-contamination while cleaning the instruments or medical devices. Due to certain circumstances some outpatient healthcare facilities may only be able to have a double sink, with one used for cleaning and the other for rinsing. These sinks must be wiped down in between uses with a bleach-based Environmental Protection Agency (EPA)-registered hospital-grade surface disinfectant after cleaning dirty instruments and before rinsing. The sinks should be equipped with a gooseneck-style faucet with winged handle controls to allow for proper water temperature adjustment. Sensor-controlled faucets are not recommended as it is difficult to obtain a precise water temperature that is adequate for cleaning and decontamination of instruments or medical devices [32].

Before placement in the disinfectant solution all items must be rinsed thoroughly to remove any residual detergent and dried completely to prevent dilution of the disinfectant solution once an instrument is immersed [9]. Once an instrument is fully immersed, if it has lumens or working channels the disinfectant solution must be flushed through with a syringe three times for internal exposure. The syringe must remain in place for the full indicated soak time [32, 16]. Exposure time ranges from 10 to 45 minutes with a solution temperature of 20–25 °C [5]. After the recommended exposure time, the instrument is transferred to an adjacent basin filled with sterile water. The instrument is fully immersed in sterile water and the external surfaces are wiped with a lint-free cloth. If the instrument has lumens or working channels the sterile water must be flushed through three times to remove any residual disinfectant solution. The final step before use or storage is to thoroughly dry the instrument and, if it has lumens or working channels, air is to be forced through with a large sterile syringe. For use in a procedure the instrument should be transferred to a sterile sheet or drape, covered in a sterile manner and transported to the point of use. If a scope is to be placed in storage it is recommended that it be hung in a well-ventilated drying cabinet that supplies forced air in cycles. Scopes are hung in a vertical position and connected to plastic tubing which enables the transport of forced air. This drying process prevents recontamination from residual fluid that may stay dormant in the scope and harbor bacterial growth, further promoting thorough drying of the internal channels of the endoscope [5]. The drying process can be enhanced with filtered, low-pressure medical air, a large syringe filled with air, or by flushing with 70% alcohol according to the manufacturer's guidelines or IFU. If the scope has detachable pieces they are to be removed prior to storage to stop residual moisture from flowing into the inner channel and aiding in growth of microorganisms [6, 7, 10, 12, 32, 33]. Monitoring of the room's temperature and humidity with a traceable digital meter is recommended by the CDC when storing flexible endoscopes [12].

According to the Association of Operating Room Nurses (AORN), the safest practice in the disinfection of endoscopes is to disinfect at the end of each day's use, again before the first use of the next day, and again before each use throughout the day [34].

Any healthcare facility that utilizes chemical disinfection must provide a safe environment for the setup and for the protection of their healthcare personnel. The solution, once activated and dispensed, must be kept in a covered container with a tight-fitting lid in a well-ventilated area. A free-standing or vented chemical fume hood is recommended for aldehyde solutions. With a free-standing fume hood, a carbon filter should be installed and must be changed and disposed of according to the manufacturers' instructions [9]. Fume hoods are available in various sizes and designs to accommodate your needs (Figures 1.4 and 1.5). A spill kit must be readily available in the event of a spillage of the chemical solution. Disposal of the chemical solution once deemed ineffective or on expiration must follow state and local

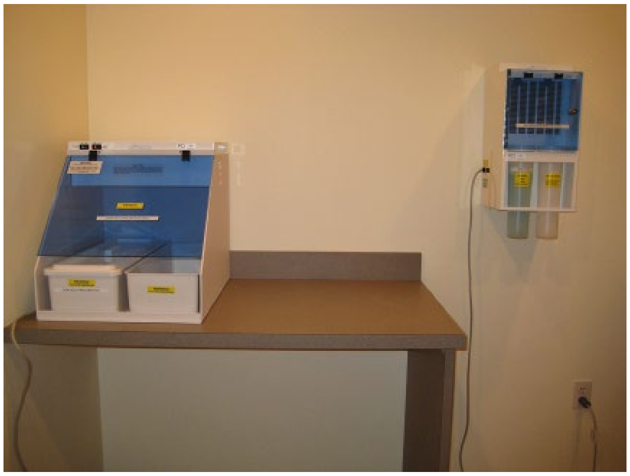


**Figure 1.4** Table-top and wall-mounted fume hoods for aldehyde solutions.

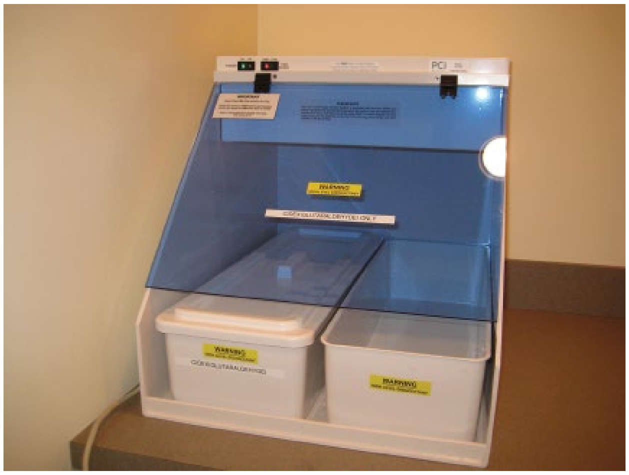


**Figure 1.5** Table-top fume hood for aldehyde solutions.

regulations. A neutralizing agent should be added to the solution to deactivate its potency. This can take from 5 to 15 minutes before disposal of the neutralized solution can occur [6].

In 2014, The American Urological Association (AUA) and the Society of Urologic Nurses and Associates (SUNA) published a joint white paper on the reprocessing of flexible cystoscopes. This is an excellent resource for any healthcare facility that utilizes flexible cystoscopes and it includes an "In-Office Disinfection of Flexible Cystoscopes Quick Reference Tool" which can help guide the instrument processing team [6].

OPA is a newer high-level disinfectant that was approved by the FDA in 1999. It is less potent than glutaraldehyde, is not an irritant to the eyes and nasal passages, and has a soak time of just 12 minutes. Prior to 2004 this chemical was ideal for the HLD of flexible cystoscopes, but due to reports of patients with bladder cancer experiencing an anaphylaxis-like reaction after cystoscopy utilizing scopes processed with OPA, this chemical disinfectant is currently contraindicated for cystoscopes and any urological instruments that will have contact with the bladder, according to the CDC and the manufacturer [6]. OPA is the disinfectant of choice for an ultrasound rectal probe, a semicritical device, which is used for guidance during a prostate needle biopsy procedure or for prostate measurement. Prior to the immersion and soak time, an ultrasound probe must be cleaned, wiped, rinsed, and dried according to the manufacturer's guidelines. A newer, alternative method of HLD for intracavity ultrasound probes is a 35% hydrogen peroxide mist system that is now available and approved by the FDA. This system not only disinfects the part of the probe (the head) that has contact with mucous membranes but it also disinfects the part of the probe used by the physician's hand to position the probe (the handle) and which therefore has the potential for contamination due to its function [33, 35, 36].

Documentation of the HLD process includes several factors. The initial setup of the HLD solution must be tested for its efficacy and level of concentration, known as minimal effective concentration (MEC). If the MEC fails the check before the intended expiration date the solution must be discarded [6]. The solution is tested every day with a reagent strip made by the solution's manufacturer, and the solution is also tested before use. The result is documented in a log book. When an item is intended for use the following information must be documented in the log: date, test strip result for effective solution concentration (positive or negative), temperature of the solution, name of the semicritical item, serial number if applicable, time it was placed in the solution, time it was removed, patient medical record number, cleaning method (manual or automated), soak station number if there is more than one on site, and name of person performing the HLD [6].

Each healthcare facility will determine which method of sterilization is best for their practice. In a hospital setting, steam, gas plasma, and peracetic acid are preferred. Some ambulatory healthcare facilities have a steam autoclave, and also use gas plasma and/or peracetic acid for sterilization methods. As for HLD semicritical items, aldehydes are used primarily to carry out this process.

Several organizations have developed guidelines for sterilization and disinfection of instruments and medical devices. The AAMI developed recommended practices for steam sterilization in healthcare facilities. The CDC put together guidelines for disinfection and sterilization in healthcare facilities and guidelines to prevent surgical infections. The AORN have recommended practices for cleaning and caring for surgical instruments, sterilization, the use and care of endoscopes and HLD in the perioperative setting. The Joint Commission has standards (IC.02.02.01) to reduce the risk of infection associated with medical equipment, devices, and supplies; this includes cleaning, disinfection, sterilization, and storage [37]. In 2013, this standard was identified as one of the top five least-adhered-to requirements for all healthcare facilities. It fell into the category of an immediate threat to life due to a break in technique of sterilization and HLD of instruments and medical devices [29]. When surveying a healthcare facility the surveyors are looking for documentation of staff orientation, training, and competency of the relevant processes. Other requirements that they will focus on are quality monitoring and adherence to the manufacturers' IFU when processing medical devices or instruments. These organizations' recommendations serve as a resource for your policy and procedure manuals and a guide to provide best practice in your healthcare facility.

Education and the training of staff is a current focus in healthcare facilities that carry out HLD and sterilization processes. In the hospital setting the staff in the central sterile department maintain certification for instrument technicians after staff have received the required training and acquired their certification. Those who work in nonhospital settings and who are not certified should receive appropriate hands-on training and education sessions to ensure they understand all aspects of the cleaning, decontamination, disinfection, and sterilization processes, including the safe use of all equipment involved. All trained staff should have a documented initial and annual competency kept in their employee departmental file for each process and piece of equipment used [15].

## Conclusion

The ultimate goals of instrument sterilization and HLD are to maintain a safe patient environment, provide quality patient care, and positive surgical or procedural outcomes with no evidence of infections. It is the responsibility of the healthcare facility to develop policy and procedures and evidence-based guidelines for the reprocessing of all critical and semicritical patient care items. These policies and guidelines should identify whether disinfection or sterilization is indicated as per the manufacturer's guidelines and the Spaulding classification system. The healthcare personnel responsible for the full cycle of reprocessing of these items should be trained and certified to perform all aspects of this task. In the physician office setting there should be designated personnel who have been trained and deemed competent to carry out the tasks of reprocessing patient care items based on the availability of soiled and clean work areas. Continuing education should occur to keep the trained and certified personnel informed of any changes in process or equipment use, and as an annual scheduled event.

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# 2

# Radiation Safety During Diagnosis and Treatment

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## Introduction

According to a 2009 National Council on Radiation Protection and Measurements (NCRP) report, the total ionizing radiation exposure to United States citizens had almost doubled over the previous two decades [1]. The report attributed this to increased exposure from computed tomography (CT) scans, image-guided fluoroscopic procedures, and nuclear medicine studies, which were estimated at 67 million, 17 million, and 18 million, respectively. During 2006, these imaging modalities constituted 89% of the total annual radiation exposure [1, 2]. On the other hand, recent studies have shown significant worldwide increase in the prevalence of stone disease [3, 4]. In the United States, prevalence increased from 5.2% in 1994 to 8.8% in 2010 [5]. Similarly, in the United Kingdom, renal colic episodes increased by 63% from 2000 to 2010 [5]. This was associated with marked decline by 83% in open surgeries and a marked increase in minimally invasive endourologic procedures such as shockwave lithotripsy (SWL), which increased by 55%, and ureteroscopy, which increased by 127% [5]. The increase in the incidence of stone disease and management with endourologic procedures is not without risks. Since ionizing radiation is not only an integral part of modern endourologic interventions but also constitutes the basis for diagnosis, preoperative planning, and post-operative follow-up, it is important for the urologists to have an intimate knowledge of radiation safety measures and to minimize ionizing radiation as much as possible to themselves, operating room personnel, and most importantly to their patients. This chapter discusses the state of the art in radiation safety measures during diagnosis, treatment, and follow-up. To follow radiation safety measures, one needs to understand how ionizing radiation is generated in the first place. Therefore, this chapter will start by explaining the anatomy of the X-ray tube and the generation of X-rays. It will then go through potential hazards of ionizing radiation. At the end of this chapter, readers will have developed strategies in lowering radiation exposure during diagnosis, treatment, and follow-up of their patients requiring endourologic procedures.

## Basic terminology and International System of Units in radiology

According to the International System of Units (SI), the absorbed dose, measured in Grays (Gy) or joules/kg, is the amount of energy absorbed per mass of tissue [6, 7]. To measure the biological effect of radiation on human tissue, the mean absorbed dose in an organ or tissue is multiplied by radiation weighting factor to calculate the "equivalent dose." The radiation weighting factor differs according to the type of radiation. For X-ray imaging (photons), it equals 1. Therefore, the mean absorbed dose and the equivalent dose are numerically equal. The SI unit for equivalent dose is the Sievert (Sv). Thus, 1 Gy equals 1 Sv. As the doses used for radiographic imaging are generally very low, milliSieverts (mSv) is used as a standard nomenclature describing doses administered [8]. The probability and severity of harmful effects from the same value of equivalent dose of radiation differ among different body organs and tissues.

The International Commission on Radiological Protection (ICRP) refers to the combination of probability and severity of harm as "detriment." In order to determine the combined detriment from stochastic effects due to the equivalent doses in all body organs and tissues, the "effective dose" is described. It is calculated by multiplying the equivalent doses in each organ by a tissue weighting factor ($W_T$), and the results are summed

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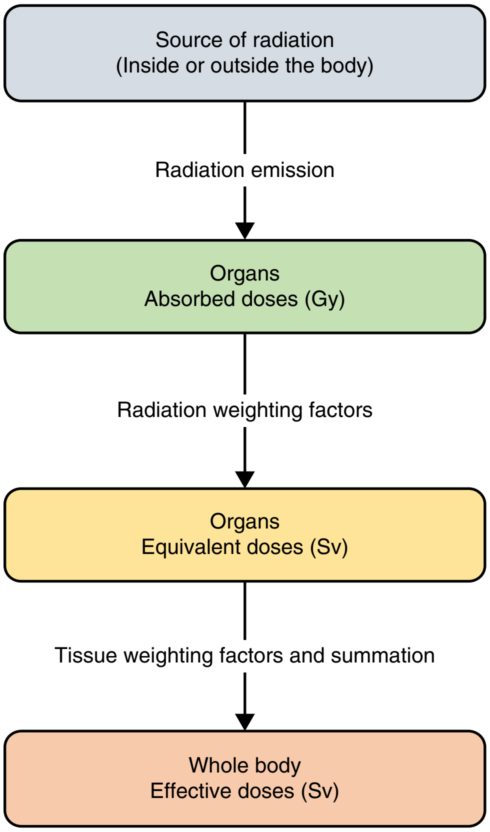

**Figure 2.1** The relationship between absorbed dose, equivalent dose, and effective dose. Reproduced with permission of Sage Publications Ltd.

over the whole body [8] (Figure 2.1). The SI unit for effective dose is also the Sievert (Sv). The weighting factors vary according the radiosensitivity of each organ and are determined by the ICRP. For example, a $W_T$ of 0.12 was described for red bone marrow, colon, lung, stomach, breast, kidney, pancreas, and prostate, a $W_T$ of 0.08 for gonads, and $W_T$ of 0.04 for the skin and brain [8].

Another factor used for estimation of radiation exposure is the dose area product (DAP), which is calculated from the radiation dose to air multiplied by the area of the X-ray field. It is expressed in $Gy/cm^2$ and it could be reliably used to estimate the effective dose by combining the DAP with the appropriate coefficient (which varies for the irradiated portion of body and the protocol used) derived from Monte Carlo simulations with anthropomorphic digital phantoms [9–11]. The size-specific dose estimate is considered as a novel method of reporting a patient's radiation dose. It is calculated by multiplying CT dose index volume (CTDIvol) by a size-dependent conversion factor. It accounts for patient size in a way that the increase in patient size decreases the size of specific dose estimates [12, 13]. The average medical imaging exposure ranges from 0.7 mSv for a single plain kidney-ureter-bladder (KUB) film to 18 mSv for a CT scan, depending upon device settings and body habitus. Even with relatively low radiation doses, the concern over excessive radiation exposure has grown recently due to the exponential rate at which medical imaging is used [14].

## How are X-rays generated?

Prior to understanding the hazards of radiation and methods of protection, it is wise to briefly consider the principles of radiation production. The basic components required for X-ray generation are (i) rotating anode (usually made of tungsten which is capable of handling a high heat load without warping or vaporizing), (ii) cathode (source of electrons), (iii) high voltage source, (iv) X-ray vacuum glass tube, (v) housing (steel casing which provides shielding to prevent leakage of stray X-rays), and (vi) collimator (which specifies the X-ray field).

Within the shielded housing, X-rays are generated when a high voltage is applied between the cathode and the rotating anode. The amount of electrons liberated from the cathode is directly proportional to the amount of current applied in milliamps (mAs). A large voltage potential (kVp) in the range of 50–120 kVp is usually required. Higher energy X-rays will penetrate deeper into tissues and penetrability of X-ray photons is directly proportional to the average energy of the photons generated. Hence, obese patients are expected to receive higher doses of radiation to obtain appropriate image quality compared with thinner ones. Therefore, the potential energy is adjusted to compensate for differences in patient body mass index (BMI). X-rays exit the housing through a narrow beryllium window, which permits the passage of only focused X-rays. Lead collimators further restrict the area of exposure, limiting the radiation area and, in turn, the amount of scattered radiation from the patient to operating room personnel (Figure 2.2) [6, 7].

The amount of X-ray photons, or radiation, generated by individual electrons varies depending on the proximity to the target material's nucleus. Therefore, a direct impact transfers a large quantity of kinetic energy and generates maximum energy X-ray photons, while a more distant interaction generates weaker X-ray photons. The X-ray photons produced is termed *bremsstrahlung*, which translates to "braking radiation." The variability of distance from the nucleus therefore creates a spectrum of energy emitted from the X-ray tube, the *bremsstrahlung* spectrum. The mean energy of the photons across the spectrum is typically equal to one-third the total potential difference generated by the voltage.

The energy of photons is an important consideration because the higher the energy of the photon, the more

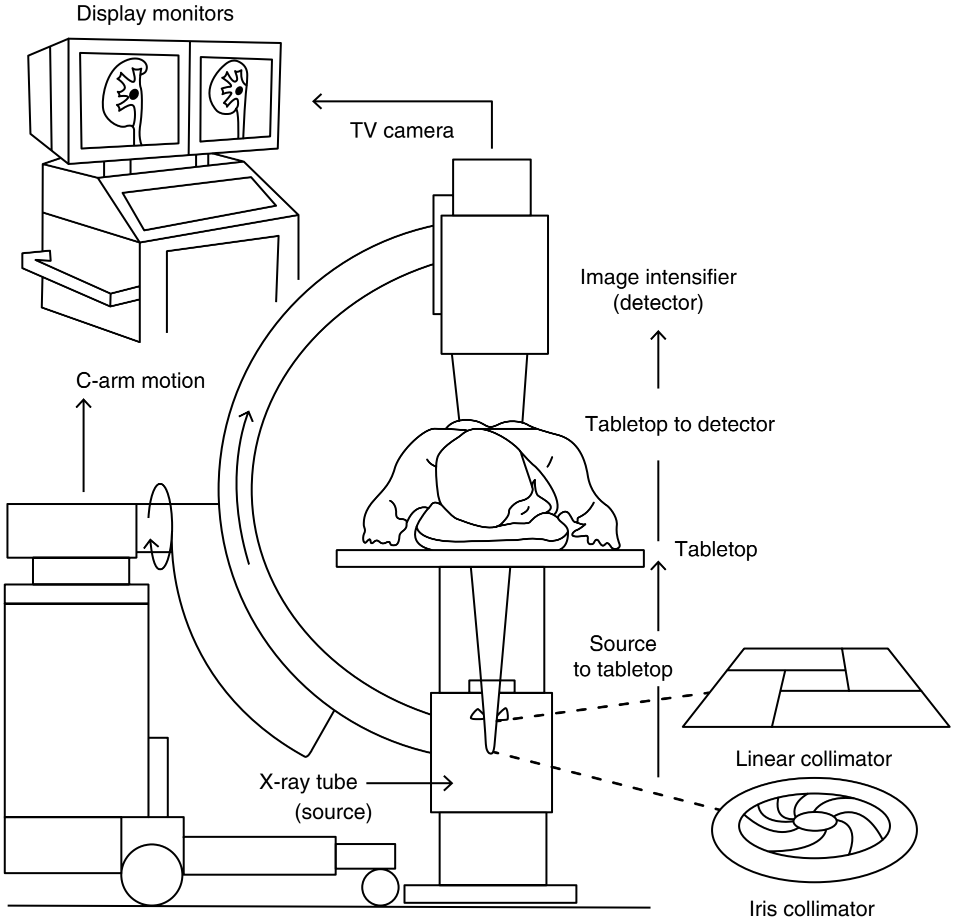

**Figure 2.2** X-ray generator set-up. Adapted from Wheeler AH. Therapeutic injections for pain management. http://emedicine.medscape.com/article/1143675-overview#a3 (accessed 15 July 2016).

shielding is required and the more readily the photon will penetrate tissue. Shielding for the X-ray housing is restricted to less than 100 mrad/hour at 1 m to prevent excessive leakage rates while the tube is operating at maximum potential difference and current. Photons leave the tube through a small opening in the shielding and are directed towards the area of interest (Figure 2.2). Filters are then generally applied to these diagnostic X-ray beams. These filters attenuate the lower-energy photons which do not have sufficient energy to reach the detector and therefore are not of clinical benefit. The electrons with energy high enough to penetrate through the filters are focused by the collimators through the tissue area of interest. Typically, the collimators further restrict exposure to the patient and the operator by eliminating radiation exposure outside the area of interest (Figure 2.2).

The quality of the image obtained is significantly reliant on the energy level and quantity of the electrons reaching the detector. X-ray photons need to be of high energy enough to penetrate through the tissue but low energy enough to limit "over-exposure" of the detector. Therefore, the most controllable aspects of diagnostic imaging equipment are (i) the potential difference (kVp), which determines the amount of energy in X-ray photons, (ii) the current (milliamps), which determines the number of electrons that create photons for a given time period, and (iii) exposure time, which combines with the current to determine the total quantity of X-rays produced. Because radiation exposure is proportional to the square of kVp and linearly related to milliamps, ideally it is better to increase kVp prior to increasing milliamps to enhance image quality. Conversely, if an initial image is "over-exposed," reducing current will greatly reduce radiation dose.

Emitted X-rays have three potential fates as they interact with living tissue: (i) some X-rays are absorbed by dense tissues such as bones, (ii) others penetrate soft tissues to reach the image intensifier, and (iii) 0.1% of X-rays are scattered 90° to the incident radiation, exposing bystanders. By placing the image intensifier above the patient and the source below the patient, the amount of scattered radiation exposure to the surgeon can be minimized. Furthermore, leakage from the tube itself is shielded and is further away from the operating surgeon's head and body (Figure 2.2).

Understanding the basic principles and mechanisms of X-ray generation provides a foundation for the understanding of radiation protection. Proper equipment maintenance and inspection of shielding and filters are requisite requirements for operators of imaging equipment. Fluoroscopy units in hospitals are usually inspected and maintained annually by biomedical engineers. Nonetheless, it is important for the urologist to understand the basic electrical parameters (kVp and current) and their effects on X-ray generation leading to optimization of the image quality while minimizing dose to patients and operators. Finally, the use of collimation to limit the exposure field to precisely target the tissue area of interest can greatly restrict unnecessary exposure.

## Potential hazards of excessive radiation exposure

There are two broad categories describing the risks from radiation exposure; namely, deterministic and stochastic.

### Deterministic effects

These generally refer to a direct cell death resulting from direct exposure of a biologic tissue to high doses of radiation. This type of tissue reaction needs a threshold dose to occur; below this threshold nothing will happen and the degree of tissue response correlates with the intensity of radiation dose above the threshold. An example is the opacification of the lens of the eye or cataract formation at a threshold of 200 rad, skin erythema and depilation at a threshold of 300–600 rad, and even skin ulceration and necrosis at a threshold of 1500–2000 rad [1, 8].

### Stochastic effects

These refer to events that are likely to occur by chance irrespective of the threshold levels of radiation, and likelihood of occurrence increases with dose. However, there is no relationship between severity of the event and the dose. The stochastic risks of greatest concern are hematologic and solid organ malignancy. The proposed explanation of these carcinogenic hazards is that X-rays, as a type of ionizing radiation, possess enough energy to overcome the binding energy of the electrons orbiting atoms. Thus this energy can knock electrons out of their orbits and create ions. In biologic material, X-rays can either ionize DNA directly or produce hydroxyl (OH) radicals from the interaction with water molecules. These hydroxyl radicals in turn interact with nearby DNA and cause epigenetic responses in the form of radiation-induced genomic instability or bystander signaling, base damage, or strand breaks. While most X-ray-induced DNA damage undergoes rapid repair by different intracellular mechanisms, occasional problems in DNA repair may happen resulting in chromosomal translocations or point mutations which may lead to induction of carcinogenesis, especially in growing cells such as in infants and children [14].

Whereas a correlation between excessive radiation exposure and deterministic dermal and ocular effects exists, models used to calculate the stochastic effects associated with radiation exposure are still debated [15]. Two recent studies assessing the risks of cancer following repeated or protracted low-dose radiation exposure among 308 297 radiation-monitored workers from United States, France, and United Kingdom [16] showed that there was a linear increase in the rate of cancer with increasing radiation exposure. Workers were selected for monitoring based on conditions of being employed for at least 1 year by the Departments of Energy and Defence in the United States, the Atomic Energy Commission or the National Electricity Company in France, and nuclear industry employers included in the National Registry for Radiation Workers in the United Kingdom. After exclusion of chronic lymphocytic leukemia, there was an excess relative risk of mortality from leukemia of 2.96 per Gy with marked association between the radiation dose and mortality from chronic myeloid leukemia (excess relative risk per Gy 10.45) and doses were accumulated at very low rates (mean of 1.1 mGy/year) [16]. Another study revealed a direct estimate of the association between solid cancer mortality and protracted low-dose exposure to ionizing radiation [17]. Another international study with 407 391 nuclear industry workers from 15 countries estimated the oncologic risks following prolonged low doses of ionizing radiation exposure. The authors found significant association between the radiation dose and all cancer mortality, with excess relative risk per Sievert (ERR/Sv) of 0.97 (90% confidence interval [CI] 0.28–1.77; 5233 deaths). Furthermore, duration of employment had a large effect on the ERR/Sv and lung cancer was the only type which had a significant association among 31 malignancies studied (ERR/Sv = 1.86 [90% CI 0.49–3.63; 1457 deaths]) [18].

In another study, the risk of cancer from diagnostic X-ray in 14 developed countries was 0.6–1.8% compared with more than 3% in Japan, which has the highest estimated worldwide annual exposure [19]. Eisenberg and co-investigators studied the risk of cancer in 82 861 patients without previous history of cancer and undergoing diagnostic or therapeutic imaging following acute myocardial infarction from 1996 to 2006 [20]. The cumulative radiation exposure was found to be

5.3 mSv/patient/year. Over a median follow-up of 5 years, a total of 12 020 incident cancers were diagnosed. Every 10 mSv of low-dose ionizing radiation was associated with a 3% increase in the risk of age- and sex-adjusted cancer with a hazard ratio of 1.003 per mSv (95% CI 1.002–1.004) [20]. Additionally, Berrington de González and coworkers estimated future cancers attributable to ionizing radiation from CT scans to be 29 000 cases in the United States in 2007. Of these, 66% were females and the largest contribution (14 000) was from abdominopelvic CTs [21]. Furthermore, Smith-Bindman and co-investigators reported that 1/600 men and 1/270 women patients who underwent CT coronary angiography at the age of 40 are at risk of cancer and this risk is halved for those who were in their sixties and doubled for those who were in their twenties [22].

## Sources of ionizing radiation encountered in urology

### Diagnostic imaging

There is no doubt that most medical diagnoses are based on ionizing radiation. However, diagnostic modalities such as ultrasound and magnetic resonance imaging (MRI) are free from radiation. Plain radiography, fluoroscopy, CT, and nuclear medicine studies are associated with various doses of ionizing radiation. Traditionally, plain radiography such as KUB films was the initial imaging modality for patients with suspected nephrolithiasis with a sensitivity of 59% and specificity of 71% [23]. This low accuracy is due to the failure of plain radiographs to detect uric acid stones. Furthermore, identification of stones might be masked by the overlying bowel gases. Advantages of KUB include low cost which rendered it available worldwide and lower radiation exposure compared to other modalities (effective radiation dose of 0.2–0.7 mSv) [23, 24]. Intravenous urography (IVU) has additional advantages over KUB such as demonstration of the anatomical and functional status of the urinary system. It is associated with higher effective radiation dose ranging from 0.7 to 3.7 mSv, depending on the number of images [24, 25]. However, IVU is time-consuming and necessitates the use of intravenous contrast materials with the risk of allergic reactions and contrast-induced nephropathy

Since being invented in 1970s, CT has been largely used in medical diagnosis and intervention. During a CT scan, multiple cross-sectional two-dimensional images of a specific area are produced by a rotating source passing X-rays through the patient’s body. Later on, these two-dimensional images can be digitally combined to yield three-dimensional images [26]. In urologic practice, CT scans play a vital role in preoperative planning of percutaneous nephrolithotomy (PCNL) and SWL. For PCNL, it provides an orientation of the pyelocalyceal system and the relationship of the kidney to the surrounding organs such as the colon, liver, and spleen. In addition, preoperative non-contrast CT (NCCT) scanning forms the basis of calculating different scoring systems assessing PCNL complexity such as the S.T.O.N.E. and Seol scoring systems [27, 28]. Regarding SWL, CT is very important for calculating the skin-to-stone distance to determine whether shock waves can reach the stone. For both SWL and PCNL, it detects postprocedural complications and presence of residual stones [29, 30]. Furthermore, it is ideal for diagnosis, staging, and follow-up of most urologic malignancies [31, 32]. In addition, NCCT is the imaging modality of choice for initial evaluation of patients with suspected urolithiasis with reported diagnostic sensitivity up to 98% and specificity up to 100% [33]. It is worth mentioning that the stone protocol CT scans performed for diagnosis and follow-up of urolithiasis patients have scan acquisition parameters that differ from traditional abdominopelvic CT scans. Therefore, patients presenting with suspected stone disease to the emergency department undergo NCCT scans with acquisition parameters different from those used in the normal stone protocol CT scans to allow emergency physicians to diagnose pathologies other than stones [34, 35].

With the exception of stones encountered in patients undergoing indinavir therapy and pure matrix stones, NCCT scan can diagnose all types of urolithiasis such as calcium, uric acid, xanthine, and cystine stones [36, 37]. Furthermore, it detects other renal and abdominal pathologies which present with acute abdominal pain resembling renal colic such as diverticulitis, appendicitis, or ovarian torsion. Therefore, it is not surprising that 10–14% of NCCTs performed in the emergency departments for renal colic were associated with alternative diagnoses [38–43].

In addition to determination of stone burden, location, multiplicity, density (Hounsfield unit), and associated hydronephrosis, dual-energy CT (DECT) technology, which has been introduced in the past decade, seems to possess the potential ability for accurate determination of stone composition [44–47]. It includes dual-energy simultaneous scanning using two different energies, which permits tissue characterization. There are two currently available DECT systems: single-source DECT (ssDECT) and dual-source DECT (dsDECT). While ssDECT is assembled with one X-ray tube with rapid kV switching between high (140 kVp) and low energy (80 kVp), dsDECT is assembled with two X-ray tubes (140 and 80 kVp) and two detectors on a single gantry perpendicular to each other [48]. Several *in vitro* and *in vivo* studies have validated DECT technology for detection of stone composition using both dsDECT and ssDECT. It allows detection of stone composition based on the variation in attenuation characteristics of stones at different X-ray energies with up to 100% sensitivity and accuracy in distinguishing non-uric acid and uric acid stones, regardless of the size of stones [44, 46, 49, 50]. Furthermore, with evolving DECT algorithms, there is an application for accurate subcategorization of renal stones [49, 51]. To reduce radiation exposure, the current DECT protocol for renal stones includes the use of single-energy mode at a low dose covering the abdomen and pelvis, to recognize possible calculi in the urinary tract. Once the urinary stone is detected, a dual-energy acquisition targeted to the anatomical area of the stone is performed [37]. It should be noted that obese patients are at higher risk of more radiation exposure from CT [52]. In a recent study by Wang and coworkers, they found that obese patients are at more than threefold-increased risk of radiation exposure compared with non-obese patients during the stone-protocol CT employing automatic tube current modulation (10.22 vs. 3.04 mSv; $P < 0.0001$) [53].

Disadvantages of CT include the high cost which limits worldwide availability, and the high radiation exposure, with effective radiation doses of 4.5–18 mSv [25]. In a study by John and colleagues, patients who underwent a CT were exposed to 14.46 mSv [54]. Furthermore, the median effective radiation dose (ERD) associated with an acute stone episode and 1 year of follow-up at two American academic centers was 29.7 mSv [55]. Moreover, it was found that 20% of patients received over 50 mSv with an average of 3.5 CTs [55]. In a similar study by Fahmy et al. assessing the ERD to which urolithiasis patients are exposed during the evaluation and follow-up over the first and second year following the acute stone episode, they found that the average ERD per CT scan was 23.16 mSv (range 4.94–72.77 mSv). Furthermore, they found that 17.3% of patients exceeded 50 mSv during the first follow-up year with mean ERD of 29.29 mSv (1.7–77.27 mSv) [56]. Another study reported that a case of acute kidney stone episode that may require radiological imaging in the form of one or two KUBs, one or two abdominopelvic CT, and one IVU during the first year of follow-up may be exposed to a total effective dose between 20 and 40 mSv [24]. In addition, it has been calculated that the effective dose from CT scan of the abdomen in adult patient is roughly equivalent to effective dose from 400 chest X-rays [25].

Even some surveillance protocols using CTs have been shown to be associated with significant radiation exposure and the risk of developing cancers. Tarin and colleagues assessed the estimated cancer risks associated with the 5-year surveillance protocol of stage I non-seminomatous germ cell tumors of the testis, as recommended by the National Comprehensive Cancer Network. They reported a lifetime cancer risk of 1.5% for different age groups with lung and colon cancer accounting for most of the risk [57].

Nuclear medicine imaging procedures such as position emission tomography CT (PET CT) scans and renal scintigraphy (renal scanning) entails the use of a radioactive material, called a radiotracer or radiopharmaceutical, which is introduced into the human body by injection, swallowing, or inhalation. This radiotracer accumulates in the area of the body being examined, where it gives off a small amount of energy that can be detected by gamma camera and provides details on both the function and structure of tissues and organs being examined. These radiotracers stay within the tissues for a period of time and liberate radiation. However, unlike other sources of ionizing radiation with a source of external radiation, nuclear studies represent a source of internal radiation. These studies are of special importance for identifying the function of organs such as the differential renal function which especially important in children with congenital renal anomalies. The ICRP reported a total of 18 million nuclear studies in the United States in 2006. Furthermore, the doubling of ionizing radiation exposure in United States over the last two decades was largely attributable to increased imaging from CT, interventional fluoroscopy, and nuclear medicine [26]. According to the US NCRP, CT scans, fluoroscopy-guided procedures, and nuclear medicine studies represent approximately 26% of the annual imaging procedures. Nonetheless, they cause 89% of the total annual radiation exposure [1, 26].

### Interventional imaging

The main interventional endourologic procedures such as SWL, ureteroscopy, and PCNL use fluoroscopic guidance. The increase in the number of these procedures over the past few decades has raised concerns regarding the amount of radiation exposure associated with these interventions. For example, in the United States, per-capita radiation exposure from medical sources increased about 600% (from 0.54 to 3.0 mSv) between 1982 and 2006 [25]. In terms of radiation exposure associated with each procedure, a study by Safak et al. found a mean ERD of 9.2 mSv (0.82–26.0 mSv) for PCNL [58]. These results were similar to the mean ERD reported by the Mancini group (9.09 mSv) [59]. Higher ERD was associated with higher BMI, larger stone burden, non-branched stone configuration, and higher number of percutaneous access (PCA) tracts [59]. Furthermore, increased stone burden, prolonged operative time, multiple access tracts, and blood loss >250 $cm^3$ have been associated with significantly prolonged fluoroscopy time (FT) [60, 61]. Concerning ureteroscopy, the mean ERD has been recently reported as 1.13 mSv, which is equivalent to that of an abdominopelvic X-ray [62]. This was lower than older studies which reported a mean ERD of 2.5 mSv [63]. The use of recent fluoroscopy devices might explain the cause behind the lower ERD in the more recent study. Predictors of prolonged FT during ureteroscopy were found to be urology trainees, male gender, ureteral balloon dilation, residual stones, use of access sheath, surgeon/trainee behavior, longer duration of the procedure (14 seconds per 10 minutes), and higher BMI [64–66]. Furthermore, the use of flexible ureteroscopes or both flexible and semi-rigid ureteroscopes in the same setting was associated with higher radiation exposure compared with semi-rigid ureteroscopy alone [63]. Regarding SWL, precise stone localization necessitates the use of fluoroscopy. SWL is associated with mean radiation exposure of 1.63 mSv [67]. Higher radiation exposures are associated with higher stone burden, higher BMI, ureteral stones locations, physician inexperience, and higher number of shocks delivered [67–69]. Moreover, radiation is used to follow-up patients with post-SWL. Recently, Kaynar and coworkers evaluated ERD of 129 patients during the first follow-up year following SWL. They reported a mean ERD of 15.91 mSv following SWL of kidney stones, 13.32 mSv following SWL of ureteral stones, and 27.02 mSv following SWL for multiple stone locations. Furthermore, SWL for multiple stone locations was associated with significantly higher radiation exposure during the first follow-up year compared with SWL of solitary renal or ureteral stones [70].

## Occupational radiation exposure for urologists

Until recently, there was paucity in the literature in terms of the amount of radiation to which urologists are exposed and its impact on their health. The 2007 ICRP guidelines recommend 50 mSv (5000 milliroentgen equivalent man or mrem) as an occupational dose limit per year or 100 mSv (10 000 mrem) averaged over 5 years [6]. Furthermore, the United States regulations (Title 10, part 20 of the Code of Federal Regulations) mandate a yearly accepted limit of 5000 mrem as deep-dose equivalent, 15 000 mrem as lens dose equivalent, and 50 000 mrem as shallow-dose equivalent. To ensure practitioners are within these guidelines, there exists a need for a controlled measurement of radiation exposure experienced by practicing urologists over a period of time. Therefore, urologists are recommended using a dosimeter to monitor their radiation exposure. A single-center prospective German study measured the radiation exposure in 12 urologists by placing two thermoluminescent dosimeters (one on the forehead and the other on the ring finger). A total of 188 patients underwent 235 endourologic procedures including 51 ureteral stent changes (USCs), 67 ureteral stent placements (USPs), 67 percutaneous stent changes (PSCs), 39 ureteroscopies, and 11 PCNLs. The authors recorded an average value of 0.04 mSv during USP and USC, 0.03 mSv during PSC, 0.18 mSv during PCNL, and 0.1 mSv during ureteroscopy using the forehead dosimeter and average values of 0.13, 0.21, 0.20, 4.36, and 0.15 mSv during USP, USC, PSC, PCNL, and ureteroscopy, respectively using a dosimeter positioned at the ring finger [71]. Furthermore, a study from North America measured the fluoroscopic radiation exposure of an experienced urologist over 9 months using a thermoluminscent dosimeter installed outside the thyroid shield. The total radiation exposure over 9 months was 87 mrems deep-dose equivalent, 293 mrem lens dose equivalent, and 282 mrem for shallow-dose equivalent [72]. Therefore, these studies showed that radiation exposure for urologists was below the annual accepted limits. Nevertheless, radiation safety protocols and recommendations should be followed to guard against the potential hazards from ionizing radiation.

## Dose-reduction strategies

Over the past two decades, reports have highlighted the increasing use of radiation in medicine. During 2000, a report from the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) found that radiation used for medical purposes accounts for more than 95% of human-made radiation exposure. Furthermore, radiological diagnostic procedures equaled or exceeded one per each individual of the population per year. It has been reported that a person who lives in United States is exposed yearly to an average of 6.2 mSv radiation from ambient sources such as cosmic rays, radon, and medical procedures [73]. While the recommended occupational radiation exposure to medical personnel should be limited to 50 mSv/year, there is no dose threshold for developing stochastic hazards [73]. According to the linear-no-threshold model (or LNT), which is used to quantify radiation exposure and set the regulatory limits for radiation protection, there is no safe dose of radiation and cancer can occur in 1/1000 individuals following exposure to an effective dose as low as 10 mSv [74]. This is because some organs such as the gonads and the eyes are more sensitive than others, such as the extremities. Thus the recommended exposure limits vary according to the body part. In addition, there are variations in radiation exposure among healthcare centers in terms of ERD for the same diagnostic procedure [75]. According to a study by Smith-Bindman and colleagues, there were wide variations among radiation doses reported for different types of medical imaging studies. For example, a mean 13-fold variation was reported between the lowest and highest dose of CT scans for adult patients across and within institutions in the San Francisco Bay area [22]. Therefore, different groups including the American Association of Physicists in Medicine, the American College of Radiology, and NCRP, together with the US Food and Drug Administration (FDA), have worked to establish nationally recognized diagnostic reference levels (DRLs) for different imaging procedures [76]. The ICRP recommended three basic principles for reducing radiation exposure. First is the *principle of justification*, which is defined as "Any decision that alters the radiation exposure situation should do more good than harm," refers to avoidance of unnecessary studies and replacing procedures associated with higher radiation with others that may play the same role, whenever appropriate. Second is the *principle of optimization*, which is defined as "The likelihood of incurring exposure, the number of people exposed, and the magnitude of their individual doses should all be kept as low as reasonably achievable (ALARA), taking into account economic and societal factors," entails performing the diagnostic or interventional procedure with an acceptable quality and lowest radiation exposure. Third, *Application of dose limits*, is defined as "The total dose to any individual from regulated sources in planned exposure situations other than medical exposure of patients should not exceed the appropriate limits specified by the Commission" [6].

## Principle of justification

Justification is a key principle for radiation safety during diagnosis and treatment using ionizing radiation. It entails several items that should be addressed. First, it is mandatory that any ionizing radiation examination prescribed by the referring clinician is required for an individual patient and that the examination has a specific objective, is risk-effective, reliable, and anticipated to influence the decision-making, patient treatment, and final outcome, and that the necessary information cannot be obtained by other modalities with lower risk. Furthermore, a single person should be responsible for the examination and this person is normally a radiologist who is trained in radiological techniques and radiological protection as certified by a competent authority. In addition, a documented request including patient's clinical information, signed or endorsed by a referring clinician, should be available before an examination is performed. In the case of a female patient in the childbearing period the potential that she may be pregnant should always be kept in mind and date of the last menstrual period should be documented and pregnancy test should be ordered in case of doubt in pregnancy [8, 77]. Furthermore, all biomedical research projects that involve the use of ionizing radiation should be institutionally approved by ethics review boards and radiation protection committees.

## Principle of optimization

Following justification of the examination or the image-guided intervention, optimization is the next step towards radiation protection. Optimization of protection is considered a forward-looking iterative process directed to performing the procedure with an acceptable quality while keeping radiation exposure as low as reasonably achievable (ALARA). It takes into account both technical and socioeconomic factors. Therefore, it is a process of "frame of mind" that always questions whether all that is reasonable has been done to reduce doses. The concept of ALARA or "as low as reasonably achievable" was described as a fundamental part of the optimization process. The basis of ALARA principles is that these measures have been compiled to minimize radiation exposure. They are cost-effective to increase compliance. They do not cause unnecessary delay to procedure, do not hinder the performance nor affect the outcome of the procedure. The three basic principles for ALARA are time, distance, and shielding.

### ALARA principles

#### *Time (minimize time)*

One of the most effective methods to reduce radiation exposure to patients and healthcare personnel is to limit the time of radiation exposure. This is particularly important during fluoroscopy where shortening of the FT leads to substantial decrease in radiation exposure. This could be achieved by multiple avenues. (i) Substitute fluoroscopy with other imaging modalities such as ultrasound-guided PCA during PCNL or totally ultrasound-guided PCNL. (ii) Use digital fluoroscopy. (iii) Use "last-image-hold" technology which has been shown to reduce radiation exposure dose by almost 10-fold (from 3000 to 400 mGy). (iv) Use pulsed fluoroscopy with fewer frames per second (such as 1 or 4 frames per second) rather than standard fluoroscopy at 30 frames per second. (v) Fluoroscopy should be turned on/off by the surgeon only during absolute key points rather than continuous stretches. (vi) Keep tracking the FT. (vii) Document the FT after each procedure [78–82] (Box 2.1).

#### *Distance (maximize distance)*

Increasing the distance is considered the cheapest and most effective way to reduce radiation to operating room personnel. It is of particular importance for healthcare

**Box 2.1 Take-home messages in radiation safety measures.**

| | |
|---|---|
| 1 | Practice ALARA principles (minimize time, maximize distance, and always use shields). |
| 2 | Use modern equipment with digital fluoroscopy with last-image hold technology. |
| 3 | Stand as far as possible from the patient to avoid scattered radiation. |
| 4 | Place the image intensifier as close as possible to the patient to minimize scatter radiation. |
| 5 | Minimize the area of radiation exposure by using collimators to narrow the field. |
| 6 | Use pulsed fluoroscopy with 4 frames per second. |
| 7 | Control the foot pedal and movement of the C-arm. |
| 8 | Limit the time of fluoroscopic exposure to a minimum during absolute key points rather than continuous stretches. |
| 9 | Track and document the amount of radiation used for each procedure. |
| 10 | Check each fluoroscopy unit annually. |
| 11 | Invest in custom-made lightweight aprons and examine each apron annually for defects. |
| 12 | Whenever possible, order imaging studies associated with lower radiation exposure such as ultrasound/KUB or low-dose CT. |

personnel. As radiation exposure has an inverse relationship with the square of the distance, doubling the distance reduces radiation to one-quarter and at a distance of 3 m the radiation dose becomes similar to background levels. Healthcare providers can increase the distance by avoiding being in the room during the procedure, whenever possible such as when performing kidney–ureter–bladder (KUB) plain radiographs, intravenous pyelography, or computed tomography (CT). Also, the use of lens-mounted video cameras decreases the distance of the surgeon from the radiation source [7, 82] (Box 2.1).

***Shielding (always use shields)***

Shielding is the third line of defense, especially for personnel who have to be in the radiation field. Shielding is made of heavy metals, most commonly lead which is capable of attenuating radiation. Examples of shields are lead-impregnated eye glasses, gloves, thyroid shields, chest and pelvic aprons, and ceiling-mounted shields. Lead aprons vary in thickness; most are 0.5 mm lead equivalent that attenuate radiation by 96.5–99.5%. Thus shielding does not provide 100% protection from radiation. Therefore, it should not be considered a substitute for other principles of ALARA [7, 83]. Lead aprons should be inspected annually for cracks. In one study, thyroid shields were found to decrease radiation exposure 23 times (from 46 to 0.02 mSv), thereby reducing radiation exposure to background levels [84]. Despite the major benefits of shielding in reducing radiation exposure, the weight of chest and pelvic aprons are associated with orthopedic problems. In 2011, Elkoushy and Andonian surveyed compliance with radiation safety measures and the prevalence of orthopedic complaints among members of the Endourological Society. Almost 64% of respondents reported orthopedic complaints in the form of back problems in 38.1%, neck problems in 27.6%, hand problems in 17.2%, and hip and knee problems in 14.2% [85]. Although there was good compliance (97%) in wearing chest and pelvic aprons, compliance with thyroid shields was only 68%. In addition, only 34.3% of respondents used dosimeters, 17.2% used lead-impregnated glasses, and 9.7% used lead-impregnated gloves [85]. Similarly, other national and international surveys have shown the lack of radiation exposure monitoring in the United States, Europe, India, Brazil, and Turkey [86–89]. Therefore, all of those studies recommended regular radiation safety courses for trainees and urologists. Radiation safety courses have been successful in reducing radiation dose with the implementation of a "radiation awareness program," where focus was placed on taking fewer "snapshots" during SWL [90]. In another study, after implementing a radiation safety education initiative, a significant decrease in dose area product and FT was achieved during pediatric procedures [82, 91] (Box 2.1).

## Principle of application of dose limits

This limit entails that the effective dose or the equivalent dose values prescribed to individuals should not be exceeded during planned exposure situations. This applies only during occupational exposure. For example, the dose limit for a surgeon or the technician should not exceed 50 mSv per year. However, limiting the dose to individual patients is not recommended because it may impact the effectiveness of the patient's diagnosis or treatment. For example, dose limits cannot be applied for patients undergoing radiotherapy, where a target is needed irrespective of the dose of radiation. Therefore, for patients, only the principles of justification and optimization apply [6]. During 2010, the FDA launched a collaborative initiative aimed at reducing unnecessary radiation exposure from medical imaging. This initiative focused on CT, fluoroscopy, and nuclear medicine as the three medical imaging modalities that are associated with highest radiation [1]. The measures included promotion of safe use of medical imaging devices through (i) establishing requirements for manufacturers of CT and fluoroscopic devices to include additional safeguards into the equipment design and developing nationwide recognized DRLs, (ii) supporting informed clinical decision making by adding requirements for manufacturers of fluoroscopy and CT devices to record radiation dose information for use in patient medical records; this may allow the physician together with the patient and the radiologist to further justify procedures which necessitate ionizing radiation, and (iii) increase patient awareness and provide them with tools to track their personal medical imaging history such as using a patient medical imaging record card [1].

During 2014, the government of Germany hosted an international conference sponsored by the International Atomic Energy Agency and the World Health Organization calling for action on radiation protection in medicine in the next decade. This conference was coined the “Bonn Call for Action” [92]. The conference recommended 10 main actions: (i) enhancing the implementation of the principle of justification by applying the 3 As (awareness, appropriateness, and audit), (ii) enhancing the implementation of the principle of optimization by ensuing the use of the DRLs for imaging procedures and strengthening the establishment of quality assurance programs for medical exposure, (iii) strengthening the manufacturers’ role in contributing to the overall safety regime, (iv) strengthening radiation protection education, (v) shaping and promoting a strategic research agenda for medical radiation protection, (vi) increasing the availability of information on medical exposure, (vii) improving the prevention of medical radiation accidents and incidents, (viii) provoking the radiation safety culture in healthcare, (ix) fostering an improved radiation risk-benefit dialogue among health professionals, patients, and the public, and (x) strengthening global implementation of radiation safety requirements [92].

## Dose-reduction strategies during diagnosis

While CT is considered the workhorse in evaluation of most non-emergent and emergent medical situations, it is the imaging modality that is associated with highest potential for radiation exposure (Table 2.1) [13, 14, 93]. Therefore, it constitutes a major concern for healthcare professionals and patients especially those who are recurrent stone-formers and are at risk of undergoing repeated CTs with the associated risks of cumulative radiation exposure [14, 56, 94, 95]. Katz et al. reported a cumulative radiation dose associated with repeated CT scans between 8.5 and 154 mSv [96]. Furthermore, reports by NRCP reported a yearly increase in the number of CTs performed in the United States of about 10% between 1993 to 2006 with estimated 62 million CT examinations performed during 2006 alone [2]. Given the importance of CT as a first-line choice for diagnosis of different urological diseases especially stone disease, and the potential hazards of the high doses of radiation associated with CT, several strategies were proposed for lowering radiation exposure. These strategies depend on either modifying the basic design of scanners and their components or the technical parameters such as slice thickness, pitch, and tube current modulation. In addition, appropriate patient centering on the gantry has been reported to decrease the dose by 20% by decreasing *z*-axis coverage. Pitch is the speed at which the table moves through the scanner gantry and increasing pitch results in radiation dose reduction. In a study by McCollough and colleagues, increasing the pitch from a standard of 1 to 1.5 resulted in 33% reduction in effective dose while still maintaining adequate image quality from a single-slice helical CT [97]. However, these results could not be achieved with multi-slice CT [98].

Furthermore, optimization of slice thickness was accompanied by reduction in radiation dose without compromising diagnostic accuracy. While slices at 0.5 mm detected stones at 70% higher than slices at 5 mm, it was associated with significantly higher radiation exposure in single-detector CT scanners [99]. Therefore, optimization of slices at 2.5 mm was proposed and it would detect most clinically relevant stones with single-detector CT scanners. However, the latest

**Table 2.1** Effective dose associated with different imaging and image-guided interventions.

| Procedure | Mean effective dose (mSv) |
|---|---|
| KUB [24, 55, 94, 111] | 0.7–1.1 |
| IVU [24, 55, 94, 111] | 1.5–3.5 |
| Standard-dose CT, abdomen [24, 55, 95] | 5–10 |
| Standard-dose CT, pelvis [55, 95] | 5–10 |
| Standard-dose CT, urogram [22, 24] | 10–31 |
| Low-dose CT, abdomen/pelvis [94, 102] | 2.0–3.5 |
| Ultra low-dose CT, abdomen/pelvis [109] | 0.5–1.5 |
| PET CT scan [24] | 14.1 |
| Diuretic renal scan [24] | 2.6 |
| Bone scan [24] | 6.3 |
| Cystography [24] | 1.8 |
| Nephrostomy tube placement [24] | 3.4 |
| SWL [127, 128] | 1–8 |
| Ureteroscopy [128, 159] | 1–7 |
| PCNL [59, 62] | 3–18 |

multi-detector CT (MDCT) scanners presented the possibility of decreasing the slice thickness without increasing radiation exposure. For example, there was no change in radiation dose among different slice thicknesses using the 64-MDCT scanner [100]. Furthermore, radiation exposure could be further decreased while maintaining an appropriate image quality by obtaining slices of 5 mm and complementing it with 3 mm coronal/sagittal reformatted images [34, 35].

Reducing the tube current has been found to be the most effective method of reducing radiation exposure. There is linear relationship between radiation dose and tube current. Therefore, a 50% reduction in tube current leads to a 50% reduction in the radiation dose. The tube current can be adjusted either manually using manual selection of a lower fixed tube current or automatically using automatic tube current modulation, optimizing the dose according to the density of tissues penetrated by radiation and patient body habitus. This could be achieved by incorporating software that uses the scout image to make adjustments in radiation output according to the patient's BMI and the tissues examined. However, reduction in tube current results in increased "noise," which is acceptable in certain situations such as stone disease. These recommendations are based on several studies that showed comparable accuracy between low-dose CT (LDCT) and standard-dose CT (SDCT) in detection of renal calculi. In one study, simulated CT reconstructions at 50 and 75% reductions from the original dose had comparable sensitivities compared with the SDCT in detection of stones >3 mm [101]. In another study by Polletti and coworkers, the accuracy in detecting ureteral calculi was comparable between LDCT and SDCT in patients with a BMI of less than 30 kg/m$^2$ with significant reduction in radiation exposure (9.6 vs. 1.6 mSv in men and 12.6 vs. 2.1 mSv in women). However, in patients with a BMI of ≥30 kg/m$^2$, the sensitivity of LDCT to detect ureteral calculi was only 50% [102]. In addition, according to a recent systematic review, LDCT scans resulted in radiation exposure ranging from 0.5 to 2.8 mSv, and had a sensitivity of 90–97% and a specificity of 86–100% for diagnosing stone disease. However, this technique may miss small ureteral stones (<3 mm), especially in obese patients (BMI >30 kg/m$^2$) [103]. Several studies confirmed the lower accuracy of LDCT for detection of ureteral calculi in obese patients [102, 104, 105].

Since 1998, MDCT scanners have been used in diagnosis and planning of treatment for patients with renal stones. It has the ability to perform three-dimensional reconstructions and multi-planar reformatting while obtaining slices down to 1 mm thick [34, 35]. In one study, using a 16-MDCT with tube current modulation, there was comparable accuracy between LDCT and SDCT in detection of urolithiasis in both non-obese and obese patients [106]. While LDCT using MDCTs was associated with relatively higher radiation dose (1.41 mSv), this radiation dose was still significantly lower than the SDCT (2.89 mSv) [106]. Furthermore, the positive correlation which was noted between ERD and BMI ($r$=0.86) was congruent with the hypothesis that radiation exposure is higher in obese patients [106]. In a recent study by Abou El-Ghar and colleagues, the use of automatic tube current modulation that is available in modern multi-slice CT scanners such as 64-MDCT made it possible to use LDCT with comparable results to SDCT even in obese patients [107]. Moreover, employing LDCT was equally sensitive to SDCT in detecting uric acid stones at very low radiation doses. Therefore, ultra-low dose protocols have demonstrated a high sensitivity and specificity (97 and 95%, respectively) in detecting calculi while reducing radiation exposure [37, 108, 109]. In a meta-analysis by Niemann and colleagues, LDCT reported to detect urolithiasis with a sensitivity of 97% and specificity of 95% [32]. Therefore, LDCT should be preferred to SDCT and be considered the first-line imaging modality in acute renal colic [32]. Based on these data, LDCT is now recommended by the American and European Urological Association guidelines as the first-line imaging modality for evaluation of non-obese (BMI <30 kg/m$^2$) patients who present with renal colic [110, 111]. Despite these recommendations for LDCT, a recent study evaluating CT studies for patients presenting with renal colic to 93 institutions in the United States demonstrated that only 2% of CTs were performed using LDCT protocols [112].

Radiation exposure could be further reduced using iterative reconstruction technology, where CT scans can be performed with lower current and lower kVp [113].

Recently, multiple iterative image reconstruction methods have been developed by almost all CT manufacturers for reducing radiation dose without sacrificing image quality. These include iterative reconstruction in image space (IRIS) by Siemens Medical Solutions, adaptive statistical iterative reconstruction (ASIR) and model-based iterative reconstruction (MBIR) by GE Healthcare, iDose by Philips Healthcare, and adaptive iterative dose reduction (IARD) by Toshiba Medical Systems. While ASIR reduces the radiation dose by 32–65% without increasing noise in the reconstructed images [114], MBIR was found to improve the spatial resolution and reduce the noise of the obtained CT images at the same time [115]. However, ASIR is much faster than MBIR. Despite the lack of published data on IRIS, IARD, and iDose, information from manufacturers suggests the potential for decreasing radiation dose in the range of 30–60%. A recent study employing ASIR reported the feasibility of performing low-dose CT scan in patients with renal colic using radiation dose equivalent to KUBs [116]. The authors found that LDCT with 70% ASIR had a sensitivity of 87% and specificity of 100% for detection of calculi of >3 mm and was associated with significantly lower radiation exposure compared with the SDCT (0.48±0.07 vs. 4.43±3.14 mSv; $P < 0.001$) [116].

The latest “digital tomosynthesis” (DT) technology is based on conventional X-ray tomography where a series of low-dose projection images are obtained with a digital detector during a single sweep of the X-ray tube. Using special software, the data are then reconstructed in a way that can provide in-depth information about the structures of interest [117]. This technology was primarily used for imaging of the chest and breast [118].

Mermuys and colleagues reported the superiority of DT compared with digital radiography for the identification of renal stones [119]. However, there was no difference between the two modalities for detection of ureteral stones. Furthermore, Wells and coworkers studied the diagnostic quality of the traditional IVU compared with DT-IVU. They found that DT-IVU was associated with better diagnostic accuracy (95.5 vs. 46.5%) and less radiation exposure compared with the traditional IVU [120]. A recent study by Astroza et al. compared the ERD of radiation accompanying KUB, IVU, stone protocol NCCT, and DT during follow-up of patients with urolithiasis [118]. They reported an ERD of 0.63 mSv with KUB, 3.93 mSv with IVU, 3.04 mSv with stone protocol NCCT, and 0.83 mSv with DT [118]. However, compared with traditional CT, DT has difficulty in identifying ureteral stones and small stones (<2 mm). Therefore, it should not be considered as a substitute for NCCT in either the evaluation of renal colic patients or the planning for surgery. Nevertheless, it provides more information when compared with KUB and it is associated with less radiation exposure than stone protocol NCCT with comparable costs. Therefore, it might be a valuable imaging modality in the follow-up of recurrent stone-formers [118].

Finally, two studies compared the diagnostic accuracy of combined ultrasound and KUB with CT in patients presenting with renal colic and reported lower sensitivity of the combined ultrasound and KUB compared with CT (79 vs. 93% in one study and 77 vs. 93% in the other) [121, 122]. Therefore, combining ultrasound with KUB would best replace CT in follow-up of patients with clinically significant radiopaque stones either during conservative treatment or in the follow-up after endourologic procedures such as SWL, ureteroscopy, or PCNL. MRI or magnetic resonance urography (MRU) is a technique that produces no ionizing radiation and can be used to evaluate the genitourinary system. MRI previously had a significant role in chronic kidney disease patients where iodinated contrast used in CT or IVU was contraindicated. MRU is now contraindicated in patients with renal impairment secondary to gadolinium’s association with nephrogenic systemic fibrosis. Nevertheless, MRI provides excellent anatomy with accurate delineation of the location and degree of obstruction and presence of perinephric fluid. However, it can’t differentiate stones from blood clots or tumors [123]. In order to overcome this, Blandino and colleagues performed a study using MRU to identify the level of obstruction, then performed targeted CT to determine the cause of obstruction. This protocol was associated with significant reduction in ERD and the sensitivity for detecting urinary stone was 98% [123]. However, this protocol is time-consuming, expensive, and MRU is not readily available. Therefore, it lacks clinical applicability. While most of dose reduction protocols focus on stone disease, patients with malignant diagnoses undergoing surveillance protocols or follow-up imaging would likely benefit from minimizing radiation exposure. The optimal parameters for patients in these situations have yet to be determined but are a potential future research direction.

## Dose reduction strategies during endourologic interventions

According to FDA regulations, all fluoroscopy units should produce similar radiation profiles at settings of a maximum potential energy of 120 kVp and current of 2 mA. Hence, radiation exposure to patients and operating room personnel depends on the operator and the type of the procedure. Generally, there are several strategies to decrease radiation exposure during endourologic interventions such as following ALARA principles, using pulsed fluoroscopy with last-image-hold technology, and collimating the beam to the region of interest.

Here are some specific radiation reduction strategies during the three most common endourologic interventions.

### SWL

Based on its noninvasive nature, few side effects, and excellent stone clearance, the latest guidelines recommend SWL as the cornerstone intervention for management of uncomplicated renal stones <2 cm and proximal ureteral stones <10 mm [124–126]. Radiation exposure during SWL is low [127]. During 50 SWL procedures, the mean FT was 204 seconds and the mean ERD during was 1.63 mSv [67]. Another study found that, SWL of renal stones was associated with higher ERD (7.23 mSV), when compared with ureteroscopy (6 mSv) [128] (Table 2.1). This is because stone localization in most SWL machines depends largely on fluoroscopy. However, it is possible to reduce radiation exposure during SWL without compromising outcomes. Therefore, recommendations to decrease radiation exposure during SWL should be followed to decrease radiation exposure to patients. Several investigations have studied radiation exposure during SWL. For example, the risk of fatal cancer from SWL was estimated to be 140/1 million of patients receiving SWL for proximal ureteral calculi and 85/1 million of patients receiving SWL for distal ureteral calculi [69]. In a study by Griffith and co-investigators, reducing the number of radiographic "snapshots" during SWL was associated with 62% reduction of radiation dose in the most obese patients (from 152 to 95 mGy per procedure) [90]. Others reported a mean skin surface radiation exposure of 178 mGy per procedure in a cohort of 298 SWLs [129].

To further reduce radiation exposure during SWL, several measures has been proposed [130]. These include the use of low-dose fluoroscopy, keeping the image intensifier close to the patient, avoiding fluoroscopy when personnel are close to the unit and when the balloons are deflated, and using intravenous contrast or retrograde pyelography for faintly radiopaque stones [130]. The other important parameter is the operator (technician or urologist) experience. In one study, there was significant impact of a technician's experience on FT and outcome during SWL [131]. Therefore, this may explain the discrepancy in ERD among different studies. Alternatively, ultrasound could be used during the localization process since modern SWL units are equipped with ultrasound guidance. This could be used as an alternative to fluoroscopy to reduce exposure to reduce radiation exposure. However, ultrasound-guided SWL was associated with lower stone-free rates ranging from 37 to 66.5% [132, 133]. Despite these disappointing results, it seems that the advancements in SWL devices incorporating ultrasound-guidance may improve SWL outcomes in the future while avoiding radiation exposure. Recently, the three-dimensional ultrasound stone locking system was found to reduce radiation exposure during SWL [134]. Abid and colleagues compared a new three-dimensional ultrasound stone locking system (Visio-Track) (EDAP-TMS) with a conventional ultrasound localizing system (Sonolith® i-sys) (EDAP-TMS) in terms of FT, radiation dose, and efficacy of SWL. They reported significantly lower FT (3.5 vs. 159.5 seconds; $P < 0.001$) and radiation dose (163 vs. 10 598 mGy/cm$^2$; $P < 0.001$) associated with significantly higher stone-free status (79.5 vs. 54.5%; $P = 0.001$) with the new three-dimensional ultrasound stone-localizing system compared with the conventional ultrasound stone-localizing device [134]. Therefore, with the latest SWL devices utilizing three-dimensional ultrasound stone-localizing systems it is possible to reduce radiation exposure without compromising outcomes during SWL.

## Ureteroscopy

Ureteroscopy is associated with significantly higher radiation exposure in obese patients [52, 66]. Other predictors of increased radiation exposure during ureteroscopy include renal flexible ureteroscopy when compared with rigid ureteroscopy, prolonged procedural time, postoperative stenting under fluoroscopic guidance, male gender, balloon dilatation of the ureteral orifice, and surgeon experience [64, 65, 135, 136].

To decrease radiation exposure during ureteroscopy, urologists should control the foot pedal and use last-image-hold technology which has been shown to decrease radiation exposure by 40 times (from 100 to 2.5 mSv) [63]. Furthermore, Greene and colleagues found that using physical markers and laser guidance resulted in 82% reduction in FT (86.1 vs. 15.5 seconds; $P < 0.001$) without affecting operative time and procedural outcomes [137]. In addition, using pulsed fluoroscopy at 4 frames/second was associated with 62.4% reduction in FT, when compared with the standard fluoroscopy at 30 frames/second during ureteroscopy (from 109.1 to 44.1 seconds; $P < 0.001$) [81]. Using a validated non-obese male model, these fluoroscopy reduction techniques were shown to decrease the mean FT down to 47 seconds with a median ERD of 1.13 mSv [62]. In order to further decrease FT during ureteroscopy, Hsi and coworkers performed ureteroscopy with only two shots of fluoroscopy to ascertain the proper stent placement bringing the median ERD down to 0.05 mSv [138]. However, a safe "fluoroless" placement of the ureteral stent following ureteroscopy was described a year prior to the Hsi et al. study [139]. Another modification in the technique was the description of radiation-free ureteroscopy or "fluoroless ureteroscopy" [140–142]. This technique entails performing ureteroscopy without the use of any source of imaging, but rather depends on visual and tactile cues. In one study, the authors were able to extract distal ureteral calculi in a fluoroless manner in 99/110 patients [140]. Others, reported the feasibility of performing fluoroless ureteroscopy in 92% of their cohort (86/92 patients) [141]. In order to avoid radiation exposure from fluoroscopic-guided ureteroscopy, other groups proposed ultrasound-guided ureteroscopy [143, 144]. This technique basically uses ultrasound to confirm the position of the ureteral stent and the guidewire. In a level 1 evidence study, the procedural outcomes during ultrasound-guided ureteroscopy were comparable with fluoroscopic-guided ureteroscopy for extracting ureteral stones <8 mm [144]. While this technique was successful in expert hands, it has limitations such as the lack of familiarity of most urologists with ultrasound and the challenge of using ultrasound guidance in obese patients.

### PCNL

The latest American Urological Association guidelines on staghorn stones recommend fluoroscopic-guided PCNL as the first-line option for treatment of large renal stones [41]. However, compared with other endourological procedures, PCNL was associated with the highest radiation exposure [7, 145–147]. Furthermore, morbidly obese patients and patients with large stone burden that necessitates multiple access tracts are even at higher risk of radiation during PCNL [59, 62]. It has been reported that, during PCNL, patients are exposed to a radiation dose similar to that during a NCCT of the abdomen or pelvis [62]. Given these findings, a patient undergoing PCNL will receive radiation during preoperative CT scan, intraoperative fluoroscopy equaling another CT scan, and a postoperative follow-up CT scan. This makes the patient at risk of receiving radiation comparable to the 50th percentile of the dose received by the victims of the Hiroshima and Nagasaki nuclear bombs in World War 2 [62, 148]. Thus PCNL patients are at a potential risk of the stochastic consequences of radiation resulting from exposure to excessive ionizing radiation [14, 20, 149, 150]. Therefore, several investigators looked at the predictors of radiation exposure during PCNL to determine factors associated with prolonged FT and ERD [59, 61, 141]. In addition, different scoring systems were introduced and validated with the aim of assessing of PCNL complexity preoperatively [27, 151–155]. Recent studies did not find significant effects of PCNL complexity on FT [156, 157].

There are several strategies for reducing radiation exposure during PCNL. For example, our group reported a significant reduction of FT during PCNL when using pulsed fluoroscopy at 4 frames/second compared with using standard fluoroscopy at 30 frames/second. This simple technique was associated with 65% reduction in FT (from 341.1 to 121.5 seconds; $P < 0.001$) [81]. Furthermore, the use of a laser-guided C-arm with fixed lower current and kVp in addition to an experienced radiology technician and pulsed fluoroscopy at 1 frame/second was associated with more than 80% reduction in FT during PCNLs (from 175.6 to 33.7 seconds) [158]. Another technique is air pyelography, which halved the mean adjusted ERD from 7.67 to 4.45 mSv [159]. Others performed percutaneous renal access under endoscopic guidance. Endoscopic-guided PCNL is a technique where the PCA is obtained using assistance via retrograde flexible ureterorenoscopy [160]. It has been shown to be associated with advantages of fewer access tracts, lower transfusion rates, and shorter operative times [161–163]. A study by Lantz et al. reported that endoscopic-guided PCNL was associated with significantly lower FT and ERD compared with standard PCNL [164]. This is because establishment of PCA contributes the most to FT during PCNL. With the presence of a pre-formed PCA is associated with a significant reduction in FT during PCNL [165]. A study by the Clinical Research Office of Endourological Society (CROES) included 5806 patients treated with PCNL to compare perioperative outcomes of PCNL using either ultrasound or fluoroscopic guidance for PCA. They compared a matched sample of 453 patients in each group. On multivariate analysis, they did not find significant difference between outcomes of both groups in terms of stone-free rates and complications [166]. Therefore, it is logical that ultrasound-guided PCA significantly reduced FT and subsequently radiation exposure during PCNL [167]. Another study confirmed that totally ultrasound-guided PCNL was feasible with comparable outcomes to fluoroscopic-guided PCNL [168, 169]. In addition, both techniques were equally feasible and safe in the hands of postgraduate trainees with comparable outcomes and significantly lower radiation exposure in the ultrasound-guided PCNL [170]. However, the lack of familiarity of most North American urologists with ultrasound guidance and lack of availability of ultrasound machines with abdominal probes may limit the applicability of this procedure. Furthermore, it may be difficult in obese patients. Others reported some success with blind access without imaging assistance. In a level 1 evidence study by Basiri and co-investigators, 50/100 patients were randomized to blind-access PCNL, when up to five punctures were attempted before fluoroscopy [171]. PCNL procedures were completed with 50% success when access was obtained blindly compared with 90% success when access was obtained with fluoroscopic guidance. In terms of outcomes, blind access was associated with more procedural time (6.6 vs. 5.5 minutes, $P < 0.01$) and lower stone-free rate (62 vs. 100%). Nonetheless, blind access was performed without the need for fluoroscopy. This approach may be reserved in case of unavailability of ultrasound and should only be performed by expert hands in certain cases [171].

## Radiation exposure during brachytherapy

Brachytherapy is an established treatment option for organ-confined, low-grade prostatic adenocarcinoma. It is a sort of internal radiation therapy that is applied for the prostate at either low dose rate using implantation seeds or high dose rate. The aim is to place radiation close to cancer cells, where the radiation can kill the cancer cells without producing marked damage to nearby healthy tissues. Temporary brachytherapy entails placing radioactive wires within the prostate gland close to the tumor for several minutes before these wires are removed. While permanent brachytherapy includes placing radioactive seeds permanently within the prostate, where they slowly release radiation. It is usually performed in collaboration with a radiation technologist and radiation oncologist. The amount of radiation exposure depends on whether the procedure is performed under ultrasound or fluoroscopic guidance (usually less than 100 mSv/minute) and on the radioactive isotope being used. For example, $^{192}$iridium has a long half-life of 74.2 days and produces an average energy level of 380 KeV [172]. Others have shorter half-lives such as $^{125}$iodine, which has half-life of 60.2 days and produces energy level of 28 KeV, and $^{103}$palladium which has a half-life of 17 days and produces energy level of 21 KeV. Brachytherapy was previously performed through an open wound; thus the surgeon's hands were receiving most of the radiation exposure at an annual rate of 18.7 mGy [173]. Recently, the amount of radiation exposure has decreased with the use of ultrasound-guided percutaneous needle placement of radioactive isotopes. However, it is important to follow the local applicable regulations for radioactive materials to minimize handling of radioactive seeds and place them in labeled metallic containers [174].

## Virtual reality simulator training and radiation exposure

The learning curve of PCNL is quite long. It is reported that 36–45 cases are needed to achieve competency and 105–115 to achieve proficiency [175, 176]. Recently, the use of virtual reality simulators for training was associated with significant decrease in radiation exposure while obtaining the percutaneous renal access. Noureldin et al. found that trainees with prior PCA experience performed better on the PERC Mentor™ simulator with significantly lower FT [177, 178]. Furthermore, Papatsoris and colleagues reported significant reduction in the FT during PCA in trainees who received training on the PERC Mentor simulator (Symbionix, Cleveland, OH, USA) compared with trainees who did not receive training (6.49 vs. 15.8 minutes; $P < 0.01$) [179]. Therefore, virtual reality simulators could be used to train urologists in obtaining PCA leading to significant reduction in radiation exposure to both patients and urologists during the early phase of the learning curve [177, 178].

## Radiation reduction strategies in special circumstances

### Pediatric urology practice

When using radiation for diagnostic or interventional purposes, it must be noted that age of the patient is important to keep in mind. This is because infants and children are at higher risk of developing cancer compared with adults receiving the same dose of radiation. There are two reasons for this: (i) the developing tissues and organs are more sensitive to the effects of radiation and (ii) infants and children have a longer expected life expectancy which gives more time for any hazards of radiation to manifest. Therefore, it is widely recognized that pediatric patients must be treated differently compared with their adult counterparts [8, 148]. Furthermore, it has been reported that approximately 25% of radiation exposure in children arises from imaging of the urinary system [180]. Therefore, during 2013, the ICRP introduced *Publication 121* to highlight "radiological protection in pediatric diagnostic and interventional radiology" [8]. It reinforced the importance of justification of imaging procedures which utilize ionizing radiation and ascertained the importance of adjusting the equipment for pediatric patients and optimizing radiation protection to significantly improve radiological protection and deliver significantly lower doses to pediatric patients [8]. This could be achieved by purchasing new imaging equipment with available dose reduction measures. In addition, special attention should be given to the unique aspects of pediatric imaging such as the wide range in patients' weight which require modification of equipment, technique, and imaging parameters. Furthermore, attention should be paid to the patient's position, field size, adequate collimation, use of protective shielding, optimization of exposure factors, use of pulsed fluoroscopy, limiting FT, and sticking to the acceptable DRLs in pediatric population. Moreover, pediatric interventional procedures should be performed by experienced hands with a specific level of training in radiological protection.

#### CT

It has been reported that 7–10% of CTs are performed for children [21]. An epidemiological study by Pearce and coworkers including a cohort of 178 604 children who underwent CT scan between 1985 and 2002 in different hospitals in the United Kingdom with average follow-up of about 10 years. They found that children who received CT scans had higher incidence of brain cancer and leukemia [181]. Furthermore, they found a significant association between the estimated radiation doses delivered by CT scans to the brain and the red bone marrow and the risk of brain tumors and leukemia, respectively. Having two or three head CT scans put the child at three times the estimated risk of brain cancer, while 5 to 10 head CT scans put the child at three times estimated risk of leukemia [181]. However, a recent multi-center cohort study including 67 274 children who had their first CT scan before the age of 10 years during the period between 2000 and 2010 questioned whether this reported increase in cancer risk in children was biased by the indications for CT scans [182]. Over a mean follow-up of 4 years, 73 cases were diagnosed with cancer, 27 with central nervous system tumors, 25 with leukemia, and 21 with lymphoma. However, 32% of children diagnosed with cancer were among those with predisposing factors. Following adjustment for predisposing factors, the excess cancer risk estimates related to cumulative doses from CT scans were reduced. Therefore, Journy and colleagues recommended that the indication for examinations, whether for predisposing factor management or suspected cancer, should be considered to avoid overestimation of the cancer risks associated with CT scans [182].

One study suggests that up to one-third of all CT scans in pediatric populations could be eliminated or replaced by alternative approaches [183]. This highlights the importance of justification on lowering pediatric radiation exposure. Furthermore, optimization of radiation protection is critical when performing CT in the pediatric population. This could be achieved by adjusting the scan parameters such as current, kVp, and pitch according to the patient's weight, age, scanned region, and study indication. Other optimization strategies include scanning only the area in question with avoidance of overlapping of scan regions, restricting multi-phase examination protocols, and the use of the state-of-the-art reduction technology such as tube current modulation, organ-based dose modulation, auto kV technology, and iterative reconstruction technology [184].

#### Voiding cystourethrography

Fluoroscopic voiding cystourethrography (VCUG) with spot films is considered the gold standard for diagnosis and grading of vesicoureteral reflux due to its acceptable sensitivity and negative predictive value [185]. Although it is associated with lower amount of ionizing radiation delivered to a child compared with other commonly performed pediatric examinations such as CT, ALARA principles recommend that radiation exposure during VCUG should be kept to minimum as children possess growing tissues and organs that are about 10 times more sensitive to ionizing radiation than adults [186]. As the fluoroscopic dose during VCUG is estimated to be 80% of the entire radiation dose, the use of fluoroscopy with spot films during VCUG was challenged. Recently, Alamdaran and colleagues evaluated the validity and radiation dose reduction using photofluorography with hard copy images compared with fluoroscopic VCUG with spot images. They found that photofluorographic VCUG was comparable to fluoroscopic VCUG in diagnosis and grading of vesicoureteral reflux with a sensitivity of 96% and specificity of 100%. Moreover, it was associated with a 50–90% reduction in radiation exposure [180]. Recently, Linke and colleagues employed an ultra low dose during 651 VCUGs using a modern flat detector. They found that with these new instruments and optimized protocols, VCUG could be performed with significantly lower radiation exposure and without obvious decrease in diagnostic image quality [187].

### Pregnant women

To better understand the hazards of radiation exposure during pregnancy, we will first cover the effects of *in utero* irradiation on the embryo/fetus. These effects are related to the absorbed dose to the embryo/fetus and at which stage of pregnancy. These include (i) lethal effects might occur as a result of radiation exposure during the pre-implantation period of embryonic development, (ii) malformations occur following exposure to a threshold of about 100 mGy during the third to eighth week of gestation which is considered the period of major organogenesis, (iii) the highest sensitivity of the central nervous system to radiation is encountered during the eighth to fifteenth week of gestation with lower sensitivity between the sixteenth and twenty-fifth week; exposure to approximately 1 Gy may cause severe mental retardation, and (iv) cancer development: throughout pregnancy, the fetus is at a potential risk of cancer from radiation exposure that is three times higher than normal populations. Given the aforementioned risks, it is important for pregnant patients to avoid diagnostic or interventional procedures using ionizing radiation and a balance between the health status of the mother and the potential health hazards on the embryo/fetus must be considered [26, 188, 189]. Moreover, there is potential risk for the mother too. Noncontrast MRI and ultrasonography are not associated with ionizing radiation; thus they are not associated with any known adverse fetal effects. However, their sensitivities and specificities in detecting ureteral calculi are low. Furthermore, the use of gadolinium contrast material to differentiate a ureteral stone from a filling defect during pregnancy is contraindicated due to its potential teratogenic effects.

According to the American Congress of Obstetricians and Gynecologists and the American College of Radiology, a single diagnostic X-ray procedure is safe and does not result in adequate radiation exposure that threaten the well-being of the developing embryo or the fetus [190]. Therefore, a KUB is associated with a small amount of radiation and can be safely performed as a diagnostic modality during pregnancy, whenever appropriate. Furthermore, it has been reported that a limited IVU of three or four films delivers around 2–2.5 mGy to the fetus and can be safely performed during pregnancy, whenever urgently needed. However, the lower part of the ureter may be masked by the fetus. Fluoroscopy is associated with considerable radiation exposure to the fetus: 15–20 mGy/minute. Therefore, it is reasonable to use ultrasound as an alternative to fluoroscopy during pregnancy, whenever possible [189]. With recent advances in CT scanners and dose reduction technologies, the use of LDCT in diagnosis of urolithiasis during pregnancy becomes permissable [191]. In a study by Johnson et al., 46 ureteroscopies were performed in 45 pregnant females at five different tertiary care institutions [192]. Imaging modalities used for preoperative assessment of the patients varied according to the center and surgeon preference. CT was accurate in detecting 95% of stones. However, ultrasound and MRI showed lower accuracies (72 and 80%, respectively) [192]. While some patients in this study underwent CT for diagnosis, there were no fetal losses. However, we do not know what happened to the delivered children afterwards. Nonetheless, the use of CT with recent techniques such as ultra-low dose with iterative technologies that significantly decrease the ERD while maintaining high sensitivity and specificity of ureteral stones may play an important role in the near future.

Regarding endourologic procedures, ureteroscopy has been shown to be safe during pregnancy with the advantage of definitive management by removing the obstructing stones rather than inserting ureteral stents or nephrostomy tubes with the need for frequent changes during pregnancy [193–196]. In 2002, Watterson and co-investigators reported the safety and efficacy of ureteroscopy and holmium laser lithotripsy in eight pregnant patients. Ninety-one percent of the procedures were successfully completed with an overall stone-free rate of 89% [193]. Half of these cases necessitated the use of fluoroscopy with an average FT of 0.19 minute while the area of the fetus and the contralateral kidney were covered with lead shields. Others reported similar outcomes in 45 patients who underwent 46 ureteroscopies during pregnancy in five tertiary care centres [192]. The most common obstetric complication was preterm labor, which may be managed conservatively without fetal loss. Others reported the feasibility of rigid ureteroscopy without the need for ureteral dilation during pregnancy [197]. In a systemic meta-analysis there was no significant difference in the outcomes of ureterosopy in pregnant and nonpregnant patients in terms of ureteral injury (0.9 vs. 3.8%) or postprocedural urinary tract infection (4.6 vs. 3.8%). However, premature uterine contractions were reported in 0.9% of pregnant females who underwent ureteroscopy and this was resolved by tocolytics [198]. Three years later, a meta-anlaysis on 116 ureteroscopic procedures in pregnant women showed similar results with 86% success rate and two major complications (one case of premature uterine contraction and one ureteral perforation) and seven minor complications (two cases of postoperative pain and five cases of postoperative urinary tract infections) [196]. Few case reports refer to the possibility of performing PCNL during the first trimester using ultrasound guidance and the second trimester of pregnancy employing strict techniques to reduce fluoroscopy with proper shielding [199]. However, SWL and PCNL remain contraindicated during pregnancy by international guidelines [124, 126].

Video 2.1 outlines radiation safety for urologists.

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## 3

# Enhanced Endoscopic Imaging

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## Introduction

Innovations and improvements in video imaging technology have paved the way for significant advancements in endourology and minimally invasive urologic surgery. Recent advances in technology have made what once appeared to be science fiction into reality. Augmented reality, three-dimensional (3D) video imaging, photodynamic and fluorescence-enhanced optics, and video image overlay are all being incorporated into current surgical practices. These technologies are not only facilitating the performance of complex surgical procedures but are allowing wider dissemination of the skills needed to perform these procedures. As these technologies continue to develop, their applications in minimally invasive endourological practice will only grow.

This chapter will review the current state of the art of video imaging systems within endourology. Technological advancements and their application in current endourological practice will be discussed. It is anticipated that this information will not only help the reader to enhance their video imaging practices today, but also prepare one for tomorrow's tremendous innovations in advanced imaging modalities.

## Digital imaging

There have been a number of major improvements which have greatly enhanced videoendoscopic surgery [1–3]. These significant advances have been the development of the charge-coupled device (CCD) chip camera and the introduction of digital video imaging. Once an optical image is focused on the CCD chip, there is a conversion of the optical (light) image to an electronic signal [4]. This electronic information, which includes both color and light (luminance), can be scanned by a video monitor to produce an image on the screen.

Standard National Television Systems Committee (NTSC) video signals utilize a limited "band width" which include both the color and luminance information in a single or "composite" signal. Problems with this format include "signal noise," which is caused by the camera having to first process color and luminance information separately and then combine the two pieces of information to create a video signal. This video noise or "crosstalk" may be the cause of decreased resolution, grainy images, and loss of information around the edges of the video image. With the advent of digital imaging, newer video formats have been introduced [5]. The first format allows the color and luminance information to be carried as two separate signals. This "component" video signal is called Y/C (S-video), with Y standing for luminance or light brightness and C referring to color. This component signal contains less crosstalk and therefore appears cleaner and sharper than images generated by composite signals. The video signal in a Y/C format is carried by a single cable, as with the NTSC format, although the color and luminance information are still separated.

Another video format is known as RGB (Red-Green-Blue). This RGB format is also a component signal, yet it is distinct from the Y/C format in that the video information (color and luminance) is separated into four signals. These include a red, green, and blue signal as well as a timing signal. Each individual signal carries its own luminance information. Separation of the video signals is performed electronically in the camera head. The RGB format requires less electronic processing than do the NTSC or Y/C formats since the color and luminance information are separate from the start. Therefore, the RGB image quality is greatly enhanced compared to the

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other two formats. Also, in contrast to the single-cable NTSC and Y/C formats, the RGB video signal is carried by four separate cables (red, green, blue, and sync). Both Y/C and RGB formats offer superior image quality.

## Standard video systems

The technical advantages created by video monitoring include binocular vision and magnification of the monitor images. Magnification may be as great as 20 times, depending on the initial optics system used. This enlarged image permits better inspection of detail and allows the operator, by virtue of the enlarged image size, to perform the procedure off the monitor rather than looking directly through the endoscope [6]. This approach significantly decreases operator strain because the surgeon no longer needs to conform his body to the angle of the viewing lens. Instead, the urologist can simply attach a video camera to the scope and manipulate the endoscope while standing comfortably and observing the video monitor [3]. Moreover, the upright position assumed by the urologist decreases the likelihood of coming in contact with potentially infected body fluids.

### Video cameras

All video systems are currently composed of a CCD solid-state chip camera, a video processor with or without a video recorder, and various video accessories. All of the chip cameras are fully immersible and shielded from electrical interference that may be created by cutting or coagulating currents during endoscopic procedures [7]. The CCD chip high-resolution camera should have an automatic white balance feature which allows one-touch color balance assuring true-to-life color reproduction. Additional features of the CCD camera may include a high-gain option which will boost the video signal to provide an exceptionally clear image, as well as a color bar option that allows the surgical team to adjust the monitors to represent accurate camera color prior to beginning the case.

Advances in CCD camera technology have significantly downsized current endoscopic video cameras, thereby allowing easier movement of the endoscope with the attached camera. With the recent significant improvements in CCD technology, tube cameras are no longer utilized due to their large size. When recording an actual endoscopic procedure, the camera may provide a remote control switch for a video recorder allowing instant fingertip pausing of the recording device during documentation. Additionally, the camera head should be designed to prevent fogging between the coupling device and the camera head. All manufacturers can supply camera-head adapters for other endoscopic systems. Finally, the entire camera head cable and edge card should be completely cold-soakable in disinfectant solutions for easy sterilization between endoscopic cases.

As noted, CCD chip cameras have supplanted tube cameras, which were the first video systems on the market. A significant improvement in CCD camera technology has been the development of the three-chip camera, which contains three individual CCD chips for the primary colors: red, green, and blue (Figure 3.1). In addition to composite SVHS and component signals, the three-chip cameras also provide an "uncoded" red, green, and blue signal. Color separation is achieved using a prism system overlying the chips [8]. This three-chip camera design provides improved color fidelity and enhanced image resolution. Moreover, three-chip cameras produce less "noise" due to the pure red-green-blue signals [9, 10]. A digital converter captures each voltage signal as an image and translates the voltage

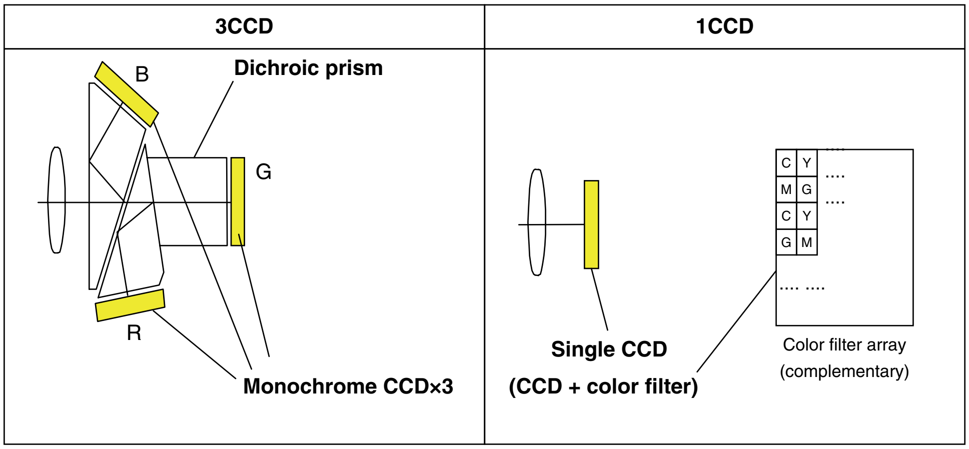


**Figure 3.1** Schematic representation of three-CCD-chip and one-CCD-chip designs. Red, green, and blue are sent to three separate CCDs by a prism. Reproduced with permission of Olympus.

values into discrete numbers, either as 0 or 1. The encoded numbers for each image element, or pixel, include information on color, light intensity, and contrast. These variables can then be modified using image-processing software within the camera [11].

Many CCD chip cameras (both single-chip and three-chip) contain electronic shuttering mechanisms that automatically adjust exposure time from 1/60 to 1/16 000 of a second (Figure 3.2). The advantage of such a sophisticated detection circuit is that the camera can react to varying light conditions almost instantaneously, reducing the flaring, "washout," and "blackout" which were noted with early video systems. Moreover, electronic shuttering mechanisms within the camera usually work more quickly than automatic light sources.

Some of the newer additions to three-chip camera technology are improved ergonomic designs (light weight and 90° rotation functionality) (Figure 3.3), wireless transmission capabilities when used with wireless monitor systems, and programmable buttons that allow high-definition (HD) image capture, video recording, image magnification, auto focus, and light source control by the operating urologist. Compatibility with the latest video-enhancing devices, such as Clarity (Stryker, Kalamazoo, MI, USA) and with modern imaging technology such as narrow band imaging (Olympus, Center Valley, PA, USA) and IMAGE 1S (Karl Storz, Tuttlingen, Germany) further improve visualization and facilitate video documentation.

## Videoendoscopes

A major advance in the endoscopic systems has been the development of the digital videoendoscope. Miniaturization

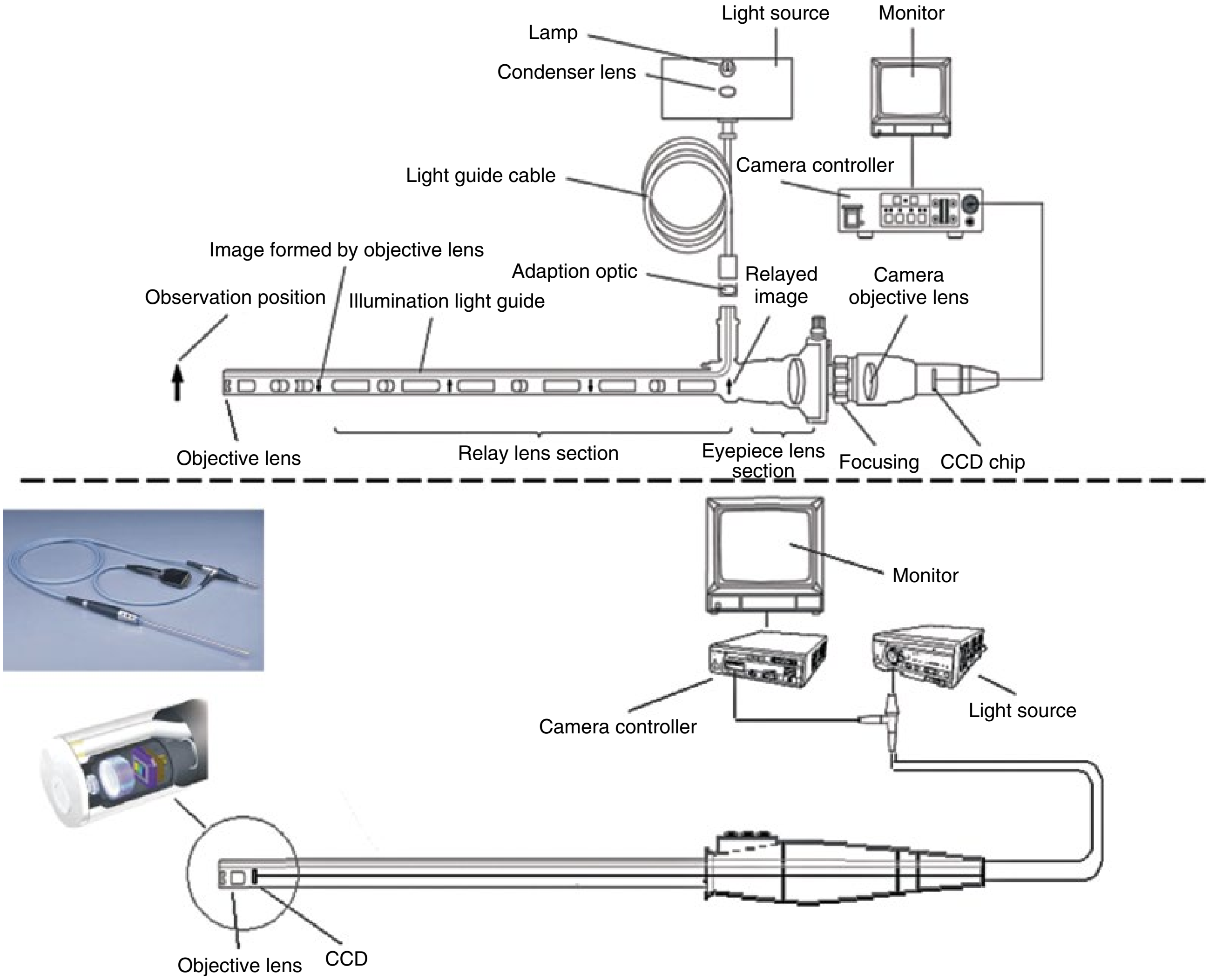

Light source
Monitor
Lamp
Condenser lens
Camera controller
Light guide cable
Image formed by objective lens
Adaption optic
Relayed image
Camera objective lens
Observation position
Illumination light guide
Objective lens
Relay lens section
Eyepiece lens section
Focusing
CCD chip
Monitor
Light source
Camera controller
Objective lens
CCD

**Figure 3.2** Traditional technology (top) compared with electronic transmission videoendoscopes (bottom). Reproduced with permission of Olympus.

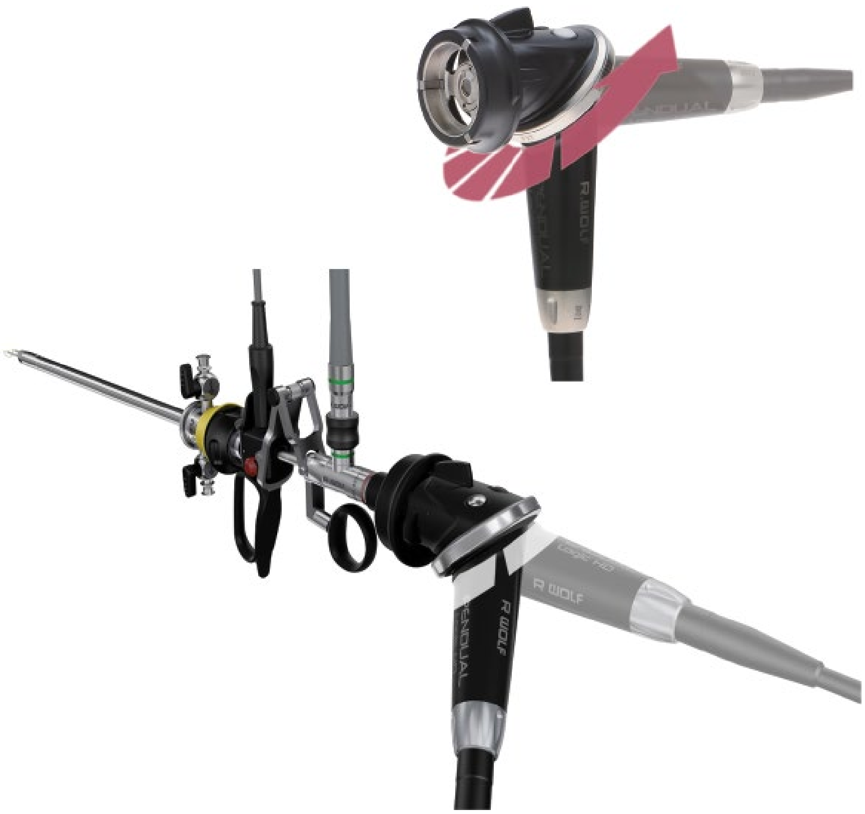


**Figure 3.3** The PENDUAL ENDOCAM Logic HD camera head from Richard Wolf. It can be rotated from a 90° angle to a straight camera head which can provide better control in different endoscopic procedures. Reproduced with permission of Richard Wolf GmbH, Knittlingen, Germany.

of chip technology now allows a CCD chip to be incorporated at the distal end of the endoscope (Figure 3.2). Instead of relaying optical images from the objective lens at the distal end of the scope to a camera attached to the eyepiece, the image is immediately captured by the CCD chip, digitized, and converted into electrical signals for transmission (chip-on-the-tip technology). This endoscope design has fewer interfaces allowing the digital information to be directly transmitted to an image display unit with minimal image loss, interference, or distortion [12, 13]. The creation of true videoendoscopes especially benefits the flexible ureteroscope and cystoscope. As internal optics are not required in the long and flexible shafts of these instruments, durable deflection mechanisms can be utilized to improve the durability of flexible endoscopes [14, 15]. With no need to attach a camera head to the eyepiece of the scope, the videoscope cable can be secured to the light cord for attachment to the video system, providing a more lightweight and convenient setup. This technology has been incorporated into larger, rigid endoscopes (laparoscopes), as well as rigid and flexible cystoscopes and ureteroscopes [16–18]. This innovation is due to recent technological advances which have now allowed miniaturization of CCD chips. One can expect to see such an integrated digital videoendoscope to replace many endourologic endoscopes in the near future.

Another development in digital camera technology includes the use of a single monochrome CCD chip with alternating red, green, and blue illumination to form a color image rather than using three chips with three separate color filters. This design reduces the space requirements and takes advantage of established high-resolution monochrome CCD chip technology [12].

Other techniques under development for image resolution enhancement include the use of complementary metal oxide semiconductor (CMOS) technology to replace the CCD sensors [19]. Both CMOS and CCD imagers are manufactured in a silicon foundry and the equipment used is similar. But alternative manufacturing processes and device architectures make the imagers quite different in both capability and performance. It is technically feasible but not economical to use a CCD processor to integrate other camera functions, like the clock driver and signal processing. These are normally implemented into secondary chips. Thus, most CCD cameras comprise several chips. On the other hand, one of the major benefits of CMOS cameras over the CCD design lies in the high level of product integration that can be achieved through virtually all of the electronic camera functions onto the same chips. Typically, a CMOS processor allows lower power usage and lower system cost. This technology is currently being used for digital ureteroscopy [20].

Several *in vivo* and *in vitro* studies have compared the new digital flexible cystoscopes to fiber-optic flexible cystoscopes in terms of their optical characteristics [21–24]. The compared optical characteristics included image resolution, grayscale imaging, color representation, color differentiation, depth of field, image brightness, and the urologist's subjective assessment of image quality. The digital flexible cystoscopes were superior to fiber-optic flexible cystoscopes in almost all optical parameters.

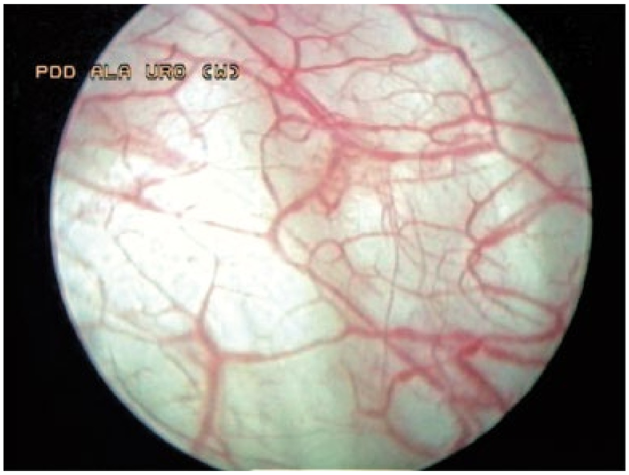
In addition to the improved imaging quality of the white light digital cystoscopes, the use of optical and video enhancing techniques, such as fluorescence cystoscopy/photodynamic diagnosis (PDD), narrow band imaging (NBI), confocal laser endomicroscopy (CLE), and optical coherence tomography (OCT) have extended the quality of information that these cystoscopes can deliver [25].

The PDD modality, or hexaminolevulinate-guided blue-light cystoscopy, uses photosensitive protoporphyrin analogues as intravesical contrast agents combined with a blue-light-source (375–440 nm) cystoscope to stimulate fluorescence. Selective accumulation of the photosensitizers by cancer cells causes tissue to appear distinctively red when visualized with blue light cystoscopy (Figure 3.4). There is evidence that the use of this modality improves detection, and consequently treatment, of non-muscle invasive bladder cancer. A newer body of evidence suggests that blue-light cystoscopy helps decrease recurrence, and even progression, rates of non-muscle invasive bladder cancer through better visualization and diagnosis and it has proven to be cost effective [26–29].

The NBI technique (Olympus) is based on a light source that filters white light into two narrow wavelengths (415 and 540 nm) that are strongly absorbed by hemoglobin, enhancing the contrast between capillaries and mucosa without the use of dye. Enhanced contrast helps differentiate the more vascularized malignant areas from normal and benign urothelium. The Olympus High Definition Flexible Cysto-Nephro Videoscope (HD CYF-VH; Olympus) is equipped with this functionality. In addition to its HD quality images, this cystonephro videoscope has a wide 120° field of view, improved deflection (220° up, 130° down), 150% increased light output, and 20% brighter NBI when compared to the previous model, CYF-V2. When compared to white light cystoscopes, NBI-supported flexible cystoscopes have been shown to improve urothelial cancer detection in multiple studies [30–34].

Based on a similar technology, Karl Storz (Tuttlingen, Germany) has recently introduced the Storz Professional Image Enhancement System (SPIES) that is used with their IMAGE 1 S camera unit. Homogenous illumination, color enhancement, and shifting the color spectrum of the image obtained by the digital flexible ureteroscope, Flex-Xc, offers clearer tissue differentiation through three different viewing options (CLARA, CHROMA, and SPECTRA) that can be displayed side by side with the traditional white light digital image. The SPIES technology is currently at early stages of clinical investigation [35–37].

(a)



(b)

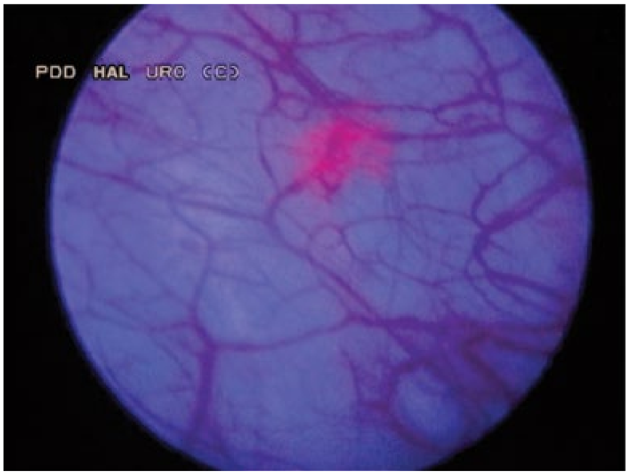


**Figure 3.4** PPD: small bladder micropapillary lesion. (a) Traditional white light cystoscopy. (b) Blue-light fluorescence cystoscopy. Reproduced with permission of Elsevier [94].

CLE and OCT are two of the newer imaging modalities. These microscopic modalities are based on fiber-optic probes used with standard cystoscopes that enable high-resolution subsurface characterization of suspected lesions, providing information on tissue microarchitecture and cellular morphology that is not possible with traditional white light, PPD, or NBI imaging technologies. The clinical validity and applicability of these technologies are still under investigation [23, 33, 38, 39].

Similar advanced optical technologies have been incorporated into the newer digital ureteroscopes. Use of the CCD and CMOS chip-on-the-tip digital technology has allowed high-definition visualization, autofocus capabilities, and digital magnification with decreased diameter of the ureteroscope shaft (Figure 3.2). Several studies have compared the currently available digital ureteroscopes with their previous generations and fiber-optic counterparts in terms of resolution, contrast, depth of field, color representation, illumination, and mechanical properties. The digital ureteroscopes have been shown to have superior visualization and imaging quality compared to the fiber-optic scopes in all of these studies [40–49].

The available modern flexible digital ureteroscopes are the Flex-Xc (Karl Storz), the URF-V2 (Olympus), and the BOA Vision (Richard Wolf, Knittlingen, Germany) (Figures 3.5–3.7). All of these flexible ureteroscopes have one or two integrated light emitting diodes (LED) light source, are capable of auto-focus and automatic adjustment of light intensity, offer wide (90°) field of view, have a 3.6 Fr working channel and can deflect 270° in both directions.

The Richard Wolf's BOA Vision and the Karl Storz's Flex-Xc ureteroscopes use CMOS, while the Olympus URF-V2 ureteroscope uses a micromini CCD, chip-on-the-tip technology. This technology eliminates the need for fibers to transmit images, which allows for decreased diameter of the scope (8.9, 8.5, and 8.4 Fr for the BOA Vision, Flex-Xc, and URF-V2 ureteroscopes, respectively).

The Olympus URF-V2 flexible ureteroscope is equipped with NBI technology that uses different light wavelengths to enhance tissue contrast, as discussed. The role of NBI technology is well established in urothelial carcinoma of the bladder. Although its role in upper tract urothelial carcinoma is theoretically promising, it is still in the early stages of investigation [50].

The Karl Storz Flex-Xc flexible ureteroscope is equipped with the Karl Storz SPIES technology that changes color enhancement and shifts the color spectrum to produce different image modalities with unique tissue enhancements. The clinical applicability and presumed advantage in detecting upper tract urothelial carcinoma using this technology has not been investigated yet. In addition to SPIES technology, the Flex-Xc flexible ureteroscope has PDD capability that uses

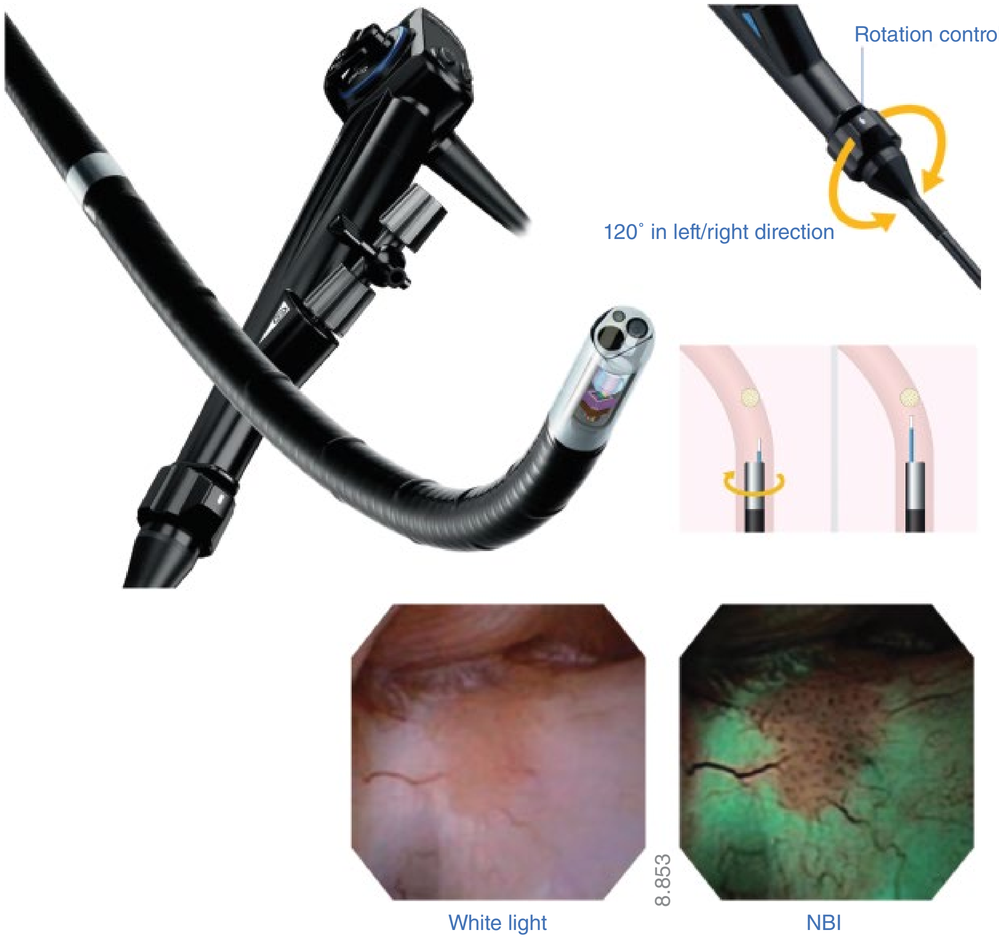


**Figure 3.5** The Olympus digital flexible ureteroscope URF-V2 with chip-on-the-tip technology, NBI, and axial rotation control. Reproduced with permission of Olympus.

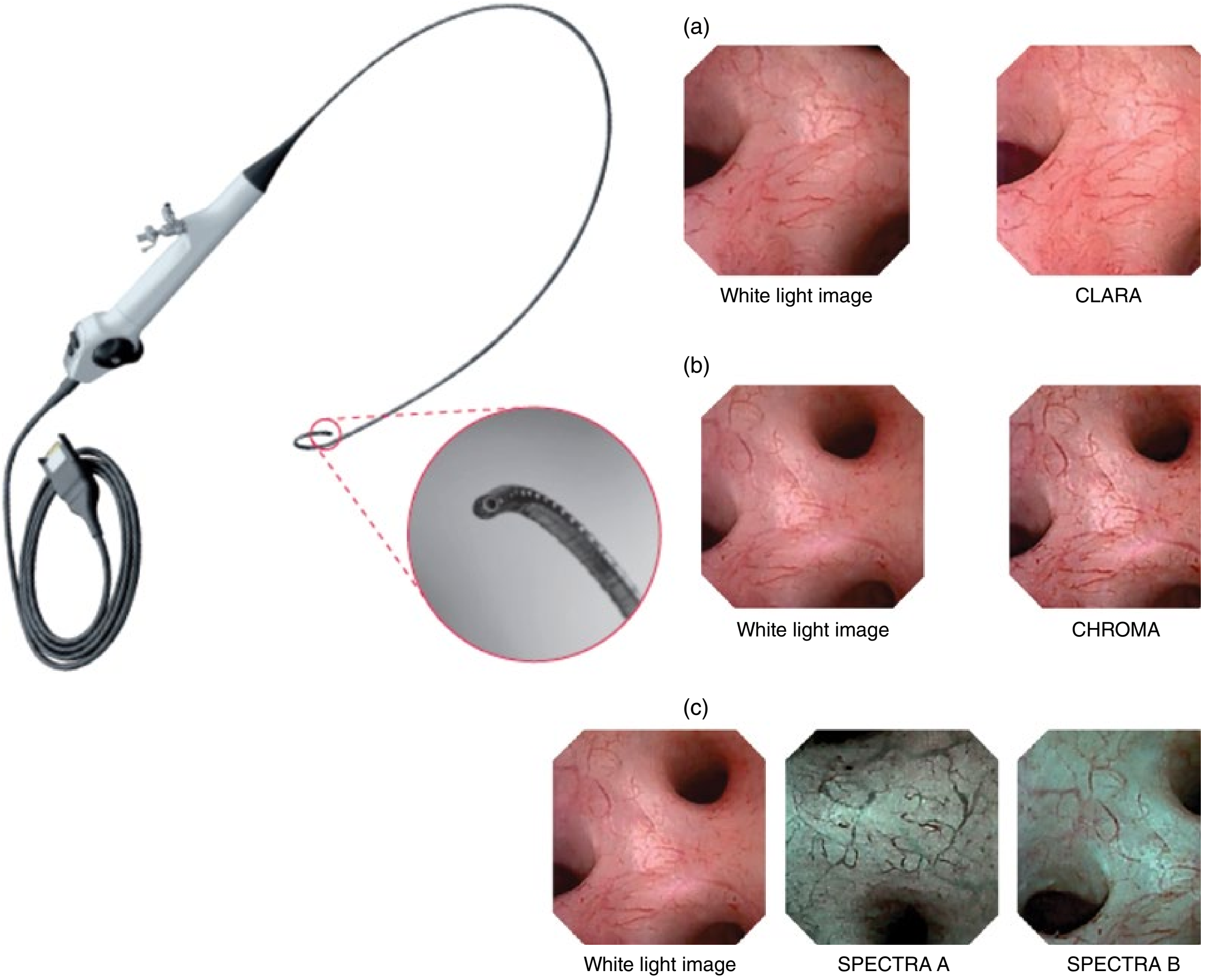


**Figure 3.6** The Karl Storz digital flexible ureteroscope Flex-Xc with chip-on-the-tip technology, Laserite ceramic insert to decrease laser thermal damage, and the Storz Professional Image Enhancement System (SPIES) modes: (a) CLARA, (b) CHROMA, and (c) SPECTRA A,B). Reproduced with permission of Karl Storz GmbH.

photosensitizers (5-aminolevulinic acid) to enhance urothelial malignant tissue fluorescence [40]. The use of this technique has been described in few reports and thus its clinical application is still under investigation [37, 51–53].

A newer addition to the flexible digital ureteorscope family is the LithoVue System (Boston Scientific, Marlborough, MA, USA), which is a single-use digital flexible ureteroscope. This ureteorscope uses CMOS chip-on-the-tip technology. Its light source is built into the handle, which is wired to a touch-screen monitor that is mounted on a mobile cart for portability (Figure 3.8). The ureteroscope has an outer diameter of 9.5 Fr and a single 3.6 Fr working channel. It can deflect 270° in both directions. Although the visibility and maneuverability of this ureteroscope has been shown to be comparable to those of a fiber-optic flexible (URF-P5; Olympus) and a digital ureteroscope (URF-V; Olympus) in one small study [54], its incorporation into daily clinical practice and cost effectiveness is yet to be explored.

Laparoscopy has witnessed similar, if not further, advancements in optical technology. HD digital laparoscopes are currently available for use and offer many significant advantages over standard-definition (SD) laparoscopes. Surgeons have subjectively rated HD images superior to SD images during laparoscopy in both the laboratory and clinical settings [55]. One recent study performed an objective comparison of performance characteristics between the Olympus HD 10 mm laparoscope (Olympus) and the Olympus SD 10 mm zero-degree laparoscope [56]. The HD laparoscope had improved resolution, decreased distortion, greater depth of field, and improved luminous flux when compared to the SD laparoscope. Given the importance of visual cues

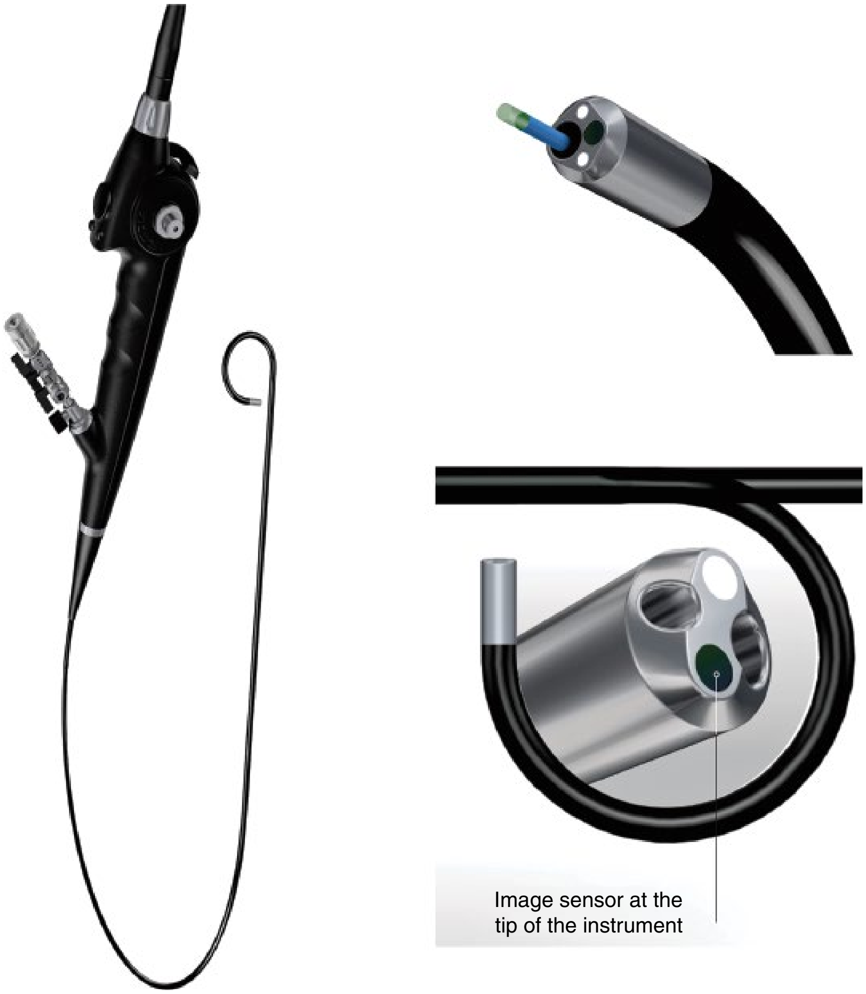


**Figure 3.7** The Richard Wolf digital flexible ureteroscope BOA Vision with chip-on-the-tip technology and dual LED light source. It is also equipped with Wolf's image sensor technology at the tip. Reproduced with permission of Richard Wolf GmbH, Knittlingen, Germany.

in performing laparoscopic surgery, these improvements could be of great significance. Laparoscopy performed with an HD camera in combination with HD monitor can improve the performance of surgical tasks, specifically laparoscopic knot tying, which requires precise depth perception [55, 57].

The newer telescopes offer HD and ultra-HD (UHD) images in wide angles. Olympus has introduced an articulating flexible tip HD videoscope (ENDOEYE FLEX LTF-S190-5; Figure 3.9) that, in many ways, resembles an ureteroscope. It also uses chip-on-the-tip technology and has built-in NBI technology. The articulating tip can bend in all directions up to 100°, which offers flexibility during surgical procedures and eliminates the need to constantly switch telescopes (for example from 0° to 30° and vice versa). It has a focus-free optical design that provides greater depth of field and eliminated the need for manual focusing. Similar to a digital ureteroscope, it has an integrated single light and camera cable that connects to the camera and the light source systems.

Another modern telescope is the EndoCAMeleon® from Karl Storz. This telescope does not have a flexible tip but it has a mobile lens with an adjustable direction of vision (0–120°). The operating surgeon can control the direction of view from the scope handle. It thus eliminates the need to switch scopes of varying angles (for example from 0 to 30° and vice versa) during surgical procedures (Figure 3.9).

The latest advancement in laparoscopic imaging technology is the introduction of the UHD 4K imaging resolution system. 4K resolution refers to a display device or content having horizontal resolution in the order of 4000 pixels and vertical resolution in the order of 2000 pixels. It offers four times the resolution of full HD and much more detailed images. This technology is introduced by the Visera 4K UHD system (Olympus). Visera 4K UHD supports both 4K UHD (3840 × 2160) and full 4K (4096 × 2160) resolution. This system generates a wider color gamut by adopting the 4K color format (BT2020) and display in a panoramic view. It allows surgeons to observe fine patterns and structures in high precision and recognize much more subtle differences in

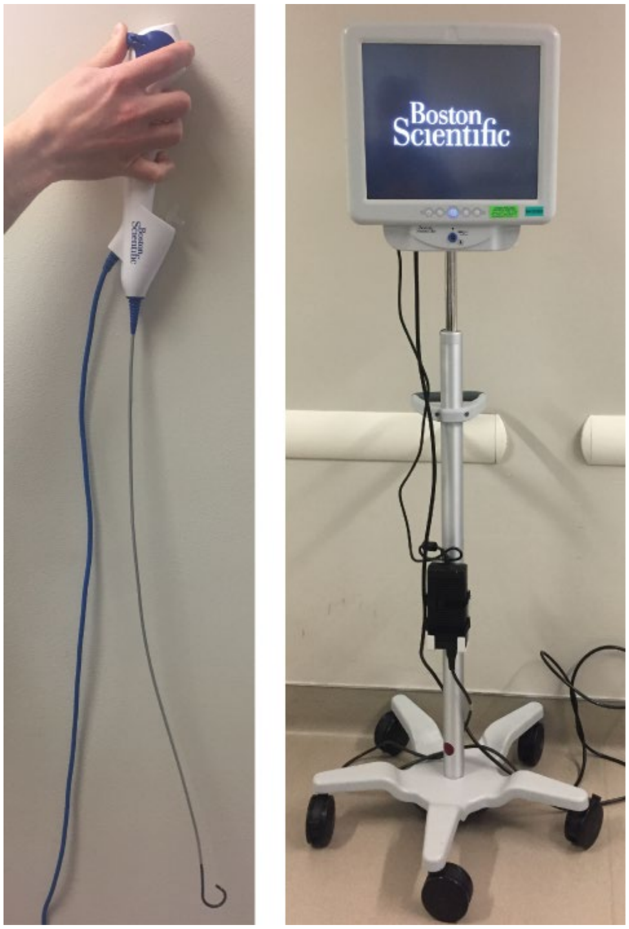


**Figure 3.8** The Boston Scientific single-use digital flexible ureteroscope LithoVue with chip-on-the-tip technology. Note the portable display cart that connects to the ureteroscope. Reproduced with permission of Olympus.

reds and yellows than conventional HD. It also has electric magnification capability that is equivalent to full HD resolution even at 2.0× zoom.

The abovementioned advancements in laparoscopic imaging technology have certainly improved the surgeon's experience in the operating room. The impact on clinical outcome has not been investigated yet.

## Video light sources

In addition to a CCD camera, a high-intensity light source, usually halogen, xenon, or light-emitting diodes (LED), should be utilized for appropriate illumination. Certain light sources have an automatic light sensing feature which quickly adjusts the light output as required by the camera. This automatic light adjustment feature is particularly helpful during endoscopic procedures, as the endoscope may be rapidly moved throughout the abdominal cavity or urinary tract, causing areas of too much or too little illumination. Light intensity will be automatically altered to maintain a pre-selected illumination level. As noted previously, some camera systems are equipped with an "automatic iris" system which will electronically increase or decrease the "aperture" of the camera shutter (Figure 3.4). If the camera system is equipped with such a light-sensing feature, there is no need for an automatic light-adjusting light source. Newer CCD or image sensor-based endoscopic cameras feature electronic exposure. This system varies the effective exposure period (i.e. light-gathering time) of the CCD as the live image is captured. Typical CCD exposure periods range from approximately 1/60 of a second to 1/10 000 of a second under very bright conditions. This electronic process can be used to maintain the brightness in the image. When the image brightness must be reduced to improve picture clarity, the image signal exposure period can be reduced electronically instead of adjusting the iris of the light source.

Shadows play an important role in depth perception and spatial orientation. Studies have demonstrated that endoscopic task performance significantly improves with video systems that provide proper illumination and appropriate shadows in the operative field [58]. Many of the current endoscopes employ a simple frontal illumination technique that produces an optically flat and shadow-less image with resultant poor contrast. Newer illumination and imaging technologies provide shadow-inducing systems using a single-point or multipoint illumination system. One of these techniques employs the use of two independent illumination fiber bundles, with one fiber bundle ending at the front lens, as designed in conventional endoscopes and the other fiber bundle ending behind the tip of endoscope. This configuration results in an improved image with better contrast due to shadow formation. Spatial orientation and perception between anatomical structures are considerably enhanced [19].

The newer endoscopic light sources generate light using LED technology. Compared to xenon lamps, LED lamps are more economic, more efficient, produce a similar light intensity that is consistent throughout the life span of the bulb, and are quieter than xenon lamps. Moreover, some manufacturers have improved on LED technology by using laser-integrated LED systems. One such example of LED Laser hybrid system is the POWER LED 300 (Karl Storz). It is claimed that this technology can deliver up to twice the light intensity of conventional LED light sources to the operative field.

Portability has recently become one of the desired features in light source technology. Recently, Cook Medical (Bloomington, IN, USA) have introduced a rechargeable, portable LED light source (VueLite® LED Light Source). This device is lightweight (approx. 85 g), small (90 mm in length), and powered by a rechargeable lithium-ion

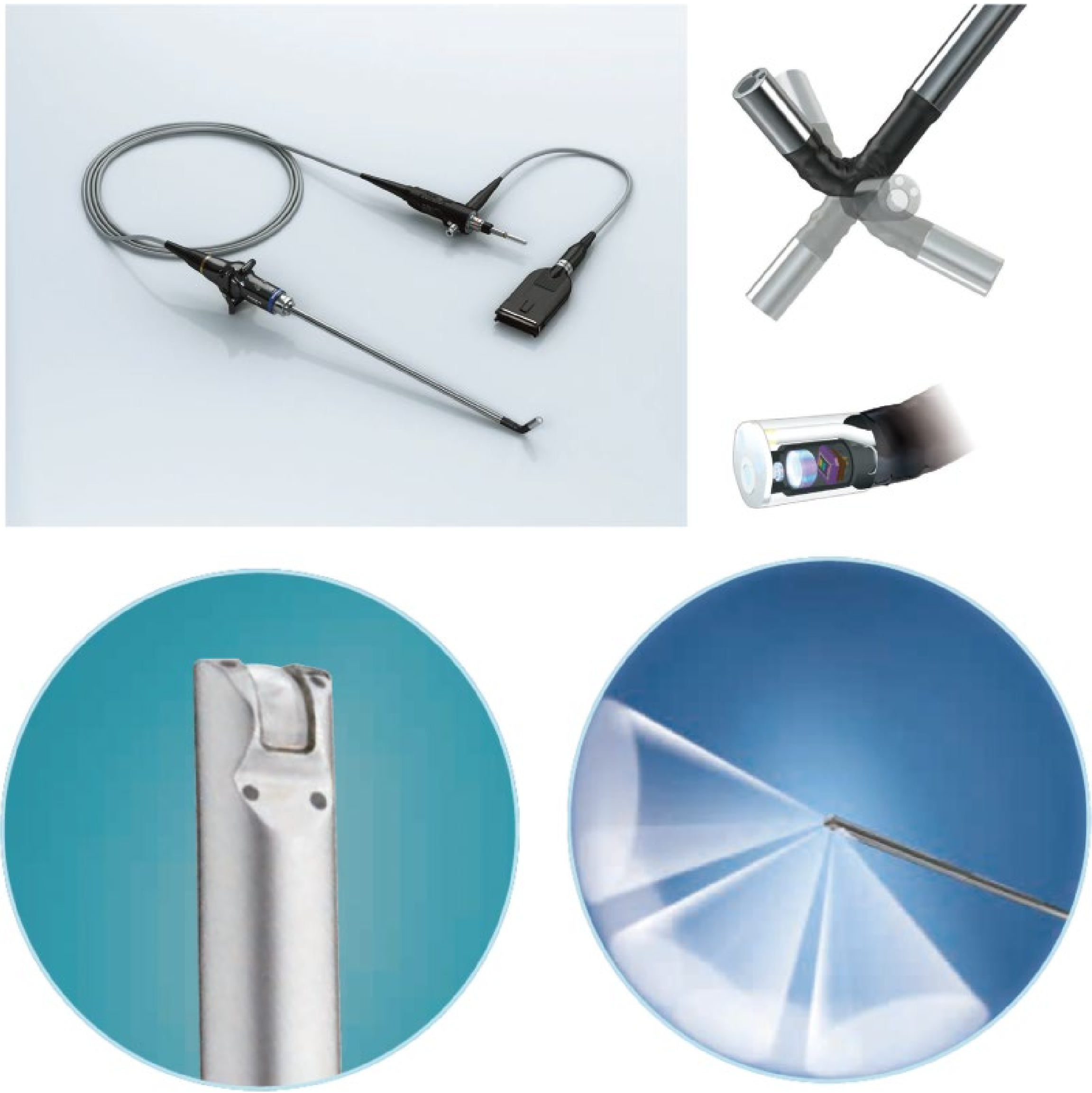


**Figure 3.9** Advances in laparoscopy. Top: ENDOEYE FLEX 2D-3D digital laparoscope with 100° articulating tip and multi-CCD chip technology (Olympus). Bottom: EndoCAMeleon telescope lens that can be adjusted in five steps from 15 to 90°. Reproduced with permission of Karl Storz GmbH.

(Li-ion) battery. It has an adjustable light intensity that, on a full 2 hour charge, can provide up to 2 hours of light for endoscopic procedures. The lifetime of the LED is around 1 million hours [59].

## Video system setup

### Video cart

An essential part of any video system should be the video cart. This cart is an integral component for the entire system, which allows one to easily transport the video documentation system from one surgical suite to another. The video cart should have room to hold the video camera electronics, the light source, and various recording devices such as a hard copy printer or digital recorder (Figure 3.10). Moreover, some video carts will also have room to hold the laparoscopic insufflator as well as electrocautery units. One should be able to adequately secure the cart during storage to prevent equipment loss. Finally, ensure that the video cart has the capability to hold $CO_2$ tanks which will be needed during laparoscopic procedures.

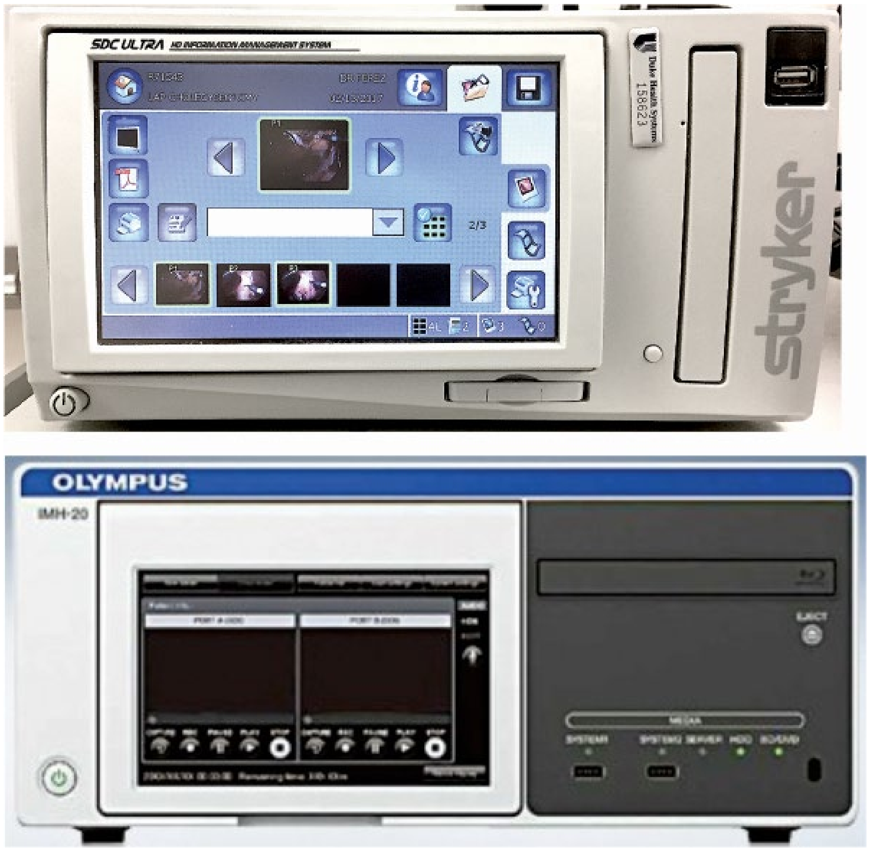


**Figure 3.10** Touch-screen, image processing, and documentation systems. They offer direct capture of high-quality still images and surgical videos on a variety of digital storage media (USB storage drives, internal hard drives, and DVD or Blu-ray discs). Top: SDC Ultra (Stryker). Bottom: IMH-20. Reproduced with permission of Olympus.

### Video setup

Traditionally, our standard operating room setup places the video cart, which contains a video camera and recorder, television monitor, and xenon light source, directly across from the operating surgeon. In addition, a second high-resolution video monitor will be placed on the other side of the table to be used by the assistants. If only one video monitor is available, it should be placed directly at the end of the operating table. All endoscopic procedures in our endoscopy suite and operating rooms are performed entirely off the video monitor(s).

With the advent of newer operating room designs, the fundamental differences between open and endoscopic or laparoscopic surgery have been recognized. Whereas in the past endoscopists and laparoscopists relied upon mobile carts traveling from room to room, today specialized rooms provide dedicated carbon dioxide lines, preventing the need to change tanks in mid-operation. Another issue relating to suboptimal operating room design is the effect of imperfect ergonomics on surgeon comfort from a musculoskeletal standpoint. Many recent studies have demonstrated significant stressors to the surgeon induced by laparoscopy. Many of these stressors are related to monitor placement, camera holding, trocar placement, and table position and height [60–63]. Operating room enhancements, such as ceiling mounted monitors and designs focused on the endoscopic and laparoscopic surgeons, allow for versatility in the ergonomics surrounding minimally invasive urologic procedures (Figures 3.11 and 3.12). Whether or not these specially designed operating rooms reduce musculoskeletal complications in surgeons has yet to be determined, but some studies indicate that this is in fact the case and that overall operating room efficiency is improved as well [64, 65]. A novel addition to the operating room of the future may incorporate high-resolution binocular face-mounted devices such as has been explored at the bench level, thus providing less surgeon neck/back strain and improved visualization and satisfaction compared to conventional standard video monitors [66].

## Future directions of endoscopic video systems

3D video systems as well as HD have been introduced to significantly improve visualization during minimally invasive surgical procedures. In addition, augmented reality techniques have been developed, which allow enhanced image processing of videoendoscopic procedures as well

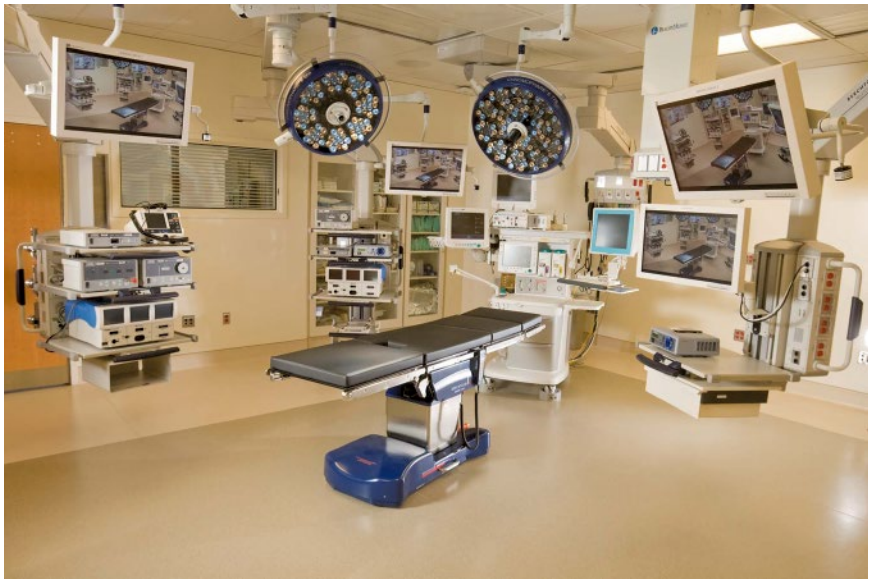


**Figure 3.11** Current operating room with HDTV monitors.

as the development of surgical simulations to aid in training of complex surgical maneuvers. The following sections will review these enhanced imaging technologies for endoscopic surgery.

## 3D video imaging

3D video imaging enhances the ability to perform delicate endoscopic maneuvers, such as dissection or precise suturing [67]. Moreover, those who are observing have a better understanding of the surgical anatomy because of the 3D image.

### Principles of 3D stereoendoscopy

In normal human vision, depth perception is a factor taken for granted. Normally, the eyes will accommodate and converge in such a way that there is intersection of the visual axes of both eyes. This intersection is known as the point of fixation. When viewed by both eyes, lateral disparity causes the viewed object to be projected in slightly different orientations on the retina of the right and left eyes. The human brain interprets this disparity on a small region of the retinal fovea (called Panum's region) as depth information. The brain then fuses these images to give the perception of depth, and this effect is called stereopsis [68].

Accommodation is the ability of the human eyes to clearly visualize objects which are both near and farther away. The eyes converge, and the lens increases its dioptic strength so that the object is brought into sharp focus on the retina. The nearest an object can be to the eye and still be in focus is called the near point, while the farthest it can still be in focus is called the far point. The region of depth is the area between the near and far points. This ability to accommodate is preserved when viewing objects with a 3D video system.

To mimic normal 3D vision, a 3D video system must therefore convey separate off-set images to each eye. The figure is captured in a slightly different orientation by the stereoendoscope and after image processing by the brain, it appears as a 3D object. Any 3D video system must therefore incorporate the principles of stereopsis [68, 69]. One potential limiting factor of 3D endoscopic systems is that the normal interpupillary distance for human vision is approximately 60 mm, while the maximum separation of two objective lenses in a standard 10 mm endoscope is approximately 8 mm. Various endoscopic designs, however, have accounted for this disparity, still allowing for adequate capture and display of 3D images.

### Stereoendoscopic image processing

Most of the 3D stereoendoscopic video systems currently available have four basic principles of stereoendoscopic image processing in common: image capture, conversion of 60 Hz to 120 Hz images, presentation of left and right images on a single monitor, and separation of the left- and right-eye images [70]. While the components of the various 3D video systems may differ slightly, they each contain the same basic principles.

### 3D display

The 3D conversion system will sequentially display the left- and right-eye images on the 120 Hz 3D video monitor. However, in order to view the left- and right-eye images on a single monitor, the images must be separated. One method involves "active" liquid crystal display (LCD) shutter glasses. These glasses are synchronized by an infrared emitter which is located on top of the video monitor. As the left-eye image is projected on the video screen, the emitter will control the shutter glasses so that

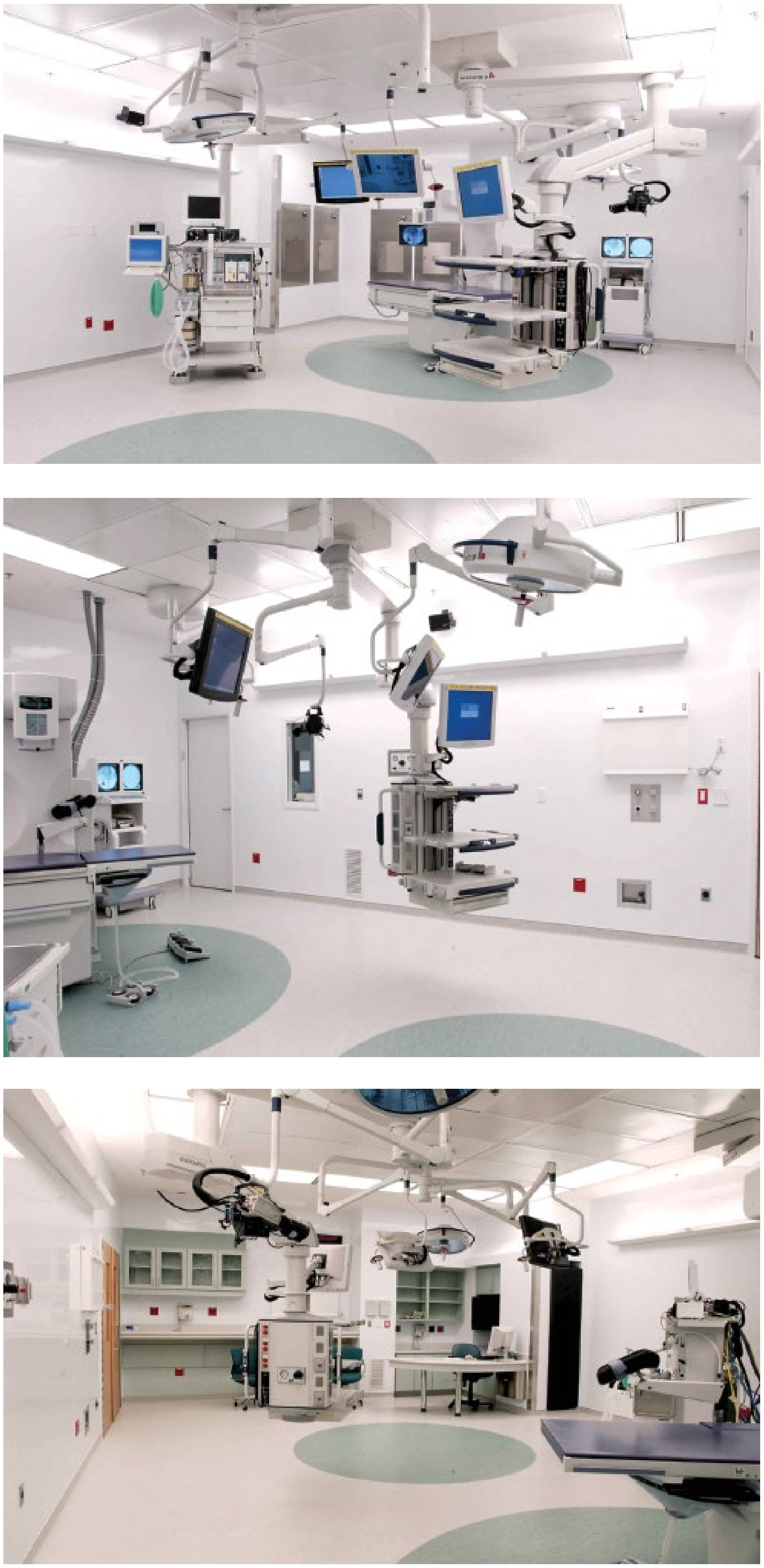


**Figure 3.12** Current operating room with HDTV monitors.

the right eye is closed and left eye open. Alternatively, when the right eye is open, the left side of the LCD glasses is blackened and the right eye image appears on the video screen. The advantage of this active system is that more light is projected to each eye and therefore the 3D image appears brighter. However, the active LCD shutter glasses require a battery, are somewhat heavy, and quite expensive.

Alternatively, "passive" polarized glasses may be worn to view the left- and right-eye images from the single video monitor [71]. This type of system requires a special polarizing filter on the video screen which will "rotate" the left- and right-eye images in different orientations thereby allowing simultaneous viewing of the left and right images. The passive polarized glasses have the advantage of significantly cheaper cost than the active LCD shutter glasses and are more comfortable to wear, but the polarizing glasses present a slightly darker 3D image than the active glasses.

An alternative to dual projection is the presentation of the two images independently to the left and right eye, much like looking through field binoculars. The images can be displayed on small screens set at the focal distance for the surgeon and mounted on an ergonomic headset [72]. This technology is currently available as part of the da Vinci robotic system [73].

#### Advantages of 3D videoendoscopy

The increased depth of field afforded by 3D endoscopic video systems facilitates intricate minimally invasive surgical procedures [74, 75]. Addition of a third dimension allows better recognition of tissue layers and may facilitate complex maneuvers such as laparoscopic suturing or knot tying [57, 76]. Indeed, skill tests performed assessing laparoscopic suturing and knot tying have demonstrated a 25% increase in speed and accuracy of these laparoscopic tasks when utilizing a 3D video system as compared to a standard two-dimensional (2D) endoscopic video system [77]. Some investigations claim that 3D video systems only facilitate surgical tasks in inexperienced laparoscopic surgeons. It appears that the reduction in time required to perform various minimally invasive surgical procedures may not be as dramatic in those individuals who have a large amount of experience with standard 2D video systems during endoscopic surgery [72]. Some studies suggest that a higher-resolution video system might be more advantageous than having 3D endoscopic imaging [78–80]. The major current use of 3D imaging systems is during robotic, more than laparoscopic, surgical procedures to allow for true stereoscopic imaging [81–83].

#### Limitations of 3D imaging systems

Late-model 3D videoendoscopic systems compared with initial 3D components provide greatly improved 3D viewing of minimally invasive surgical procedures. Yet, they still provide reduced resolution and lower-light images as compared to standard single-chip or three-chip 2D video camers. The decrease in image brightness and resolution is due to the fact that most 3D video systems use two optical channels which are significantly smaller than a single-lens system in a standard 10 mm laparoscope. Moreover, since most 3D video systems incorporate two separate camera systems, the camera head is significantly larger than a single-camera system and, therefore, more cumbersome to work with during minimally invasive surgical procedures.

Cost continues to be a limitation of 3D videoendoscopy. Most 3D video systems are two to three times more expensive than standard 2D endoscopic video cameras. While 3D video imaging systems are more costly than conventional 2D video equipment, the enhanced depth perception produced by 3D endoscopes has been demonstrated to improve the performance of minimally invasive surgical procedures [84, 85]. 3D imaging also facilitates the training of minimally invasive surgery and may lessen the learning curve of these technically demanding procedures [86]. It is anticipated that 3D video imaging may improve the performance of current endoscopic procedures as well as facilitate the development of more advanced, minimally invasive surgical techniques [67].

### Image-guided surgery

Image-guided surgery (IGS), computer-assisted surgery (CAS), or augmented reality (AR) involve the integration of preoperative radiologic imaging with real-time intraoperative surgical views (Figure 3.13). It allows the surgeon to "see" subsurface information which is inaccessible through ordinary endoscopic imaging. Augmented reality and imaged guided surgery have many potential advantages to conventional endoscopic surgery. AR has the potential to replace the loss of haptic feedback in robotic and laparoscopic surgery by allowing surgeons to see anatomic and spatial relationships that are not obviously apparent through standard or 3D views. In addition, AR and IGS have the potential to predict surgical results beforehand [87]. These features have the potential to minimize the loss of healthy tissue while maximizing oncological efficacy.

Various techniques have been described for the implementation of IGS and AR. Real-time virtual sonography (RVS) has been described, allowing synchronization of preoperative computed tomography (CT) or magnetic resonance imaging (MRI) images with intraoperative real-time ultrasound images [88, 89]. The system displays the real-time ultrasound image and the corresponding image of a 3D reconstructed CT or MRI. This technology is especially useful for percutaneous ablative procedures for the kidney or prostate.

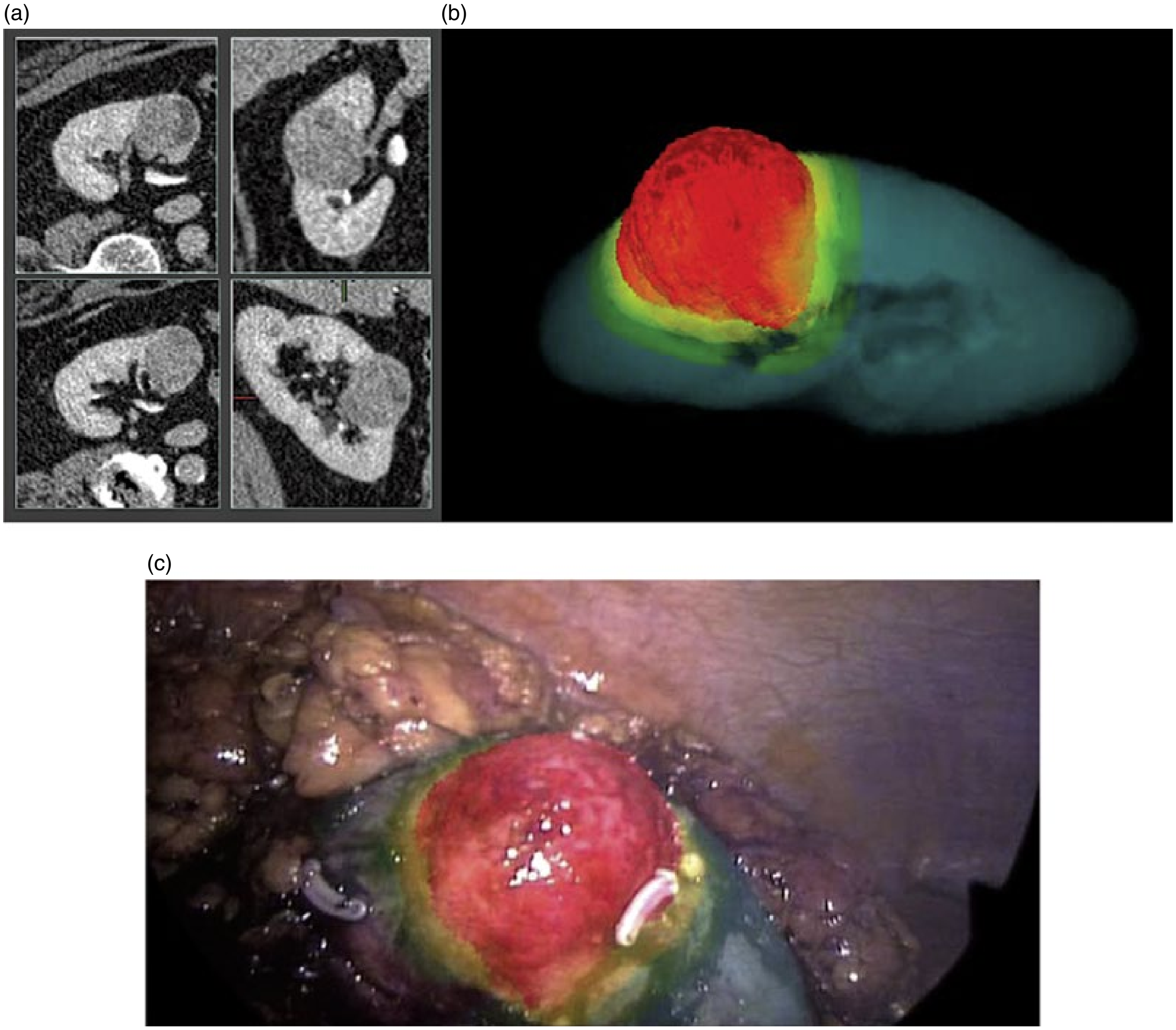


**Figure 3.13** Example of augmented reality navigation during laparoscopic partial nephrectomy. (a) Original CT images. (b) Four-color coded surgical model. (c) Augmented-reality image is superimposed onto the real-time surgical view. Reproduced with permission of Elsevier.

Other investigators have reported on the use of AR for laparoscopic partial nephrectomy [89]. They utilized an optical tracking system for their surgical instruments combined with a computer workstation to overlay preoperative 3D reconstructed images onto their surgical view. For laparoscopic partial nephrectomies, the images were displayed with colored zones corresponding with the tumor and various margins. Other techniques have been described for coordinating the preoperative images to the intraoperative view. One system placed navigation in the target organ for better localization and to account for organ movement [90]. This technique has been coined as the “inside-out tracking system.” The tracking system was able to overlay images onto the operative field with a 0.5 mm error margin.

Recently, Rassweiler et al. reported the use of marker-based navigation technique to obtain percutaneous access to the kidney for urinary stone treatments [91]. They used an iPad (Apple Inc., Cupertino, CA, USA) as a wireless video output source and, simultaneously, as the computer and display device to show enhanced virtual reality of the patient’s anatomy. Although interesting, the application of this technique in clinical practice has not been widely adopted yet.

AR has also been applied to robotic-assisted laparoscopic partial nephrectomy [92]. The system allows overlay of 3D models constructed from preoperative CT scans onto the 3D intraoperative video recordings. The advantage of this system is it did not require external tracking devices. Another model for AR utilized the da Vinci robot system as a single localizer [93]. This system demonstrated decreased removal of benign tissue in an *in vitro* model.

All of these systems currently allow for 3D reconstructed, preoperative images to be displayed onto real-time endoscopic surgical views. The major limitation is accounting for organ motion and deformity. The future of AR and IGS is predictive surgical navigation. Ukimura and Gill described surgical radar and surgical body-GPS [88]. Surgical radar involves displaying color-coded zones over the real-time image of an intended surgical target. The trajectory of an instrument, endoscopic scissors for example, can be used to predict whether the current path of that instrument will violate an undesirable structure, such as a tumor. Surgical body-GPS allows for monitoring of real-time organ position. The surgeon can be alerted to how real-time movement of the organ alters the line of excision for an intended target. The aim of this technology is to maximize normal tissue preservation and oncological efficacy.

## Conclusions

The application of video technology to endoscopic procedures provides several advantages in both the teaching and private practice settings not previously available to the urologist. Improved magnification and image quality facilitates performance of the procedure by the surgeon, as well as coordination of the assistants and ancillary personnel to provide a smoother, safer, and potentially shorter operation. Video monitoring facilitates teaching both during and after the procedure, as well as provides preoperative patient education. Moreover, videoendoscopic procedures also increase the safety of the procedure for the operating urologist.

As newer technologies, such as HDTV and 3D videoendoscopy, become more widespread, an increasing number of videoendoscopic procedures will be performed. The dissemination of the surgical skills needed to perform these surgical procedures is becoming increasingly important. Technologies such as augmented reality simulation and telementoring may become commonplace in the near future for the training of future urologists. These technologies allow for more rapid acquisition of skills necessary to perform complex endourological and laparoscopic procedures in a safe environment with reduced risks of adverse events for patients. Future technologies such as image-guided or computer-assisted surgery should only further improve the safety and efficacy of videoendoscopic procedures. With the advent of new technology for video imaging and documentation patient care provided by the endourologist and minimally invasive surgeon should rapidly improve.

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## 4

# Preoperative Antibiotics and Prevention of Sepsis in Urologic Endoscopic Surgery

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## Introduction

Sepsis from a urinary source is one of the most feared complications in urologic practice due to its potential for increased morbidity and mortality after urologic surgery. In this chapter, we will discuss the importance of appropriate preoperative workup, use of adequate antibiotic prophylaxis, as well as intraoperative and postoperative measures to help prevent the development of adverse events related to infection and sepsis.

According to the European Section for Infection in Urology, the prevalence of hospital-acquired infections varies between 3.5 and 9%. The prevalence of hospital-acquired urinary tract infections (HAUTI) was found to be 9.4% over an 8-year period between 2003 and 2010. The most common presentation was asymptomatic bacteriuria in 27%, followed by cystitis in 26%, and pyelonephritis in 20%. Some 10.3% of all cases presented as urosepsis [1]. Among those patients with nosocomial urinary tract infections (UTIs), almost 80% had a prior history of urologic surgery; endourologic procedures had been undergone in 50%, open or laparoscopic surgery in 45%, and prostate biopsies in 5% [2]. These data suggest that preventive measures, such as a strict preoperative evaluation and correct antibiotic prophylaxis in surgical patients, must be improved.

The prophylactic use of antibiotics can reduce the risk of surgically related infection. The European Association of Urology (EAU) and American Urological Association (AUA) have both published guidelines for best practice in antibiotic prophylaxis in urologic surgery. The AUA most recently updated their guidelines in 2009 and the EAU in 2014 [3, 4]. These guidelines are extremely helpful to standardize the administration of antibiotics prior to surgery. However, local practice should be based on or adjusted according to local or even hospital microbiologic patterns and requirements, so it is crucial that each center and department reviews regularly its infection patterns and antibiotic resistance.

There is currently no uniformly accepted definition in the literature to delineate infection versus sepsis, which may account for the wide range of incidences reported [5]. After any diagnostic or therapeutic urologic procedure, UTIs can be present as a simple bacteriuria with limited clinical symptoms or they can result in severe sepsis or even septic shock. It is difficult to predict in which patient a serious complication will develop, but several publications describe potential risk factors that can contribute to this scenario. It is crucial to recognize patients at risk of complications with a complete preoperative evaluation to establish a prompt diagnosis and proper treatment in the event of a postoperative infectious complication.

## Pathogenesis of urosepsis

Classically, urosepsis is defined as a sepsis caused by UTI; this occurs in 7–25% of all septic cases [6]. An infectious complication is triggered during urologic surgery when urinary bacteria and their products enter the bloodstream via a vascular, lymphatic, or urothelial disruption. Manipulation of infected urine or infection stones with an increase in pressure mainly in the collecting system causes an intense liberation of bacteria and endotoxins via direct absorption, pyelovenous–lymphatic or pyelotubular backflow, and forniceal rupture, triggering a systemic inflammatory response [7].

There is a neurohumoral generalized pro- and anti-inflammatory response. This begins with cellular activation of monocytes, macrophages, and neutrophils that interact with endothelial cells through numerous

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pathogen-recognition receptors [8]. A further host response includes the mobilization of plasma substances, such as tumor necrosis factor (TNF), interleukins (ILs), caspases, proteases, leukotrienes, kinins, reactive oxygen species, nitric oxide, arachidonic acid, platelet activating factor, and eicosanoids. TNF-α and IL-1 are the most important proinflammatory cytokines and exhibit similar biologic properties. They influence the temperature regulatory centers in the hypothalamus, resulting in fever. They also have an effect on the formation reticularis in the brainstem, which renders the patient somnolent and comatose. Release of corticotropin in the pituitary gland is increased, which stimulates the adrenal gland. These factors also stimulate hematopoietic growth factors, which leads to the formation of new neutrophils and the release of stored ones. The neutrophils are additionally activated and produce bactericidal substances, such as proteases and oxygen radicals. B and T lymphocytes are stimulated for the synthesis of antibodies and cellular immune reaction. In the continuing septic process, however, apoptosis of B cells, CD4 helper cells, and follicular dendritic cells causes an anti-inflammatory immune suppression, called transient immune paralysis [9].

Activation of the complement and coagulation cascades further amplifies this chain of events. There is microvascular injury, thrombosis, and loss of endothelial integrity (capillary leak), resulting in tissue ischemia. This diffuse endothelial disruption is responsible for the multiple organ dysfunction and global tissue hypoxia that accompany severe sepsis/septic shock [10].

## Bacteriology of urinary infections and sepsis

The pathogens associated with UTIs and urosepsis have not varied greatly over the last decades and concern centers around the considerable changes in resistance patterns [1]. A continuous assessment of local patterns is important to establish the most appropriate antibiotic regimens to prevent infectious complications most efficaciously. *Escherichia coli* remains the single most common microorganism to cause urinary infection. This is followed by *Klebsiella* and *Pseudomonas*, frequently associated with stone disease. Furthermore, the increasing presence of Gram-positive bacteria such as *Enterococcus* and *Staphylococcus* should be noted [1].

DasGupta et al. reported that 40% of urology inpatients had Gram-positive organisms, with *Enterococcus* accounting for 27% [11]. Several reports have shown that other organisms have increased not only their incidence, but also their resistance to antibiotics commonly used in urology, including trimethoprim, quinolones, cephalosporins, and aminoglucosides, such as gentamicin; this is the case for *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* [12], *Serratia* spp., and *Clostridium difficile.* Many common antibiotics once prescribed for uncomplicated urinary infection such as ciprofloxacin and trimethoprim now have high resistance rates. The rates of resistance from 2000 to 2008 to ciprofloxacin rose in Germany (2 to 21%), Spain (15 to 31%), Sweden (0 to 7%), and the UK (1 to 15%), as well as to trimethoprim in Germany (23 to 37%), Spain (25 to 37%), Sweden (9 to 17%), and the UK (13 to 46%) [13]. This rise in resistance of urinary pathogens towards quinolones has been reported worldwide and might be the consequence of its overuse due to its efficacy in treating other infections and uncomplicated UTIs, as well as its misuse as prophylaxis in some urologic diagnostic procedures. In cases of urosepsis, resistance to commonly prescribed antibiotics was high and rates ranged from 8% (imipenem) to 62% (aminopenicillin/β-lactamase inhibitors); 45% of Enterobacteriaceae and 21% of *P. aeruginosa* were multidrug-resistant [14].

## General measures of sepsis prevention in genitourinary surgical patients

In recent years, the incidence of sepsis has increased, but the associated mortality has decreased, suggesting improved management of patients [15]. Besides correct management, the role of prevention is of great importance and it is imperative to identify preoperative risk factors, apply adequate prophylaxis, and try to minimize intraoperative risks, in order to reduce the incidence of septic episodes or allow early recognition of the features that can lead to one.

The EAU in its Guidelines on Urological Infections recommends the following basic preventive measures of proven efficacy in any urologic patient undergoing surgery [4]:

- Isolation of all patients infected with multiresistant organisms to avoid cross-infection.
- Prudent use of antimicrobial agents, both in prophylaxis and in treatment of established infections, to avoid selection of resistant strains. Antibiotic agents should be chosen according to the predominant pathogens at a given site of infection in the hospital environment.
- Reduction in hospital stay. It is well known that long inpatient stays prior to surgery lead to a greater incidence of nosocomial infections.
- Early removal of indwelling urethral catheters, as soon as allowed by the patient's condition.
- Nosocomial UTIs are promoted by bladder catheterization as well as by ureteral stenting.

- Antibiotic prophylaxis does not prevent stent colonization, which appears in 100% of patients with a permanent ureteral stent and in 70% of those temporarily stented.
- Use of closed catheter drainage and minimization of breaks in the integrity of the system.
- Use of the least-invasive method to release urinary tract obstruction until the patient is stabilized.
- Attention to simple everyday techniques to ensure asepsis, including the routine use of protective, disposable gloves, frequent hand disinfection, and infectious disease control measures to prevent cross-infections.

## Preoperative evaluation

All patients who are being considered for genitourinary surgery should be evaluated with a complete medical history, physical examination, and laboratory tests, including an obligatory urine culture; this will identify those patients with a high risk for development of an infectious complication [16].

### Risk factors for infectious complication

There are well-recognized risk factors that for academic purposes can be categorized under the following headings (Table 4.1).

#### *Related to the patient*

There are several patient characteristics known to increase the risk of infectious complication after surgery. These include patients who are immunosuppressed secondary to diverse causes, among others; those with malignant or autoimmune diseases receiving chemotherapy or chronic use of corticosteroids usually have impaired infection resistance. Also patients of advanced age or poor nutritional status, with diabetes, obesity, significant kidney or liver diseases, and female patients have a higher risk [6]. Other related factors are the presence of a coexistent infection at another site at the time of surgery or prolonged hospitalization.

#### *Related to urinary tract diseases*

Urinary diseases or their management increase the possibility of colonization and chronic bacteriuria. Risk factors in urologic patients are anatomic anomalies, voiding dysfunction, urinary diversion, active UTI, obstruction of the urinary tract, stone disease, indwelling catheters, and endogenous material, such as ureteral stents and nephrostomy tubes.

Many of these patients will have a positive urine culture and must receive preoperative antibiotics appropriately tailored to culture-specific organisms; at the end of treatment urinary evaluation must be repeated. Rao et al. reported that bacteriuria and pyuria are risk factors for bacteremia; they also found that preoperative bacteriuria had a positive predictive value (PPV) of 0.53 for detection of endotoxemia, another important risk factor for the development of urosepsis [17].

#### *Related to procedure*

Any procedure performed in patients with urolithiasis has a potential risk for postoperative infection due to bacterial colonization of the urinary tract, infection stones, or urinary drainage obstruction and indwelling catheters. Prolonged surgical time, high intrapelvic pressures during endourologic procedures, such as percutaneous or retrograde renal surgeries, and bleeding during procedure carry a high risk of postoperative infection. Open or laparoscopic surgeries, which involve the gastrointestinal or genital tract, such as urinary diversions or vesicovaginal fistula repair, also should be considered high-risk procedures for infection.

These factors frequently act in an additive manner, compounding their impact. The likelihood of bacterial invasion is also affected by the amount of bacteria at the site of the surgical procedure. All procedures invading the urinary tract are considered "clean–contaminated." The likelihood of bacterial invasion is increased if bacteriuria is present or adequate wound preparation and surgical techniques are not employed [9].

**Table 4.1** Risk factors associated with postoperative infectious complications in genitourinary surgery.

| Related to patient | Related to urinary tract diseases | Related to procedure |
|---|---|---|
| Immunosuppression | Chronic bacteriuria | Stone disease management |
| Malignancy | Voiding dysfunction | Incisional therapy |
| Autoimmune diseases | Urinary diversion | Surgery of long duration |
| Chronic corticosteroid use | Obstruction | Involvement of genital tract |
| Diabetes mellitus | Stone disease | Involvement of gastrointestinal tract |
| Poor nutritional status | Indwelling catheters | Prosthesis |
| Severe kidney or liver dysfunction | Endogenous material (ureteral stents) | |
| Advanced age | Anatomic anomalies | |
| Female | Impaired urinary flow | |
| Distant coexistent infection | | |
| Prolonged hospitalization | | |

## Antibiotic prophylaxis

Prophylaxis means a brief course of antibiotics administered before or at the start of an intervention, and is used to minimize the infectious complications resulting from diagnostic and therapeutic interventions. While the rationale for the use of antibiotics is well accepted, possible side effects and development of antimicrobial resistance patterns are potential risks. Therefore, an antibiotic prophylaxis policy should be well considered and based on high levels of evidence [18].

Surgical antimicrobial prophylaxis is recommended only when the potential benefit exceeds the risks and anticipated costs; it has been demonstrated in a variety of settings that surgical antimicrobial prophylaxis, by reducing the incidence of surgical site infections, reduces costs. Conversely, excess and/or inappropriate antimicrobial prophylaxis increases costs, which is reversed by measures to improve compliance with evidence-based recommendations [19]. A multicenter study looked a the rate of antibiotic resistance, daily antibiotic dose, and cost after implementation of antibiotic guidelines. The rate of resistance of *E. coli* to piperacillin/tazobactam (9.1 vs. 5.4%), gentamicin (18.3 vs. 11.2%), and ciprofloxacin (32.3 vs. 19.1%) decreased significantly after guideline introduction. The defined daily dose (DDD) use of ciprofloxacin fell from 4.2 to 0.2 DDD per 100 patient days after implementation, and antibiotic drug costs (€76 980 vs. €36 700) and costs related to postoperative infections (€45 870 vs. €29 560) decreased following introduction of the guideline [20].

In considering prophylactic treatment, the surgical site and the properties of the antimicrobial agent should be taken into account. The agent should achieve serum and tissue levels that exceed the minimum inhibitory concentration for organisms characteristic of the operative site. Furthermore, the optimal agent should have a long half-life so as to maintain sufficient serum and tissue concentrations for the duration of the procedure without the need for redosing. It should be safe, inexpensive, and unlikely to promote bacterial resistance [3].

For prophylactic antimicrobial administration to be optimally effective, timing and dosing are critical. Infusion of the first dose should begin within 60 minutes of the surgical incision (with the exception of 120 minutes for intravenous fluoroquinolones and vancomycin). Correct dosing is equally important. Some drugs should be adjusted to the patient's body weight. Oral administration is as effective as the intravenous route for antibiotics with sufficient bioavailability. This is recommended for most interventions, when the patient can easily take the drug between 1 and 2 hours before intervention. Additional doses are required intraoperatively if the procedure extends beyond two half-lives of the initial dose [21]. With few exceptions, the published literature suggests that antimicrobial prophylaxis is unnecessary after wound closure or upon termination of an endoscopic procedure; in most cases, antimicrobials should be given in a single dose, or at least discontinued within 24 hours of the end of the procedure [22].

Three circumstances in which a longer duration of antimicrobials is frequently considered include the placement of prosthetic material, the presence of an existing infection, and the manipulation of an indwelling tube [23]. In cases where an existing infection is present, a therapeutic course of antimicrobials should be administered in an attempt to sterilize the field. In the absence of pre-existing bacterial colonization, there is no evidence that prophylaxis should extend beyond 24 hours following a procedure. In cases where prolonged catheterization follows the procedure (e.g. radical prostatectomy), antimicrobial therapy at the time of catheter removal may be therapeutic rather than prophylactic, since colonization has likely occurred. An alternative is to culture the urine 24–48 hours prior to the intended catheter removal, and administer culture-directed therapy. This is not practical in cases of catheterization for only 48–72 hours. An option then is to administer antimicrobial treatment empirically [3].

The use of preoperative antibiotics can reduce the risk of surgically related infection. Table 4.2 summarizes the recommendations for best practice in antibiotic prophylaxis in urologic surgery from the published EAU and AUA guidelines [3, 4].

## Preoperative antibiotics and preventive measures of sepsis in specific procedures

### Transurethral surgery

#### Transurethral resection of prostate

UTIs and other infectious complications can be present in 1–26% of patients treated with transurethral resection of prostate (TURP). Risk factors associated with postoperative bacteriuria are operative time, disconnection of the closed urine drainage system, prolonged postoperative catheterization (≥3 days), and preoperative catheterization (within 1 month prior to surgery) [24, 25]. TURP is the most studied procedure regarding the use of antibiotic prophylaxis. Two large meta-analyses have been published which include 38 and 32 randomized clinical trials respectively, and both concluded that the benefit obtained from antibiotic prophylaxis in TURP is sufficiently well demonstrated [26, 27]. The incidence of bacteriuria is reduced (26 to 9%), as is that for clinical sepsis

**Table 4.2** Recommended antimicrobial prophylaxis in genitourinary surgery and procedures. Data from [3, 4].

| | Indication | | Antibiotic scheme | | | |
|---|---|---|---|---|---|---|
| **Procedure** | **AUA** | **EAU** | **First choice** | **Alternative** | **Duration** | **Remarks** |
| **Diagnostic procedures** | | | | | | |
| Cystography, cystoscopy, ureteroscopy, urodynamics | If risk factors | If risk factors | Fluoroquinolone or 2nd-generation cephalosporin or TMP–SMX | Aminoglycoside ± ampicillin or amoxicillin/clavulanate | ≤24 hours | If urine culture is negative, antimicrobial prophylaxis is not necessary |
| Prostate biopsy | All | All | Fluoroquinolone or TMP–SMX | Aminoglycoside + metronidazole or clindamycin | ≤72 hours | |
| **Endourologic surgery and shock-wave lithotripsy** | | | | | | |
| Shock-wave lithotripsy | All | If risk factors | Fluoroquinolone or TMP–SMX or 2nd/3rd-generation cephalosporin | Aminoglycoside ± ampicillin or amoxicillin/clavulanate | ≤24 hours | Patients with ureteral stent, nephrostomy obstruction and infection stone |
| TURP/TURBT | All | If risk factors | Fluoroquinolone or TMP–SMX or 2nd/3rd-generation cephalosporin or aminopenicillin/BLI | Aminoglycoside + ampicillin or 1st-generation cephalosporin or amoxicillin/clavulanate | ≤24 hours | Consider in large necrotic tumors |
| Ureteroscopy | All | If risk factors | 2nd/3rd-generation cephalosporin or TMP–SMX or aminopenicillin/BLI or fluoroquinolone | Aminoglycoside ± ampicillin or 1st-generation cephalosporin or amoxicillin/clavulanate | ≤24 hours | |
| Percutaneous renal surgery | All | All | 2nd/3rd-generation cephalosporin or TMP–SMX or aminopenicillin/BLI | Ampicillin/sulbactam or fluoroquinolone or 1st-generation cephalosporin | ≤24 hours | Length of short course to be determined, intravenous route suggested |
| **Open or laparoscopic surgery** | | | | | | |
| Clean operations | If risk factor | All | 1st-generation cephalosporin | Clindamycin | Single dose | Consider in high-risk and short postoperative catheter treatment |
| Clean–contaminated opening of urinary tract | All | All | 2nd/3rd-generation cephalosporin or aminoglycoside + metronidazole or aminopenicillin/BLI | Ampicillin/sulbactam<br>Fluoroquinolone | Single perioperative dose | |
| Contaminated (involving bowel) | All | All | 2nd/3rd-generation cephalosporin or aminoglycoside + metronidazole or clindamycin | Ampicillin/sulbactam<br>Ticarcillin/clavulanate<br>Pipercillin/tazobactam<br>Fluoroquinolone | ≤24 hours | For surgery involving the colon, bowel preparation with oral neomycin plus either erythromycin base or metronidazole can be added |
| Implanted prosthetic devices | All | All | Aminoglycoside + 1st/2nd-generation cephalosporin or vancomycin | Ampicillin/sulbactam<br>Ticarcillin/clavulanate<br>Pipercillin/tazobactam | ≤24 hours | |

TURP, transurethral resection of prostate; TURBT, transurethral resection of bladder tumor; TMP–SMX, trimethoprim–sulfamethoxazole; BLI, β-lactamase inhibitor.

### Box 4.1 Key points in prevention of infection/sepsis in transurethral resection of prostate (TURP)/transurethral resection of bladder tumor (TURBT).[a]

1) Identify high-risk patients.
2) Treat any positive preoperative urine cultures.
3) Obtain a preoperative negative urine culture (ideally).[b]
4) Antimicrobial prophylaxis in all cases:[c]
   - maintain closed urinary drainage system
   - avoid prolonged catheterization (>3 days).

[a] Applicable to other transurethral procedures with manipulation.

[b] With chronic bacteriuria or in catheterized patients administer 3–7 days of culture-sensitive antibiotics before surgery.

[c] For TURBT, EAU guidelines recommend antimicrobial prophylaxis only in the presence of risk factors or large and/or necrotic tumors.

(4.4 to 0.7%). Wagenlehner et al., in a large, prospective multicenter study, compared two antibiotics regimens with a control group; they found that the patients receiving antibiotics showed lower levels of bacteriuria compared with controls and demonstrated that the presence of bacteriuria post TURP (CFU $>10^4$/ml) is a risk factor for infectious complications [28]. There was no statistical difference between antibiotic regimens. Bacteriuria is not considered to be an infectious complication but the last study showed that there is a correlation between bacteriuria and the development of infectious complications.

The AUA guidelines recommend the use of antimicrobial prophylaxis in all patients. The suggested antimicrobial prophylaxis is fluoroquinolone or trimethoprim–sulfamethoxazole as antimicrobial of first choice, and alternatively a first- or second-generation cephalosporin, aminoglycosides ± ampicillin or amoxicillin/clavulanate, before the start of TURP and until less than 24 hours postoperatively [3]. The EAU guidelines recommend a very similar antibiotic regimen in all patients other than those at low risk or with a small prostate [4] (Box 4.1).

#### Transurethral resection of bladder tumor

The AUA guidelines recommend the same regimen of antimicrobial prophylaxis mentioned above for TURP in all patients undergoing transurethral resection of bladder tumor (TURBT). In contrast, the EAU guidelines recommend that antimicrobial prophylaxis for TURBT is unnecessary unless the patient has some risk factors for infectious complications, or a large tumor requiring a prolonged resection time, or a necrotic tumor. Scientific evidence supports the recommendation by the EAU in two studies that did not show any difference between antibiotics and placebo in terms of reduction of the rate of bacteriuria [29, 30]. Yokoyama et al., in a prospective, randomized study in patients with no risk factors for complications, corroborated these findings; no differences were found in terms of infectious complications between groups given antibiotics or placebo. The authors concluded that antibiotics might be deferred and only given to patients who develop postoperative infections [31]. In contrast to this, a retrospective review of patients undergoing TURBT looked at factors that lead to unplanned hospital readmission rates. On multivariable analysis, the use of preoperative antibiotics was found to be significant [32]. This finding is likely related to development of hematuria related to UTI but was not specifically elucidated. There is little evidence for any benefit of antibiotic prophylaxis in TURBT. However, antibiotic prophylaxis should be considered in patients with large tumors with a prolonged resection time, and those with risk factors for infection [30, 33, 34].

#### Other transurethral procedures

Other transurethral procedures involving manipulation, like bladder biopsy, laser prostatectomy, and internal uretrotomy, may be similar in terms of tissue trauma, and the AUA guidelines suggest that data regarding TURP and TURBT could be extrapolated to these procedures.

## Management of nephrolithiasis

Although infection or sepsis may occur despite a sterile preprocedure urine culture, every effort should be made to sterilize the urinary tract before instrumentation. Preoperative treatment with culture-specific antibiotics and subsequent documentation of successful treatment is imperative. While having a negative preoperative urine culture is desirable for all endourologic procedures, this is not always possible, mainly because of stone or urinary tract colonization. In these cases, oral culture specific antibiotic therapy should start at least 1 week before the planned procedure or intravenous therapy at least 24 hours prior to the planned procedure.

Patient-related risk factors associated with the development of postoperative infections include:

- immunosuppression secondary to malignancy, or autoimmune diseases
- chemotherapy or chronic use of corticosteroids
- diabetes mellitus
- advanced age, poor nutritional status, obesity
- significant kidney or liver diseases
- female patients
- presence of a coexistent infection at another site at the time of surgery
- prolonged hospitalization.

Whereas urinary tract-related risk factors include:

- anatomic anomalies and voiding dysfunction
- urinary diversion
- presence of obstruction to the urinary tract
- presence of indwelling catheters, ureteral stents, nephrostomy tubes.

### Shock-wave lithotripsy

The use of prophylactic antimicrobial treatment in patients who undergo shock-wave lithotripsy (SWL) is debated in the literature. The AUA Best Practice Policy guidelines on antibiotic prophylaxis recommends preoperative antibiotic prophylaxis for all patients undergoing SWL [3]. This recommendation was based on a 1997 meta-analysis by Pearle and Roehrborn [35] combining data from eight randomized controlled trials. This study found that the post-SWL urinary tract infection rate for the placebo/no-prophylaxis patients was 5.7% (range, 0–28%) compared to 2.1% (range, 0–7.7%) for patients who were given preprocedural prophylaxis. The relative risk of UTI with prophylaxis was 0.45 ($P = 0.0005$).

The EAU based their contemporaneous recommendations [4] on a narrower list of randomized control trials that focused on the effects on antibiotic prophylaxis rather than the treatment itself. Along with follow-up studies they found that the rates of post-SWL symptomatic UTI and asymptomatic bacteriuria were low both with and without prophylaxis [18]. Their ultimate recommendation is against antibiotic prophylaxis prior to SWL in patients without stents or positive urine cultures.

Since the time of the original AUA guideline statement, Lu and colleagues re-examined the available data in their own meta-analysis including nine randomized trials (1364 patients) [36]. Lu showed that antibiotic prophylaxis did not significantly reduce the risk of fever (relative risk [RR] = 0.36, $P = 0.31$) or overall asymptomatic bacteriuria (RR = 0.77, $P = 0.17$). There was a trend toward protection against UTI (RR = 0.54, $P = 0.05$); however, there was no difference in UTI rates for patients with preoperative ureteral stents (RR = 0.85, $P = 0.75$).

Duvdevani et al. has supported the recommendation that antibiotics prophylaxis is only indicated in patients with risk factors such as those listed in Table 4.1 or those undergoing a concomitant urologic procedure at the time of the SWL [37]. Although the rate of bacteremia post-SWL is reported to be as high as 14%, the rate of sepsis is less than 1%, and the use of prophylaxis remains controversial [38]. The key points in prevention are listed in Box 4.2.

Thus in light of the most recent publications, prophylactic antibiotics are recommended only in high-risk stone groups with infected stones, recent instrumentation, nephrostomy tubes, positive urine cultures, and a history of recent UTI or sepsis. In addition, special consideration should be given to certain high-risk patient groups such as those with as advanced age, anatomical anomalies of the urinary tract, poor nutritional status, chronic smokers, chronic steroid users, immunodeficiency, externalized catheters, and prolonged hospitalization. In general, SWL should only be performed if the patient's urine is sterile and when there is no distal obstruction to minimize infective complications. Currently, prophylactic antibiotics should be considered only in high-risk patients.

### Box 4.2 Key points in prevention of infection/sepsis in SWL.

1) Identify risk factors.
2) Rule out active UTI prior to the procedure.
3) Obtain preoperative negative urine culture (ideally).[a]
4) Antimicrobial prophylaxis if one of the following:[b]
   - obstruction
   - presence of an indwelling stent or catheter
   - infection stones
   - periprocedure stone or urologic manipulation (stone mobilization, double-J stent insertion).

---

[a] In bacterial persistence or chronic bacteriuria administer at least 3 days of culture-specific antibiotics before SWL.

[b] AUA guidelines recommends antimicrobial prophylaxis in all cases.

### Ureteroscopy

A 2003 randomized control trial by Knopf et al. which included 113 patients found a single prophylactic oral dose of fluoroquinolone prior to ureteroscopy reduced the incidence of postoperative bacteriuria (1.8% vs. 12.5%, $P = 0.02$) [39]. There were, however, no incidences of symptomatic UTI. This study guided the AUA Best Practice Policy in recommending antibiotic prophylaxis prior to ureteroscopy for the management of stone disease [3]. The guideline committee states that the potential risk of bacteriuria is 30% and UTI ranges from 4 to 25% without prophylaxis. Practice studies have shown that there is no difference in efficacy between oral fluoroquinolone and intravenous cefazolin [40].

With regard to postoperative prophylaxis for patients with stents, Ramaswamy and Shah retrospectively reviewed their experience between two groups that had received different post-procedural prophylaxis [41]. The first group was covered with fluoroquinolones for 1 week post-ureteroscopy until stent removal, while the second group received 3 days of cephalexin immediately prior to ureteral stent removal within 1 week of surgery. They observed no differences in asymptomatic bacteria or symptomatic UTI rates (2% for both groups). Unfortunately, this series did not examine whether any antibiotics were indicated post-ureteroscopy or not.

A Korean group reviewed their experience with infectious complications following ureteroscopy and identified several risk factors [42]. They noted an overall UTI rate of 3.8%. Furthermore, they found hydronephrosis, bacteriuria, and an indwelling ureteral stent or nephrostomy tube was associated with an increased risk of post-procedural fever. Administration of antibiotics after the procedure was not as effective as preprocedural prophylaxis. Martov et al. assessed the CROES database and examined the rate of infection after ureteroscopy [43]. They noted that the overall rate of infection for patients with negative urine culture was only 2.2% and there was no significant difference in infection rates for patients who did not receive prophylactic antibiotics. Current AUA and EAU recommendations for antimicrobial prophylaxis are given in Table 4.2.

As with other endourological procedures, the routine use of antimicrobial prophylaxis for ureteroscopy in patients with a sterile preoperative urine culture is controversial. Assessment of urine for sterility by midstream urine specimen (MUS) culture and sensitivity (C&S) is recommended by most endourologists as an essential prerequisite for endoscopic stone treatment. Nevertheless, MUS cultures do not always correlate with obstructed urine or stones, and sepsis may present in 1% of cases which have a negative MUS culture. Mariappan et al., in a prospective study, cultured MUS, renal pelvic urine, and obstructing ureteric stones from patients who had undergone ureteroscopic lithotripsy [44]. Clinical bacteremia was seen in 19%. Of these, 58.3% developed features of systemic inflammatory response syndrome (SIRS). Blood and stone C&S were positive in 25% of cases and pelvic urine C&S was positive in 66.7%, but none had a positive MUS C&S ($P = 0.04$).

Moreover, there has been increased interest in stone cultures and their increased sensitivity over voided urine in predicting UTI or sepsis. The bulk of the literature has focused on stone cultures in patients undergoing percutaneous nephrolithotomy (PCNL). However, in a recent publication, one group also examined their role in patients undergoing ureteroscopic procedures. Eswara and colleagues retrospectively reviewed their experience with stone cultures in patients undergoing ureteroscopy ($n = 274$) or PCNL ($n = 54$) [45]. They found that while preoperative urine cultures were only positive at some point in 7% of patients, stone cultures were positive in 29%. Their overall sepsis rate was about 3–4% for all patents. In patients with positive stone cultures, the sepsis rate was significantly higher at 8% compared to only 1% in those who had negative stone cultures. Ultimately, urine cultures had a sensitivity of 11% versus 64% in stone cultures and there was a concordance of 64% between the stone culture pathogen and the one causing sepsis compared to only 9% of preoperative urine cultures. Despite the correlation of stone cultures and postoperative infection, their utilization in guiding clinical practice is limited in that it takes several days following the removal of the stone for cultures to results. They are most helpful following the development of UTI to help guide antibiotic choice.

As a consequence of the potential risk for infection from the presence of infected stones, antibiotic prophylaxis is indicated for any ureteroscopic intervention performed for the treatment of urinary tract calculi. Indications for antibiotics are less clear for diagnostic ureteroscopy or treatment of tumors. The risk of infection and sepsis, albeit low (3.4 and 0.3–2%, respectively), outweighs the potential benefits, such as cost savings, that may be associated with no antibiotic administration for therapeutic proposes [46].

Modifiable intraoperative factors may influence infectious complications (Box 4.3). During ureteroscopy, the hydrostatic pressure generated by the irrigation fluid results in bacterial and endotoxin translocation into the systemic circulation; therefore, a low-pressure irrigation system can reduce the incidence of systemic infection. Only enough irrigation to maintain adequate visibility should be used, and renal pressure should be kept as low as possible with the use of a ureteral access sheath (UAS) or angiographic catheter, or periodic drainage of the collecting system through the ureteroscope. In addition, continuous or intermittent bladder drainage with a small-caliber bladder catheter will help maintain low intrarenal pressures during ureteroscopy [46]. Auge et al. found that by using a UAS during ureteroscopic stone surgery, pressures in the urinary tract could be significantly reduced. Flexible ureteroscopy was performed with and without the aid of the UAS while pressures were measured via the nephrostomy tube connected to a pressure transducer. With the ureteroscope positioned in the distal ureter, the mean intrarenal pressure without the UAS was 60 compared with 15 mmHg with the UAS; with the ureteroscope in the renal pelvis the pressures were 94.4 and 40.6 mmHg, respectively [47].

### Percutaneous renal surgery

PCNL has become the treatment of choice for large and complex (staghorn) stones. The most common composition for staghorn stones is struvite [48], which results from the presence of urea-splitting organisms in the urinary tract. Large non-struvite stones may also harbor bacteria. Additionally, PCNL, while minimally invasive, still traverses through skin, retroperitoneal, and renal tissue to access the urinary tract and stone and utilize large volumes of irrigation relative to ureteroscopy. These factors, taken together, make a strong case for preoperative

### Box 4.3 Key points in prevention of infection/sepsis in therapeutic ureteroscopy.

1) Identify high-risk patients.
2) Treat preoperative positive urine cultures:
   - *never* perform stone manipulation or incision therapy in active UTI
   - relieve urinary obstruction, treat infection, and carry out a staged treatment.
3) Ensure a preoperative negative urine culture (ideally).[a]
4) Antimicrobial prophylaxis in all cases.
5) Maintain low intrarenal pressure during procedure. Options:
   - periodic drainage through ureteroscope or use of ureteral access sheath or angiographic catheter
   - continuous or intermittent bladder drainage.

[a] In chronic bacteriuria administer at least 3 days of culture-sensitive antibiotics before instrumentation.

### Box 4.4 Key points in prevention of infection/sepsis in percutaneous renal surgery.

1) Identify high-risk patients.
2) Treat preoperative positive urine cultures:
   - *never* perform stone manipulation or incision therapy when there is active UTI!
3) Ensure sterile urine preoperatively (ideally).[a]
4) Antimicrobial prophylaxis in all cases.
5) Stop procedure if purulent fluid is obtained at puncture, leave a nephrostomy tube, and stage treatment.[b]
6) Maintain low intrarenal pressure during procedure:
   - use only enough irrigation to maintain adequate visibility
   - use a wide renal access sheath, ideally 4 Fr wider than nephroscope.
7) Limit quantity of irrigation fluid and operative time.

[a] In chronic or asymptomatic bacteriuria administer at least 7 days of culture-sensitive antibiotics before surgery.
[b] Obtain pelvic urine culture and treat infection completely.

antibiotic prophylaxis. It is generally agreed that patients who are scheduled for PCNL must have a negative urine culture before surgery. Unfortunately, this is not always possible to adhere to because of stone or urinary tract colonization; in these patients, appropriate antibiotic therapy should start at least 1 week before the planned procedure (Box 4.4).

The practice of prophylaxis was reinforced by the CROES group, who retrospectively identified 162 patients from multiple institutions who underwent PCNL without preoperative antibiotics and matched them to patients who did receive antibiotics [49]. All patients had negative preoperative urine cultures and matching was based on infectious risk factors such as diabetes, nephrostomy tubes, and staghorn stones. They found that antibiotic prophylaxis led to fewer fevers (2.5 vs. 7.4%) and other complications (1.9 vs. 22%) and higher stone-free rate (86.3 vs. 74%).

Gutierrez et al. assessed 5354 consecutive patients undergoing PNCL from the CROES database between 2007 and 2009 [50]. Some 10.4% of the patients developed a fever: 8.8% of those with negative preoperative cultures, and 18.2% with positive preoperative cultures. In this study, factors found on multivariate analysis to increase the risk of fever included a positive urine culture (adds ratio [OR] 2.12), staghorn calculus (OR 1.59), preoperative nephrostomy (OR 1.61), lower patient age (OR 0.99 for each year), and diabetes (OR 1.38).

Other studies that compared limiting antibiotics to preoperative prophylaxis with continuing until nephrostomy tube removal found no difference in infection-related outcomes [51–53]. Bag and colleagues randomized high-risk patients (stone ≥2.5 cm and/or hydroureteronephrosis) to immediate preoperative antibiotic prophylaxis versus 1 week of nitrofurantoin plus prophylaxis prior to PCNL. The patients who received nitrofurantoin were more likely to have sterile pelvic urine (RR = 4.95) and stone cultures (RR = 3.64), and less likely to have endotoxemia (RR = 0.22) or experience SIRS (RR = 0.31) [54].

The published literature suggests that antimicrobial prophylaxis is unnecessary after wound closure or on termination of an endoscopic procedure, but because PCNL can be associated with a pre-existing infection, infectious stone, or manipulation of an indwelling catheter the subsequent course of antimicrobials that is therapeutic rather than prophylactic might extend beyond 24 hours from the conclusion of the procedure. In the absence of pre-existing bacterial colonization, there is no evidence that prophylaxis should extend beyond 24 hours. Deshmukh et al. [22] studied whether compliance with AUA guidelines for prophylactic antibiotics increased infection rates compared to those who received 5–7 days of antibiotics. No difference was seen in infection rates for those who received prolonged antibiotics versus those who only received ≤24 hours of antibiotics.

In cases where prolonged catheterization follows the procedure (i.e. nephrostomy tube), antimicrobial therapy at the time of catheter removal may be therapeutic rather than prophylactic, because colonization likely has occurred. A recommended antimicrobial regimen is given in Table 4.2.

Results of urine cultures from patients with stones are not predictive of stone bacteriology, especially in those with struvite stones. Therefore, this group should receive broad-spectrum antibiotic therapy that is specific to the cultured bacteria but also likely to be effective against urease-producing organisms residing in the stone. Mariappan et al. demonstrated that stone and pelvic urine cultures obtained during surgery are better predictors of potential urosepsis than bladder MSU [55]; they found that bladder urine cultures were positive in 11.1% of cases versus 35.2 and 20.4% of stone and pelvic urine cultures, respectively. Stone culture showed the greatest positve predictive value (0.7). Infected bladder urine did not always carry identical bacteria to those found in the upper tract. Patients with pelvic or stone positive cultures showed a relative risk for urosepsis at least four times greater than the rest of the cohort. In this study, bladder urine did not predict SIRS. Also, they found that preoperative hydronephrosis and stones larger than 20 mm correlated with positive stone and pelvic urine cultures.

Renal pelvic pressure (RPP) greater than 30 mmHg has also been shown to result in pyelovenous–lymphatic backflow. Troxel and Low, in a prospective study that included 31 patients, found that during PCNL pressures greater than 30 mmHg were recorded in only eight (26%) patients and no association was seen between RPP and postoperative fever [56]. Contrary to this, Zhong et al. demonstrated that mean intrapelvic pressure greater than 20 mmHg and accumulated time of RPP greater than 30 mmHg may cause enough backflow to contribute to bacteremia and postoperative fever [57]. Low RPP during surgery is achieved using an open low-pressure access system, such as operating through an Amplatz sheath (operating instrument 4 Fr sizes smaller than the access sheath). Inflow of irrigant should be at gravity and never pressurized. We also recommend the use of forced diuresis (furosemide 20 mg at the beginning of irrigation and every 60 minutes of surgery and irrigation time) to reduce further the pyelorenal reflux that potentially causes fluid overload and bacteremia. Others factors that have been related to postoperative fever and risk of bacteremia are long operative time, large stone burden, and large amounts of irrigating fluid.

Manipulation of infected stones can cause sepsis due to endotoxemia. McAleer et al. measured endotoxins levels in renal stones and found markedly higher levels in infection stones [58]. Interaction of bacteria with different intracorporeal lithotripters may have antibacterial effects. *In vitro* studies have shown a decrease of bacteria viability after use of intracorporeal lithotripsy and laser [59]. We reported that extracorporeal shock-wave or intracorporeal lithotripsy, using all the alternatives currently available, are significantly effective at reducing the viability of bacteria located inside artificial stone models, including struvite stone models infected with *Proteus mirabilis* [60–62]. Whether this bactericidal effect is desirable is still to be answered, because reduction in the number of bacteria may represent an increase in the presence of proteins/endotoxins liberated from bacterial cell lysis, therefore increasing the risk of urosepsis.

In the presence of an obstruction at the ureteropelvic junction or intrarenal segments (stone, stricture, or tumor), infected urine may be encountered despite previous negative cultures of the voided urine. In such instances, treatment has to be postponed, the urine cultured, and the renal collecting system drained under antibiotic coverage until eradication of the infection is documented. According to Ramsey et al. in a recent evidence-based review [63], the effects on the resolution of infected hydronephrosis are similar if a ureteral stent or a nephrostomy tube is used; nevertheless, Mokhmalji et al., in a prospective randomized study, reported prolonged fever and catheter placement time in the group of patients treated with ureteral stent, and suggest that percutaneous nephrostomy is superior to ureteral stents for diversion of hydronephrosis [64].

Small case series have been reported that explore the possibility of continuing the surgery even if purulent urine is encountered incidentally. Aron et al., in a group of 19 patients, reported no difference regarding the incidence of postoperative fever or sepsis between patients with one-stage versus staged surgery with collecting system drainage and 3–7 days of intravenous antibiotic coverage before a second procedure [65]. Hosseini et al. divided 45 patients into two groups: in group 1 ($n = 29$) stones were removed during the first session and in group 2 ($n = 16$) a nephrostomy tube remained in place and stone removal was accomplished 3–5 days later when results of urine and nephrostomy fluid cultures were negative [66]. They reported no intraoperative or postoperative complications, other than transient fever in 10.3 and 12.5% in groups 1 and 2, respectively. In spite of these recent reports, there are neither sufficient evidence nor well-designed clinical trials to recommend other conduct than performing a staged procedure with drainage and broad-spectrum antibiotic therapy until infection has resolved.

Therefore, these studies suggest that when the preoperative urine culture is negative, a single dose of antibiotics appears to be as effective in preventing postoperative infections as multiple doses irrespective of the type of antibiotic used. A systematic review published in 2008 concluded that in the presence of a negative preoperative culture there was a low evidence of postoperative UTI, suggesting a more favorable outcome after PNL by using antibiotic prophylaxis and that, when prophylaxis was used, there was no advantage for any specific antimicrobial regimen [18].

## Open and laparoscopic urologic surgery

Surgical wound classification into the categories clean, clean–contaminated, contaminated, and dirty seems as relevant to urologic surgery as it is for general surgery [67].

**Clean surgery**

This category involves surgery performed in uninfected tissues without opening of the urinary tract and with primary closure of the wound. Montgomery et al., in a prospective but nonrandomized trial, compared 424 hand-assisted laparoscopic nephrectomies with and without antimicrobial prophylaxis (cephalosporin preoperatively), and found that omission of antibiotic prophylaxis was significantly associated with an increased rate of incision site infections (13 vs. 5.4%) [68]. Steiner et al. randomized a group of 83 patients undergoing open transabdominal radical nephrectomy to a single dose of intravenous third-generation cephalosporin ($n=39$) versus no antimicrobial prophylaxis ($n=44$) and found a significantly lower overall infection rate in the prophylaxis group (7.7 vs. 27.3%) [69]. Togo et al. [70] evaluated 4677 consecutive cases of which 1277 were clean. In the group that received a single dose of prophylactic antibiotic, the rates of surgical site infection, UTI, and remote infection were all 1%.

**Clean–contaminated surgery**

In this category, the urinary tract is entered under controlled conditions and there are no infected tissues or bacteriuria. Surgery involving bowel tissue is also classified as clean–contaminated. According to the EAU guidelines for UTI, prophylactic antibiotics are not recommended for open procedures that do not involve bowel segments, except in patients who are at increased risk of infection, as occurs with long-term urinary drainage. The expected rate of febrile UTI in surgeries that enter the urinary tract is close to 10% without prophylaxis; antimicrobial prophylaxis can be expected to significantly reduce this rate to 2–3% [71]. Regarding the optimal duration of perioperative prophylaxis, one randomized controlled trial confirmed that 1 day of intravenous second-generation cephalosporin was as effective as 4 days of the same agent in the prevention of postoperative infections after radical prostatectomy [72]. Stranne et al. also found in a prospective study that a single dose of antibiotic (a quinolone) given before radical retropubic prostatectomy appears to be sufficient prophylaxis [73]. Togo found the rates of surgical site infection, UTI, and remote infection were 3, 3, and 2% respectively after having received a single dose of prophylactic antibiotic [70].

**Contaminated and dirty surgery**

The contaminated category includes the presence of an untreated infection, including UTI, or the gross spillage of fecal matter. When purulence is present, the surgery is labeled as dirty. In *contaminated* and *dirty* operations, antimicrobial agents are given with a therapeutic intention. Infected urine is a very high risk factor for both surgical site infections in, for example, open prostatectomy, and febrile UTI after TURP. Casey et al. reported an incidence of infectious complication of 20% in patients with chronic bacteriuria undergoing major urologic surgery, and they found that wound infections were as common in patients whose urine cultures revealed multiple unsuspected organisms as in those who were resistant to the perioperative antibiotics [74]. Patients with an indwelling catheter, nephrostomy tube, or other stent device should be considered as having bacteriuria and must be treated in advance (between 3 and 7 days prior to the procedure) in order to favor sterile urine at the time of surgery. The patient should be covered well beyond the intervention (7–10 days or longer), depending on the type of operation and patient factors [75]. Since infectious complications are potentially serious when they involve prosthetic material, antibiotic coverage is advocated irrespective of surgical category [67]. The rates of surgical site infection, UTI, and remote infection were found to be 17, 30, and 10% respectively for clean–contaminated cases in which a single dose prophylactic antibiotic was given [70].

## Use of antibiotics in patients with indwelling catheters, stents, and drainage tubes

The most important risk factor in the development of catheter-associated bacteriuria is the duration of catheterization. Most episodes of short-term catheter-associated bacteriuria are asymptomatic and are caused by a single organism. Multiple organisms tend to be acquired in patients catheterized for more than 30 days. The clinician should be aware of two priorities: the catheter system should remain closed and the length of catheterization should be minimal. While the catheter is in place, systemic antimicrobial treatment of asymptomatic catheter-associated bacteriuria is not recommended, except for some special cases. Routine urine culture in an asymptomatic catheterized patient is also not recommended because treatment is in general not necessary. Antibiotic treatment is recommended only for symptomatic infections [76].

Long-term antibiotic suppressive therapy is not effective in this group of patients. Antibiotic irrigation of the catheter and bladder is also of no advantage. Routine urine cultures are not recommended if the catheter is draining properly. A minority of patients can be managed with the nonreturn (flip) valve catheter, which avoids the need for a closed drainage bag. Such patients may exchange the convenience of on-demand drainage for an increased risk of infection.

Alternatives to indwelling urethral catheters that are less prone to cause symptomatic infection should always be considered. In selected patients, suprapubic catheters, condom drainage systems, and intermittent catheterization are preferable to indwelling urethral catheters [4]. Intermittent catheterization is recommended whenever the patient is able to self-practice this alternative. Prophylactic antimicrobials have not been demonstrated to be beneficial in patients undergoing clean intermittent catheterization [75]. The rate of bacteriuria even in short-term catheterized patients is 5–10% for each day that the catheter is in place [77].

When continuous urinary drainage is required after surgery, perioperative antibacterial prophylaxis is not recommended unless a complicated infection requiring treatment is suspected. Asymptomatic bacteriuria (bacterial colonization) is only to be treated prior to surgery or after removal of the drainage tube. Treatment of a patient at the time of removal of an external urinary catheter should be based on culture-directed antimicrobials. An analysis in the Cochrane Database of Systematic Reviews concluded that there is limited evidence that antimicrobials during the first three postoperative days, or from postoperative day 2 until catheter removal, reduces the rate of bacteriuria and other signs of infection in surgical patients [78].

In patients with indwelling double-J stents, two randomized controlled trials showed that the rate of bacterial colonization depends directly on underlying pathologies, time of stenting, and female sex [79, 80]. Low-dose antibiotics for patients with temporary double-J stents are not recommended and have been shown to increase the risk of acquiring bacterial resistance [81]. Recent advances in stent design have lead to the development of some drug-eluting catheters with the aim of reducing the biofilm and thus the stent colonization. In a rabbit model, triclosan reduced bacterial growth and *P. mirabilis* survival, preventing stent-related UTIs [82]; unfortunately these stents are not commercially available.

## Postoperative sepsis: early identification and initial treatment

Early recognition and management of sepsis optimizes outcome. Therefore, patients in whom this problem is suspected after genitourinary surgery should be prioritized and receive timely care. To diagnose sepsis and severe sepsis/septic shock as early as possible, it is necessary to have clear definitions of infection, organ dysfunction, and global tissue hypoxia, and to recognize the clinical and laboratory findings that are indicative of these conditions.

Sepsis is defined as the presence of SIRS caused by a documented or suspected infection. SIRS is defined as the presence of two or more of the following: (i) temperature greater than 38 °C or less than 36 °C; (ii) heart rate greater than 90 beats/minute; (iii) respiratory rate greater than 20 breaths/minute (or $P_aCO_2 < 32$ torr); and (iv) white blood cell count greater than 12 000/mm$^3$ or greater than 10% immature band forms. Severe sepsis is defined as the presence of sepsis and one or more organ dysfunctions. Organ dysfunction can be defined as acute lung injury, coagulation abnormalities, thrombocytopenia, altered mental status, renal, liver, or cardiac failure; or hypoperfusion with lactic acidosis. Septic shock is defined as the presence of sepsis and refractory hypotension, i.e. systolic blood pressure less than 90 mmHg and unresponsive to a crystalloid fluid challenge of 500 ml.

As mentioned above, clinical and laboratory recognition of septic problems is mandatory. Procalcitonin is a propeptide of calcitonin, but lacks hormonal activity. During generalized infections with systemic manifestations, its level may rise considerably. In contrast, during severe viral infections or inflammatory reactions of noninfectious origin, procalcitonin levels show little or only a moderate increase in levels. Its exact site of production during inflammatory response is still unknown. The documentation of high levels of early biochemical markers, such as procalcitonin and protein C, in the initial postoperative period may help identify a severe inflammatory response to surgical stress from bacteremia, SIRS, or sepsis/septic shock, and prompt the institution of adequate and opportune therapeutic measures [83].

Cytokines are involved in the pathogenesis of sepsis syndrome. They are peptides that regulate the amplitude and duration of the host inflammatory response. They are released from various cells including macrophages, monocytes, and endothelial cells, in response to various infectious stimuli. When they become bound to specific receptors on other cells, cytokines change their behavior in the inflammatory response. The complex balance between pro and anti-inflammatory responses is modified in severe sepsis. An immunosuppressive phase follows the initial proinflammatory mechanism. Other cytokines that are associated with sepsis are interleukins (IL-1, 6, and 8) and TNF-α. Sepsis may indicate an immune system that is severely compromised and unable to eradicate pathogens or a nonregulated and excessive activation of inflammation. The mechanisms of organ failure and death in patients with sepsis remain only partial understood [84].

Appropriate therapy is a continuum of infection management ranging from drainage (maintaining indwelling catheter or opening the nephrostomy tube in cases of percutaneous renal surgery), broad-spectrum antibiotics, aggressive fluid resuscitation, and invasive monitoring with medical management in the intensive care setting until the causative agent is found and eradicated (Figure 4.1).

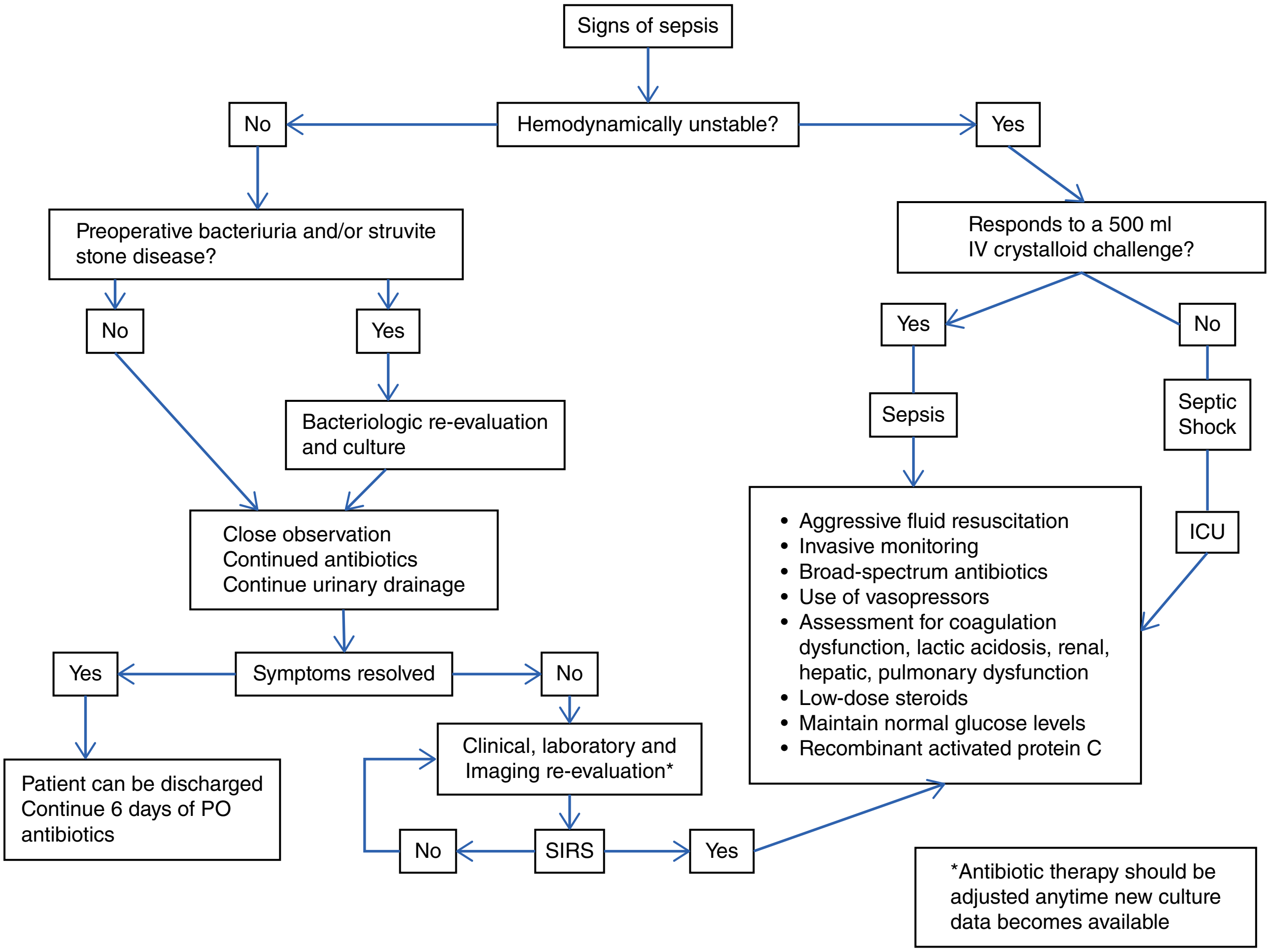
Signs of sepsis
Hemodynamically unstable?
No
Yes
Preoperative bacteriuria and/or struvite stone disease?
No
Yes
Bacteriologic re-evaluation and culture
Close observation
Continued antibiotics
Continue urinary drainage
Symptoms resolved
Yes
No
Patient can be discharged
Continue 6 days of PO antibiotics
Clinical, laboratory and Imaging re-evaluation*
SIRS
No
Yes
Responds to a 500 ml IV crystalloid challenge?
Yes
No
Sepsis
Septic Shock
ICU
• Aggressive fluid resuscitation
• Invasive monitoring
• Broad-spectrum antibiotics
• Use of vasopressors
• Assessment for coagulation dysfunction, lactic acidosis, renal, hepatic, pulmonary dysfunction
• Low-dose steroids
• Maintain normal glucose levels
• Recombinant activated protein C
*Antibiotic therapy should be adjusted anytime new culture data becomes available

**Figure 4.1** Postoperative management of a patient suspected of or diagnosed with sepsis. ICU, intensive care unit; IV, intravenous; PO, *per os*.

Continuous monitoring of vital signs, pulse oximetry, urine output, and initial laboratory testing to assess the severity of global tissue hypoxia and organ dysfunction, including assessment for lactic acidosis, renal and hepatic dysfunction, acute lung injury, and coagulation abnormalities, should be instituted as soon as possible in patients in whom severe sepsis/septic shock is suspected to facilitate the earliest recognition of this condition.

The usual bacteria cultured from urinary sources are aerobic Gram-negative bacilli and enterococci. If patients present with SIRS or sepsis, preoperative cultures should be reassessed to possibly redirect antibiotic therapy. These patients should be recultured with two sets of blood cultures and urine cultures from each drainage tube (including urethral and/or nephrostomy if present). If results are not available, empiric broad-spectrum antibiotics should be initiated as soon as possible to cover the most likely pathogens. Suggested primary regimens include the usage of ampicillin/gentamicin, piperacillin–tazobactam, or carbapenems (doripenem, imipenem, or meropenem); the duration of treatment is determined by the patient's clinical response. It is imperative to modify the antibiotic regimen to a culture directed one as soon as possible.

If severe sepsis/septic shock is recognized, besides empiric antibiotic therapy, prompt treatment in the intensive care unit should include repletion of intravascular volume with large amounts of crystalloid intravenous fluids. If necessary, vasopressors can be administered to maintain blood pressure and ensure adequate tissue perfusion. A central venous catheter can be placed and central venous pressures monitored for goal-directed fluid resuscitation although a Cochrane review demonstrated that invasive pressure monitoring did not change overall mortality rates [85]. Bicarbonate and low-dose steroids may be used and tight blood glucose control maintained. Tight blood glucose control by administration of insulin doses up to 50 U/hour is associated with a reduction in mortality. Multidisciplinary treatment is essential to obtain good results [7, 10, 86].

## Conclusions

Septic complications in genitourinary surgery are a life-threatening scenario that urologists wish to avoid during their practice. To achieve this goal or to minimize the risk of sepsis, a thorough medical history must be performed to identify patient risk factors; it is necessary to assess the appropriate time to perform surgery according to the potential infectious sources and to provide correct preoperative prophylaxis and follow-up. Once an infectious complication is suspected, it is imperative to act fast and accurately in a multidisciplinary fashion to avoid the progression of the natural history of sepsis and to provide a better opportunity for recovery.

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## 5

# Management of the Anticoagulated Patient

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## Introduction

In the early part of the twentieth century, infectious diseases were the most common causes of death across the globe. Technological advances such as improved sanitation and decreased pollution led to dramatic changes such that by the end of the twentieth century chronic, noncommunicable diseases accounted for the greatest number of deaths [1, 2]. Greater longevity can also be attributed to many of these changes. Diminished smoking, declining homicide rates, improved emergency and trauma care, and declining cancer rates have all contributed to the declining mortality rates. As living standards improved, life expectancy continued to increase such that the average life expectancy at birth was 71.4 years for the global population in 2015 [3].

In the United States, the top four causes of death can be attributed to chronic, age-related conditions such as heart disease, cancer, chronic respiratory diseases, and stroke [4, 5]. With an aging population and increasing prevalence of chronic diseases comes an ever increasing burden of complex comorbidities that challenge the physicians managing them with other more acute concurrent illnesses [4, 5]. IMS Health, a market research firm, released global sales data for the most prescribed drugs of 2015. Anticoagulants ranked 11th of the top 20 global therapy areas for pharmaceuticals. Out of top 20 prescribed drugs globally, Xarelto (rivaroxaban), an anticoagulant, was ranked 17th [6].

The increasing prevalence of chronic diseases, especially cardiovascular diseases, translates into increasing use of anticoagulants and antiplatelets and the so-called novel oral anticoagulants (NOACs) in clinical practice. It is not uncommon for surgeons to encounter patients using these agents who need surgical care. Intimate knowledge and mastery of the issues concerning their management in the perioperative setting is imperative. This chapter will articulate the pharmacological mechanisms of action, the indications and clinical applications, and the appropriate interval for interruption and bridging perioperatively. The risks of perioperative bleeding balanced against the risk of thromboembolic events will also be discussed.

## Challenges

It is estimated that there are over 6 million patients in the United States on anticoagulation medication for prevention of thromboembolism, and an ever-increasing number of patients are on dual antiplatelet therapy; 10% of these patients are purported to undergo surgery annually [7, 8]. Discontinuing anitcoagulants or antiplatelets is not without risk. Valve thrombosis carries a 10–20% mortality risk associated with emergency valve replacements. Coronary stent thrombosis carries a greater than 50% mortality in association with a myocardial infarction [9]. Compounding the issues further, hemorrhagic events carry a 9–13% mortality rate; however, long-term permanent disability is rare [5, 10]. For patients who experience a stroke, 20% are fatal while another 50% result in permanent neurological deficit [5]. The goal is balancing the risks of increased bleeding associated with surgery on anticoagulation while minimizing the risk of thromboembolic events.

## Anticoagulants and mechanisms of action

### Heparin

#### Unfractionated heparin

Heparin is supplied in two general formulations. Unfractionated heparin is a heterogenous mixture of

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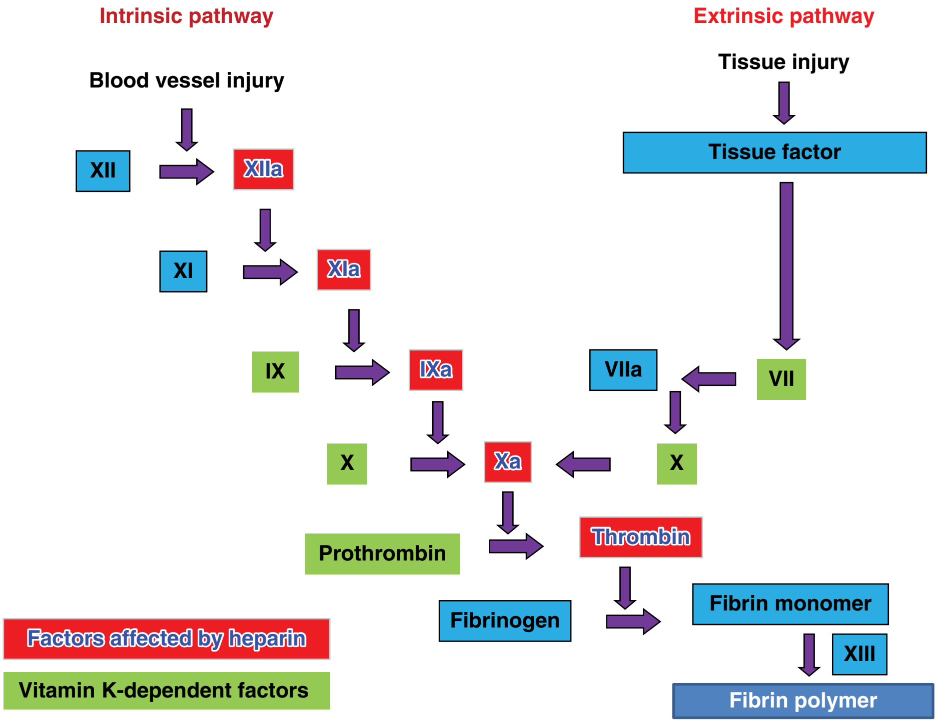

**Figure 5.1** Coagulation cascade.

glycosaminoglycans with varying molecular weights from 3000 to 30 000 Da with a mean of 15 000 Da, one-third of which will be biologically active. Heparin acts by binding to antithrombin and facilitating rapid inactivation of thrombin and factor Xa (Figure 5.1). The complexing of antithrombin and thrombin dissociates heparin and returns it to the circulation. Heparin also acts to inhibit platelet aggregation by its action on inhibition of thrombin [11, 12].

#### Low molecular weight heparin

Low molecular weight heparins (LMWH) are produced from unfractionated heparin by either chemical or enzymatic depolymerization. They have a molecular weight of 2000–10 000 Daltons with a mean of 4000–6500 Daltons. They are composed of mainly short-chain heparin molecules. They are unable to bridge antithrombin and thrombin, and mediate their effects mainly by the inhibition of factor Xa [11, 12].

#### Mechanism of action

Antithrombin has a low level of activity at baseline, mediated by an arginine center that binds to active serine proteases of the coagulation cascade. The bindings of heparin to antithrombin facilitates it inactivation of thrombin and factor Xa. The binding is specific and reversible and does not inactivate heparin. Once antithrombin is complexed with thrombin, the heparin molecule dissociates and returns to the circulation. Heparin also impairs platelet aggregation by directly binding to platelets. The high molecular weight heparins are the molecules thought to be most active in this mechanism. Reversal of heparin is accomplished by withholding the drug. For emergent cases or when supratherapeutic, protamine sulfate is used as a reversal agent [11, 12].

### Warfarin

Warfarin is the most commonly used vitamin K antagonist. It acts via the intrinsic pathway by inhibition of factors II, VII, IX, and X, and proteins C, S, and Z (Figure 5.1). Warfarin is available as an intravenous preparation, but is most administered orally, is water soluble, and rapidly absorbed. It has high bioavailability and reaches maximal serum concentration within 90 minutes of administration. It has a half-life of 36–42 hours. It circulates bound to albumin and other plasma proteins and is eliminated by the liver. Therefore, its activity is highly influenced by drug–drug interactions, diet (particularly foods rich in vitamin K), comorbidities, genetic variability, and diet. After initial administration, there is a period of hypercoagulability as a result of the transient reduction of vitamin K-dependent anticoagulant proteins. Hence, initiation of warfarin therapy is often accompanied by a period of concomitant heparinization with unfractionated or LMWH. The full anticoagulation effect of warfarin may not be seen for 6 days. Frequent prothrombin time and international normalized ratio (PT/INR) monitoring is done until full therapeutic dose is achieved. Warfarin is indicated for the treatment of atrial fibrillation, atrial flutter, venous thromboembolism (VTE) prophylaxis, deep venous thrombosis (DVT), pulmonary embolism, hypercoagulable states, and valvular disease [11, 12]. Reversal of the effect of warfarin is accomplished by withholding the medication. The PT/INR will slowly normalize over a period of 5 days. More rapid reversal can be achieved by oral administration of low-dose vitamin K (2–2.5 mg) as recommended by the guidelines of the American College of Chest Physicians (ACCP) [8]. Administration of fresh frozen plasma may be required also.

## Dabigatran

Dabigatran etexilate is an oral direct factor IIA (thrombin) inhibitor (Figure 5.1). Once ingested, dabigatran etexilate is converted to its active form, dabigatran, a potent, competitive, and reversible direct inhibitor that binds to the active site on thrombin, thereby inactivating both fibrin-bound and unbound thrombin. Plasma levels reach a peak at 1.25–3 hours after ingestion. Therapeutic effect is achieved 2–3 hours after ingestion and it has a half-life of 12–14 hours. Excretion is predominantly renal; therefore, dosing is adjusted according to creatinine clearance. It is not recommended in patients with a creatinine clearance of <15 ml/minute. Discontinuation of dabigatran should be done 24–48 hours before surgery, and preferably 5 days ahead for cases where severe risk of bleeding is expected. Reversal of the action of dabigatran is possible with a newly approved monoclonal antibody antidote, idarucizumab (Praxbind), which directly targets dabigatran and can reverse the anticoagulant effects of dabigatran within minutes of administration [11, 12].

## Rivaroxaban

Rivaroxaban is an oral selective inhibitor of factor Xa. It targets both free factor Xa and bound factor Xa in the prothrombinase complex (Figure 5.1). The half-life of rivaroxaban is 11–13 hours and reaches peak plasma concentration 2–4 hours after oral administration. As with dabigatran, bridging with heparin is not needed when discontinued or restarted after interruption. It is approved for stroke prevention in patients with nonvalvular atrial fibrillation. Clinical indications have been expanded to include treatment of DVT and VTE events, prevention of DVT, and pulmonary embolism after hip or knee arthroplasty. Cessation prior to surgery is recommended 24–48 hours before surgery and resumption 6–10 hours after surgery, or when hemostasis is deemed adequate or the risk of severe hemorrhage has diminished [11, 12].

## Apixaban

Apixaban is another oral selective direct inhibitor of free and clot-bound factor Xa (Figure 5.1). After oral administration, peak plasma concentrations are achieved within 1–4 hours. It is predominantly metabolized by the liver and has several important drug interaction cautions against concomitant usage with drugs affecting CYP3A4. It has no antiplatelet activity. It is currently approved for the prevention of stroke and thromboembolic events in patients with nonvalvular atrial fibrillation. It is used for prophylaxis against DVT and pulmonary embolism after recent knee or hip replacement, and treatment of DVT and pulmonary embolism, and there is a reduction in risk of recurrence following initial therapy [11, 12].

## Edoxaban

Edoxaban is another oral anticoagulant drug which acts as a reversible, direct factor Xa inhibitor, that binds to blocks the active site of factor Xa. It inhibits free factor Xa and prothrombinase complex activity and inhibits thrombin-induced platelet aggregation (Figure 5.1). Primarily, it is excreted as unchanged drug in urine; metabolism and biliary/intestinal excretion account for the remainder of its clearance. Peak plasma concentration is achieved within 1–2 hours of oral administration. The half life of edoxaban is 10–14 hours, achieving total clearance in about 22 hours. Therefore, cessation is advised at least 24 hours prior to invasive or surgical intervention. Parenteral anticoagulant administration is advised prior to initiation of edoxaban. Edoxaban is approved for the treatment of DVT and pulmonary embolism, prevention of stroke, and systemic embolism in patients with nonvalvular atrial fibrillation [11–13].

## Clopidogrel

Clopidogrel is a prodrug which upon activation by CY2C19 acts by irreversibly inhibiting the P2Y12 subtype of the adenosine diphosphate (ADP) receptor on platelet cell membranes. The P2Y12 subtype of the ADP receptor is important in activation of platelets and eventual crosslinking by the protein fibrin. Platelet inhibition can be seen 2 hours after oral administration of a single dose. However, the onset of action is slow, hence a loading dose is recommended if rapid effect is needed. The elimination half-life of clopidogrel is 0.5–1.0 h. Some 50% was excreted in the urine and 46% in the feces in the

5 days after dosing. It inhibits aggregation for the life of the platelet, typically 7–10 days. Bleeding time and platelet function return to baseline after 5 days. Cessation is recommended 7–10 days prior to any planned surgery [11, 12].

### Ticlopidine

Ticlopidine is another oral thienopyridine, similar in action and mechanism to clopidogrel. It exhibits high bioavailability up to 80% with rapid absorption. The drug is metabolized into its active form which irreversibly blocks the ADP receptor on the surface of platelets. Antiplatelet effect is demonstrated within 2 days of initiation of therapy and reaches maximum effect after 6 days. The drug is metabolized by the liver, with elimination via renal and fecal routes. After the first dose the half life is 12.6 hours, but this is prolonged to 4–5 days with repeated dosing. The effects persist for 3 days after discontinuing ticlopidine although it may take 1–2 weeks for platelet function to return to normalize [11, 12].

### Prasugrel

Prasugrel is yet another oral thienopyridine class of ADP receptor inhibitors, Similar in mechanism and action to clopidorgel and ticlopidine, it acts by irreversible binding to P2Y12 receptors in platelets and thus prevents platelet aggregation. Prasugrel is a prodrug that is rapidly metabolized by esterases in the intestine and blood serum to an inactive thiolactone, which is then further converted to a pharmacologically active metabolite via CYP450-mediated oxidation, primarily CYP3A4 and CYP2B6. It has an elimination half-life of 2–15 hours. Antiplatelet activity is seen within 1 hour of oral administration. Maximal effect is seen after about 3–5 days of dosing at 10 mg daily following a loading dose of 60 mg. Platelet aggregation returns to baseline in 5–9 days after cessation of the drug. Since the inhibition is irreversible, the return to normal platelet function reflects the production of new platelets [11, 12].

### Ticagrelor

Ticagrelor blocks ADP receptors of subtype P2Y12. Its binding site is different from ADP and the binding is reversible. It does not rely on hepatic activation via the CYP2C19 enzyme; therefore, it is potentially more useful in patients with genetic variants of the enzyme. Ticagrelor, once administered orally, reaches its peak concentration after about 1.5 hours. The main metabolite is formed quickly via CYP3A4 and peaks after about 2.5 hours. Both ticagrelor and its metabolite are pharmacologically active. Excretion of the drug and its metabolite are mainly via bile and feces [11, 12].

## Safety of antithrombotics and risk stratification

The decision of whether or not to interrupt or hold anticoagulants and antiplatelets before surgery can sometimes be complex and prove to be a significant challenge for the surgeon. Interrupting or reversing anticoagulation therapy may lead to transient rebound hypercoagulability as a result of stopping and subsequently restarting anticoagulation therapy. Therefore, the risk of cessation needs stratification and to be weighed against the risk of bleeding from the surgery if the patient is to remain on anticoagulation throughout. The indication for anticoagulation therapy and the length of therapy must be evaluated. Before coming to a decision on interruption and resumption of anticoagulation, the indications for surgery need to be considered, alternatives to surgery and other surgical options assessed, and the associated bleeding risks evaluated. The underlying disease requiring the anticoagulation and coexisting cardiovascular diseases need to be considered in conjunction with the risk of thrombosis.

## Atrial fibrillation, risk of thromboembolism, and bleeding risk

The most commonly used method to predict thromboembolic risk in atrial fibrillation is the CHA2DS2-VASc score. It was developed by the American College of Cardiology (ACC) in conjunction with the American Heart Association and European Society of Cardiology. The acronym stands for Congestive heart failure, Hypertension, Age >75 (2 points), Diabetes, and Stroke or transient ischemic attack (TIA) or thromboembolism (2 points), and VASc stands for Vascular disease (peripheral arterial disease, previous myocardial infarction, aortic plaque), Age 65–74 (1 point), and Sex category (female gender 1 point). It allows for an individualized approach to the prediction and the selection of antithrombotic agents for the prevention on the basis of patient risk for stroke and risk for intracranial hemorrhage. Each risk factor receives 1 point except age > 75 and stroke/TIA which receive 2 points. The more points on the CHA2DS2-VASc score, the higher the annual stroke risk in general [14–16]. Other predisposing factors such as the presence of mechanical heart valves, underlying diseases causing a hypercoagulable state, renal impairment, cardiomyopathy, atrial thrombus, and concurrent malignancy should also be considered when evaluating the risk of thromboembolism.

## Bleeding risk

Several tools have been proposed and used for the assessment of bleeding risk in atrial fibrillation patients on anticoagulation. The HAS-BLED score represents the most recent tool for this purpose and stands for Hypertension (uncontrolled systolic blood pressure >160 mmHg), Abnormal renal or liver function, Stroke, Bleeding history, Labile international normalized ratios, Elderly, and concomitant Drugs and/or alcohol excess [17]. Each risk factor assigns 1 point and scores range from 0 to 9. Scores of ≥3 indicate a high risk of bleeding at 1 year. For these patients, caution with anticoagulation use is recommended. The HAS-BLED score can be a guide for surgeons in the evaluation of bleeding risk in atrial fibrillation patients.

## Pulmonary embolism and deep venous thromboembolic disease

Patients suffering from pulmonary embolism are particularly challenging to manage. The risk of a recurrent thromboembolic event can be immediately catastrophic. Not unlike atrial fibrillation, the length of therapy is important when considering cessation or interruptions in anticoagulants. The risk of recurrence with temporary cessation is lowest in patients who have been treated for at least 1 month, and preferably longer. For those patients who have been treated for less than 1 month, alternatives to surgery and, if possible, delaying surgery should be considered. If emergent or urgent surgery is indicated, then these patients need to be bridged as the risk of recurrence or propagation is highest in this group [18, 19].

## Mechanical heart valves

Patients with mechanical heart valves an especially complex group since they all need to remain anticoagulated. Common types of heart valve prostheses include the St Jude's Medical bileaflet valve, the Starr–Edwards ball-and-cage design, the Bjork–Shiley tilting disc design, and the stented porcine prosthesis. The type and position of the heart valve needs to be considered as they influence risk of thrombosis. Thromboembolism risk is higher with the Starr–Edwards ball-and-cage design than with the Bjork–Shiley tilting disc. Bileaflet prosthetic valves such as the St Jude valve have the lowest risk of thromboembolism. Mitral valve replacement carries the higher rates of thromboembolism compared to aortic valve replacement. Patients with any mitral valve replacement or a mechanical aortic valve replacement requiring anticoagulation will need to be bridged with unfractionated heparin which can then be held 1–4 hours before the surgery [20].

## Hypercoagulable states

The risk of thromboembolism is particularly vexing in patients with inherited and acquired thrombophilia. They often require special preparation due to the increased risk of thrombosis associated with interrupting and resuming anticoagulation. These patients should be considered at high risk for adverse for interrupting anticoagulation. Careful preparation and individualized approach to bridging and management in conjunction with a hematologist, to minimize the risk.

## Coronary stents

Bare metal stents (BMS) and drug-eluting stents (DES) are designed to combat the problem of acute reocclusion or re-stenosis after percutaneous coronary balloon angioplasty. Both types of stents reduce the risk of reocclusion and re-stenosis. It has been stated that up to 30% of patients with BMS develop re-stenosis within the first year due to intimal hyperplasia. DES, which have a polymer coating that binds antiproliferative drugs such as sirolimus, paclitaxel, or everolimus to the stent and releases the drug, reduces risk of stent re-stenosis by up to 70% [9, 21, 22]. However, due to this same mechanism, the length of time to complete endothelialization of the stent is prolonged in DES, thus increasing the risk of acute stent thrombosis. Thus prolonged antiplatelet therapy is required in DES, compared to BMS. The ACC recommends dual antiplatelet therapy for at least 14 days after balloon angioplasty, 1 month for BMS, and 6–12 months for DES. Coupled with the increasing use of intracoronary stents there is an increasing incidence of these patients presenting for noncardiac surgeries while still within the mandatory time recommended for antiplatelet therapy. The risks of significant hemorrhage and ischemia under these circumstances is not insignificant and pose a particular challenge for the surgeon. For certain subgroups of these patients who have severe coronary disease and carry the greatest risk of a major adverse cardiac event, the cardiologist may insist on life-long antiplatelet therapy. The ACC guidelines recommend delaying surgery if the period of dual antiplatelet therapy is less than 1 month for BMS or less than 3 months for DES. For patients with DES, if surgery is within 3–6 months of initiation of dual antiplatelet therapy after percutaneous coronary intervention, then the risk of delaying surgery should be weighed against the risk of stent thrombosis [23].

## Risk of thrombosis

The 2012 guidelines of the ACCP stratify patients into the following thrombotic risk categories (see

**Table 5.1** Summary of ACCP 2012 Guidelines for risk categorization and perioperative bridging.

| Risk category | Atrial fibrillation | Mechanical heart valve | VTE |
|---|---|---|---|
| High (must bridge; >10% annual risk of thromboembolism) | CHADS2 of 5 or 6 | Any mitral valve prosthesis | Recent VTE (within 3 months) |
| | Recent stroke or TIA within 3 months | Any caged ball or tilting disc aortic valve prosthesis | Severe thrombophilia<br>• Protein C, protein S, or antithrombin deficiency<br>• Antiphospholipid antibodies<br>• Multiple abnormalities |
| | Rheumatic valvular heart disease | Recent stroke or TIA (within 6 months) | |
| Moderate (consider bridging based on patient and surgery-specific factors; 5–10% annual risk of thromboembolism) | CHADS2 of 3 or 4 | Bileaflet aortic valve prosthesis and one or more risk factors:<br>• Atrial fibrillation<br>• Prior stroke or TIA<br>• Hypertension<br>• Diabetes<br>• Congestive heart failure<br>• Age >75 years | VTE within the past 3–12 months<br>Non-severe thrombophilia:<br>• Heterozygous factor V Leiden<br>• Prothrombin gene mutation |
| | | | Recurrent VTE |
| | | | Active cancer (treated within 6 months or palliative) |
| | | | VTE >12 months and no other risk factors |
| Low (no bridging needed; <5% annual risk of thromboembolism) | CHADS2 of 0–2 and no prior stroke or TIA | Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke | |

Table 5.1): low risk (less than 5% risk of thrombotic events per year), moderate risk (5–10% risk of thrombotic events per year), and high risk (greater than 10% risk of thrombotic events per year) [8]. According to the panel, patient at high risk should undergo bridging, patients at moderate risk should be considered for bridging, while patients at low risk do not need to be bridged [8].

## Perioperative management of patients receiving vitamin K antagonist (warfarin) therapy

### Interruption and resumption before surgery

For patients who require temporary interruption of warfarin before surgery, the panel recommends stopping warfarin approximately 5 days before surgery. For patients requiring temporary interruption of warfarin before surgery, resuming warfarin is recommended approximately 12–24 h after surgery and when there is adequate hemostasis [8, 23].

### Need for bridging anticoagulation during interruption of therapy

For those patients with mechanical heart valves, atrial fibrillation, or VTE who are considered at high risk for thromboembolism, the panel suggests bridging anticoagulation when interrupting warfarin therapy. In patients with a mechanical heart valve, atrial fibrillation, or VTE at moderate risk for thromboembolism, the decision to bridge or not to bridge is based on an assessment of the individual patient and surgery-related factors. For patients with mechanical heart valves, atrial fibrillation, or VTE considered to be at low risk for thromboembolism, the panel does not recommend bridging anticoagulation when interrupting warfarin therapy (Table 5.1) [8, 23].

### Perioperative management for patients who require minor procedures

When the surgery is considered to be minor and carrying a low risk of hemorrhage, the panel suggests continuing warfarin with concomitant oral prohemostatic agent or interrupting warfarin 2–3 days before the procedure, optimizing local hemostasis [8, 23].

## Perioperative management of patients who are receiving antiplatelet drugs

### Non-cardiac surgery and aspirin

In patients considered to be at moderate to high risk for cardiovascular events who are on aspirin and require noncardiac surgery, the panel recommends continuing aspirin around the time of surgery instead of stopping aspirin 7–10 days before surgery. In patients at low risk for cardiovascular events who are receiving aspirin therapy, the panel suggest stopping aspirin 7–10 days before surgery instead of continuation [8, 23].

### Patients with coronary stents having surgery

Patients with a coronary stent who are receiving dual antiplatelet therapy and require surgery, the panel recommends deferring surgery for at least 6 weeks after placement of a BMS and for at least 6 months after placement of a DES instead of undertaking surgery within these time periods (Figure 5.2). In patients who require surgery within 6 weeks of placement of a BMS or within 6 months of placement of a DES, the panel suggests continuing dual antiplatelet therapy around the time of surgery instead of discontinuing dual antiplatelet therapy 7–10 days before surgery. One should note that the most recent guidelines from the ACC, published in 2016, shortened the mandatory time period during which surgery must be delayed to 1 month after placement of BMS and 3 months for DES before interruptions of dual antiplatelet therapy can be considered [23]. This is discussed elsewhere in this chapter in the section on coronary stents [8, 23].

## Perioperative use of bridging intravenous unfractionated heparin and LMWH

In patients who are receiving bridging anticoagulation with therapeutic-dose unfractionated heparin, the panel suggests stopping unfractionated heparin 4–6 hours before surgery. For those patients who are being bridged with therapeutic-dose subcutaneous LMWH, the panel recommends administering the last preoperative dose approximately 24 hours before surgery. For those patients being bridged with therapeutic doses of subcutaneous LMWH and are undergoing surgeries with high risk for hemorrhage, the panel recommends resuming

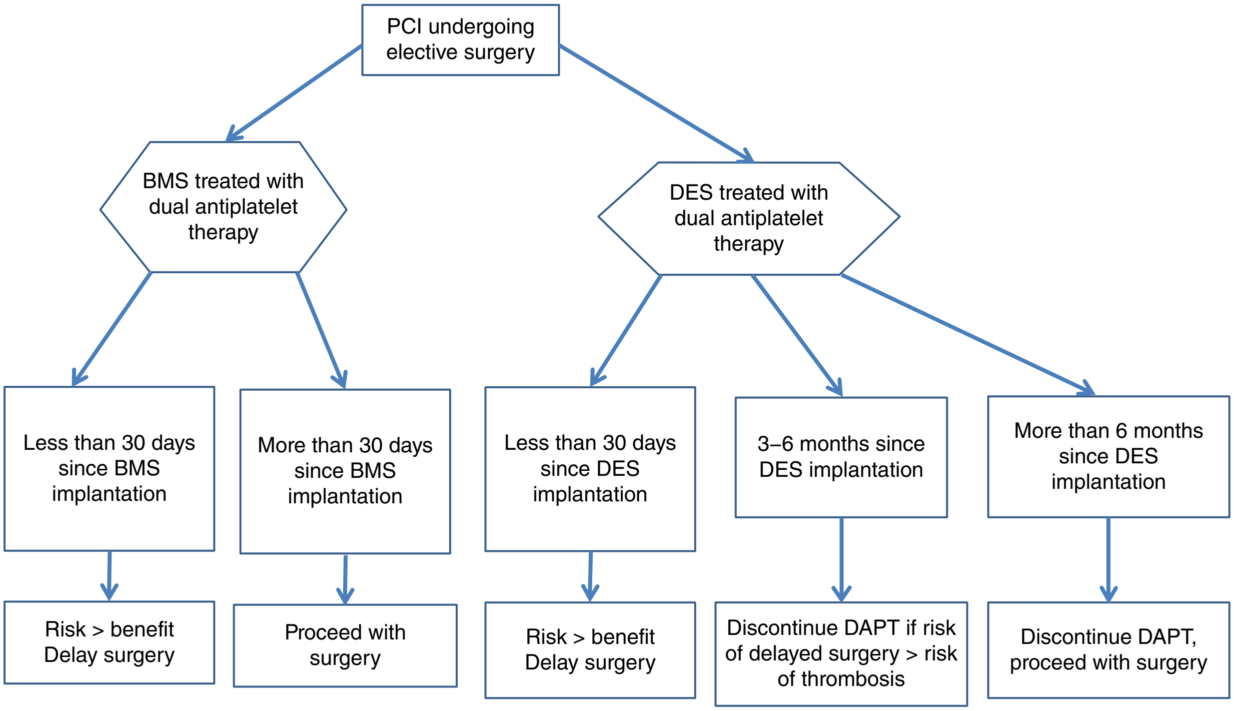
PCI undergoing elective surgery
BMS treated with dual antiplatelet therapy
DES treated with dual antiplatelet therapy
Less than 30 days since BMS implantation
More than 30 days since BMS implantation
Less than 30 days since DES implantation
3–6 months since DES implantation
More than 6 months since DES implantation
Risk > benefit Delay surgery
Proceed with surgery
Risk > benefit Delay surgery
Discontinue DAPT if risk of delayed surgery > risk of thrombosis
Discontinue DAPT, proceed with surgery

**Figure 5.2** 2016 ACC/American Heart Association treatment algorithm for timing of elective noncardiac surgery in patients with coronary stents [23]. DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention.

therapeutic-dose LMWH 48–72 hours after surgery instead of resuming LMWH within 24 hours after surgery. If the surgery poses a low risk of significant hemorrhage, resuming therapeutic-dose LMWH approximately 24 hours after surgery is recommended [8, 23].

## Antiplatelet and anticoagulant use in urological surgery

There is very limited evidence-based literature on the perioperative management of patients who are scheduled for urological surgery. In deciding on a management scheme for interrupting and resuming antiplatelets and anticoagulation during elective urological surgery, certain patient and procedural risk factors need to be considered. The risk of thromboembolic event or stent stenosis needs to be considered along with comorbid conditions. Patients with severe coronary artery disease with multiple stents, stent re-stenosis, poor ejection fraction, and renal failure need to be weighed against the risk of bleeding or significant hemorrhage associated with the planned surgery. Consultation and comanagement with the patient's cardiologist and hematologist, as well as the anesthesiologist, is necessary to minimize the risk of adverse outcomes.

In Table 5.2 the most common types of urological surgery are categorized according to bleeding risk. Table 5.2 categorizes the patients into low-, moderate-, and high-risk groups according to the ACC and ACCP guidelines. For most cases, aspirin can be continued perioperatively in patients with intracoronary stenting, as prematurely interrupting aspirin is a risk factor for acute coronary syndrome and stent thrombosis. However, if the risk of bleeding is considered to be severe, aspirin should be interrupted for the surgery and then resumed as soon as the window for severe bleeding has elapsed. Several studies of perioperative aspirin and anticoagulation use during transurethral resection of the prostate have demonstrated an increased rate of postoperative bleeding, likewise for transurethral laser enucleation techniques [24–29]. However, for transurethral vaporization techniques, there does not appear to be a significantly increased risk of bleeding for patients receiving clopidogrel, aspirin, or warfarin compared to controls [24–29]. Pregnancy and uncorrected coagulopathy are the two absolute contraindications for shock-wave lithotripsy. It can carry a high risk of hemorrhagic complications including postoperative perirenal hematomas and life-threatening renal hemorrhage, resulting in transfusion, renal embolization, and nephrectomy. The rate of asymptomatic perirenal hematomas can be as high as 25% when sensitive abdominal computed tomography scanning is used postoperatively, and rate of symptomatic hematomas have been reported to be 0.7% [30–32]. Patients that cannot discontinue anticoagulants and antiplatelets are usually managed with other modalities [33–36]. Several series have reported results of the use of the anticoagulants and antiplatelets in conjunction with shock-wave lithotripsy, some with catastrophic outcomes [37]. In patients undergoing transrectal ultrasound-guided prostate biopsy (TRUS Bx) there is an increased the risk of prolongation of rectal bleeding, hematuria, and hematospermia in association with antiplatelets and anticoagulants use [29, 38–40]. A prospective randomized trial published in 2007 found that the median duration of hematuria and rectal bleeding was statistically significantly greater in uninterrupted aspirin use (group 1) and interrupted but bridged with LMWH (group 2) compared to interrupted aspirin (group 3): 6, 4, and 2 days and 3, 2, and 1 days, respectively. The number of patients still reporting hematospermia at 30 days after TRUS Bx was 21.4, 18.5, and 9.3% in groups 1, 2, and 3, respectively [38].

Ureteroscopy is considered safe in the face of anticoagulation and antiplatelets. Turna et al. published a retrospective case-control study of flexible ureteroscopy and holium:YAG laser lithotripsy [41]. They identified 37 patients on warfarin (38%), clopidogrel (13%), or aspirin (49%) who underwent surgery without interruption of antithrombotic therapy. There were no bleeding-related complications in either group [41].

**Table 5.2** Bleeding risk categories for common urological surgeries.

| Low risk | Moderate risk | High risk |
|---|---|---|
| Cystoscopy | Laser enucleation of prostate | Cystectomy |
| Ureteroscopy/renoscopy | Transurethral resection of prostate | Partial and total nephrectomy |
| Laser lithotripsy | Transurethral resection of bladder | Prostatectomy |
| Laser vaporization of prostate | Transrectal biopsy of prostate | Penile prosthesis |
| Urethral bulking | Urethral sling and sphincter placements | Penectomy |
| | Prolapse repair | Shockwave lithotripsy |

Several series have also been published on use of aspiring during other high-risk procedures [42, 43]. Leyh-Bannurah et al. reported on a retrospective series of 137 open retropubic and robot-assisted radical prostatectomy (RARP) in patients on uninterrupted aspirin therapy compared to controls matched by propensity score. The authors did not observe a statistically significant increase in blood loss in the aspirin group. However, they did observe that aspirin was an independent predictor of blood transfusion [42]. Likewise for robot-assisted laparoscopic radical nephrectomy (RALRN) and RALRP, Parikh et al. reported on 51 patients who underwent RARP while continuing aspirin compared to 44 controls. There was no significant difference in estimated blood loss, and there were no transfusions in either group. Results were similar for the RALRN group which had 14 patients with uninterrupted aspirin versus 12 controls [44].

In contrast to aspirin, clopidogrel, cilostazol, and warfarin were associated with an increased risk of thrombotic events postoperatively in patients undergoing open or laparoscopic partial nephrectomy in a retrospective series of 47 chronically anticoagulated patients who had the anticoagulation interrupted [45]. In that series, the transfusion rates were similar to the matched control group. Similar findings were observed in patients with a percutaneous nephrolithotomy [46]. However, a recent series of uninterrupted aspirin therapy in patients undergoing percutaneous nephrolithotomy did not show an difference in bleeding complications compared to controls [47].

## Conclusion

With the increasing prevalence of patients with coronary stents and who are on antiplatelet therapy or anticoagulation, urologists are increasingly more likely to be needed to perform surgeries. Sometimes the underlying indication for surgery can be life threatening, creating an incredibly complex set of difficult medical choices. Taken together, the evidence base upon which to draw conclusions and guide management is sparse and of suboptimal quality. It thus becomes imperative to categorize the patient's risk group and to balance the risk of hemorrhagic consequences with the risk of thromboembolic events. A multidisciplinary approach is essential for optimal management of these patients.

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# SECTION 2

# Percutaneous Renal Surgery

# Part 1 Perioperative Considerations

## 6

## Surgical Anatomy of the Kidney for Endourological Procedures

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## General anatomy

The kidneys are paired organs lying retroperitoneally on the posterior abdominal wall. Each kidney has a characteristic shape, with a superior and an inferior pole, a convex border placed laterally, and a concave medial border. The medial border has a marked depression, the hilum, containing the renal vessels and renal pelvis.

### Renal morphometry

In adults, the left kidney is larger than the right, and this agrees with morphometric findings in fetal kidneys [1]. The right kidney has a mean length of 10.97 cm and 3.21 cm mean thickness at the hilum, in comparison to 11.21 cm and 3.37 cm, respectively, for the left kidney [2].

An interesting finding is that the superior pole has a greater width (mean, 6.48 cm) than the inferior pole (mean, 5.39 cm). Also, there is a statistically significant correlation between kidney length and an individual's stature [2].

### Position of the kidneys

Because the kidneys lie on the posterior abdominal wall, against the psoas major muscles, their longitudinal axis parallels the oblique course of the psoas (Figure 6.1). Moreover, since the psoas major muscle has a cone shape, the kidneys also are dorsally inclined on the longitudinal axis. Therefore, the superior poles are more medial and more posterior than the inferior poles (Figure 6.1). Also, because the hilar region is rotated anteriorly on the psoas muscle, the lateral borders of both kidneys are posteriorly positioned. This means the kidneys are angled 30–50° behind the frontal (coronal) plane (Figure 6.2) [3].

### Perirenal coverings

The kidney surface is enclosed in a continuous covering of fibrous tissue, the renal capsule ("true renal capsule"). Each kidney within its capsule is surrounded by a mass of adipose tissue, lying between the peritoneum and the posterior abdominal wall (Figures 6.2 and 6.3). This perirenal fat is enclosed by the renal fascia (the so-called fibrous renal fascia of Gerota). The renal fascia is enclosed anteriorly and posteriorly by another layer of adipose tissue, the pararenal fat, which varies in thickness (Figure 6.3).

The renal fascia is made up of a posterior layer (a well-defined and strong structure) and an anterior layer (a more delicate structure, which tends to adhere to the peritoneum) (Figures 6.2 and 6.3). The anterior and posterior layers of the renal fascia (fascia of Gerota) subdivide the retroperitoneal space into three potential compartments: (i) the posterior pararenal space, which contains only fat; (ii) the intermediate perirenal space, which contains the suprarenal glands, kidneys, and proximal ureters, together with the perirenal fat; and (iii) the anterior pararenal space, which unlike the posterior and intermediate spaces, extends across the midline from one side of the abdomen to the other. This latter space contains the ascending and descending colon, the duodenal loop, and the pancreas [3] (Figure 6.4). Inferiorly, the layers of the renal fascia end weakly fused around the ureter (Figures 6.3 and 6.5). Superiorly, the two layers of the renal fascia fuse above the suprarenal gland and end fused with the infradiaphragmatic fascia (Figure 6.5). An additional fascial layer separates the suprarenal gland from the kidney (Figure 6.5). Laterally, the two layers of the renal fascia fuse behind the ascending and descending colons. Medially, the posterior fascial layer is fused with the fascia of the spine muscles. The anterior fascial layer merges into the connective tissue of the great vessels (aorta and inferior vena cava) (Figures 6.2 and 6.4).

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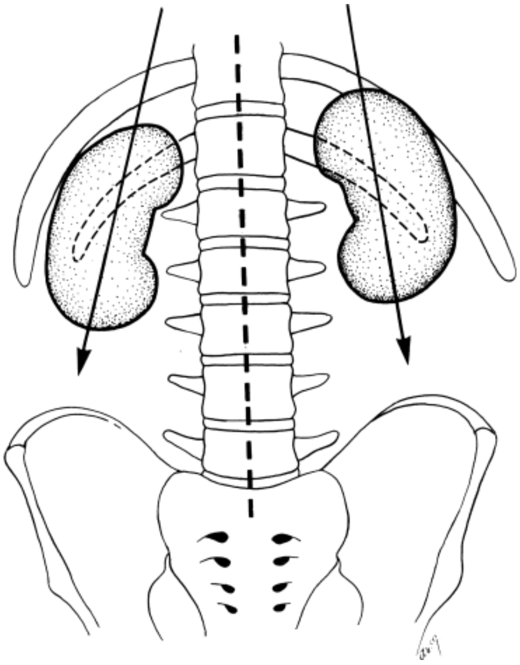

Figure 6.1 Schematic of an anterior view of the kidneys in relation to the skeleton showing that the longitudinal axes of the kidneys are oblique (arrows), with the superior poles more medial than the inferior poles. The dashed lines mark the longitudinal axis of the body. It can also be seen that usually the posterior surface of the right kidney is crossed by the 12th rib and the left kidney by the 11th and 12th ribs.

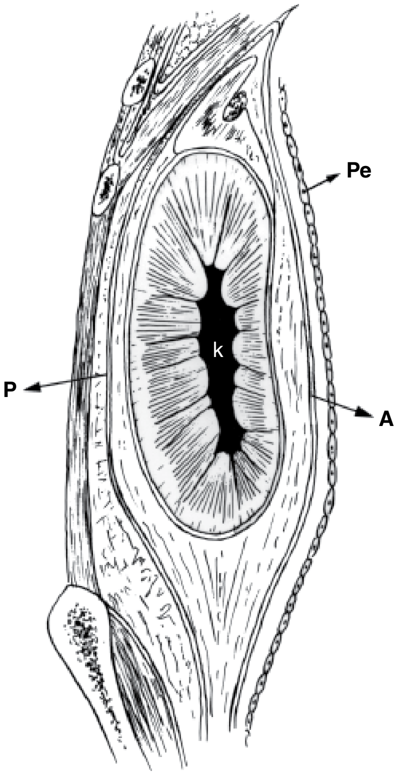

Figure 6.3 Schematic of a lateral view of a longitudinal section through the retroperitoneum showing the posterior (P) and anterior (A) layers of the renal fascia. Pe, peritoneum; k, kidney.

These anatomic descriptions of the renal fascia show that the right and left perirenal spaces are potentially separated and, therefore, it is exceptional that a complication of an endourologic procedure, e.g. hematoma, urinoma, or perirenal abscess, involves the contralateral perirenal space [3].

## Relationship of kidneys to the diaphragm, ribs, and pleura

The kidneys lie on the psoas and quadratus lumborum muscles. Usually, the left kidney is higher than the right kidney, with the posterior surface of the right kidney crossed by the 12th rib and the left kidney crossed by the 11th and 12th ribs (Figure 6.1). The posterior surface of the diaphragm attaches to the extremities of the 11th and 12th ribs (Figure 6.6). Close to the spine, the diaphragm is attached over the posterior abdominal muscles, and forms the medial and lateral arcuate ligaments on each side (Figure 6.6). In this way, the posterior aspect of the diaphragm (posterior leaves) arches in a dome above the superior pole of the kidneys, on each side. Therefore, when performing an intrarenal access by puncture, the endourologist may consider that the diaphragm is traversed by all intercostal punctures, and possibly by some punctures below the 12th rib (Figure 6.7). Also, it can be

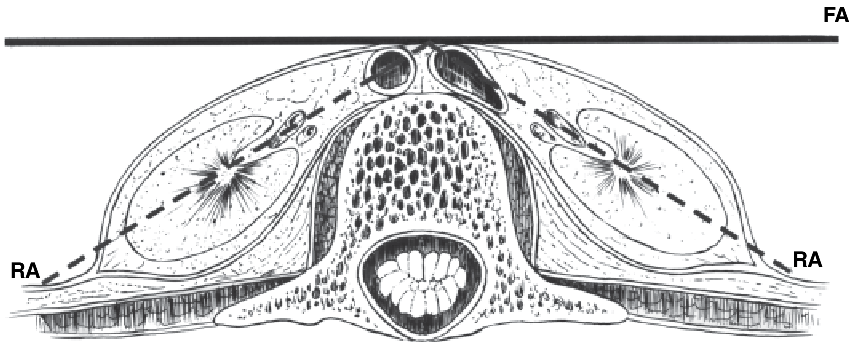

Figure 6.2 Schematic of a superior view of a transverse section of the kidneys at the level of the second lumbar vertebra showing that the kidneys are angled 30–50° behind the frontal (coronal) plane of the body (FA). RA, renal frontal (coronal) axis.

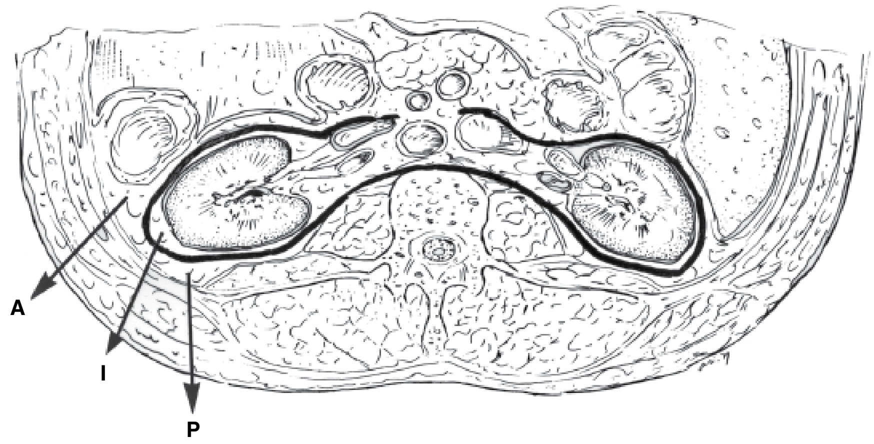

**Figure 6.4** Schematic of a superior view of a transverse section of the kidneys at the level of the second lumbar vertebra showing the three compartments of the retroperitoneal space. P, posterior pararenal space, which contains only fat; I, intermediate perirenal space, which contains the suprarenal glands, kidneys, and proximal ureters, together with the perirenal fat; and A, anterior pararenal space, which unlike the posterior and intermediate spaces, extends across the midline from one side of the abdomen to the other, and contains the ascending and descending colons, duodenal loop, and pancreas.

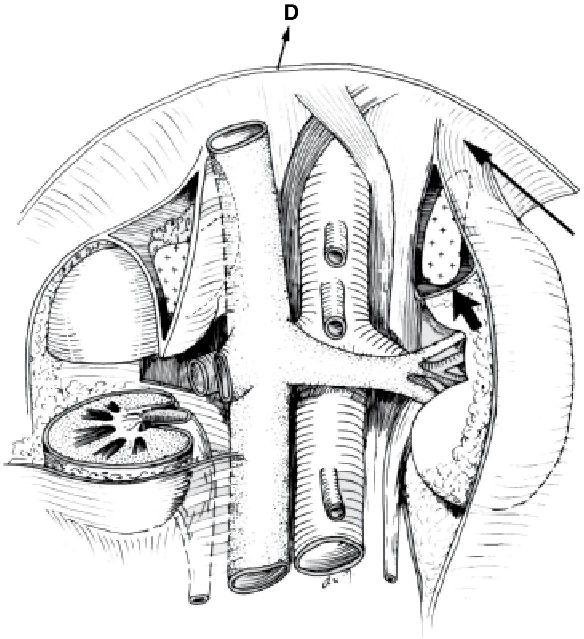

**Figure 6.5** Schematic of an anterior view of the renal fascia (Gerotas' fascia) and kidneys. This shows that the two layers of the renal fascia fuse above the suprarenal gland and end fused with the infradiaphragmatic fascia (long arrow). Note a dependence of the fascia separating the suprarenal gland from the kidney (short arrow). D, diaphragm muscle.

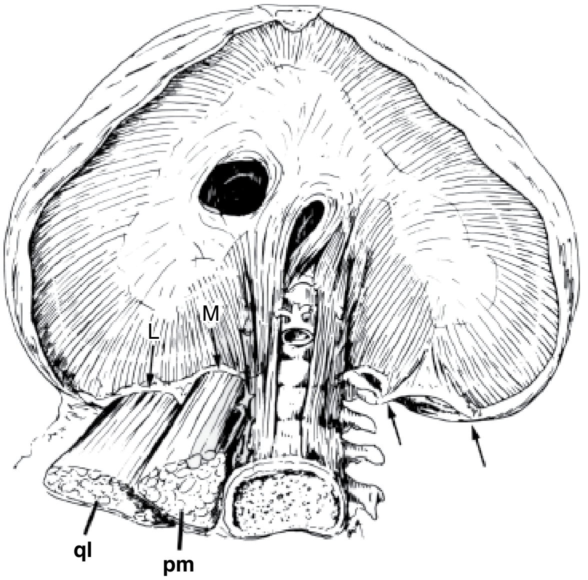

**Figure 6.6** Schematic of an inferior view of the diaphragmatic dome. The arrows point to the diaphragmatic attachments to the extremities of the 11th and 12th ribs. M, medial arcuate ligament; L, lateral arcuate ligament; ql, quadratus lumborum muscle; pm, psoas muscle.

expected that the pleura is transversed without symptoms in most intercostal approaches [4].

Generally, the posterior reflection of the pleura extends inferiorly to the 12th rib; nevertheless, the lowermost lung edge lies above the 11th rib (at the 10th intercostal space) (Figure 6.7). Regardless of the degree of respiration (mid or full expiration), the risk of injury to the lung from a 10th intercostal percutaneous approach to the kidney is prohibitive [4]. Any intercostal puncture should be made in the lower half of the intercostal space, in order to avoid injury to the intercostal vessels above.

## Relationship of kidneys to the liver and spleen

The liver on the right side and the spleen on the left may be posterolaterally positioned at the level of the suprahilar region of the kidney, because at this point these organs have their largest dimensions (Figure 6.8). Therefore, it should be remembered that a kidney puncture performed high in the abdomen will allow little space for the needle entrance [4]. If the intrarenal puncture is performed when the patient is in mid or full inspiration, the risk of injury to the liver and spleen is increased [4]. This knowledge is particularly important in patients with hepatomegaly or splenomegaly, in whom a computed tomography (CT) scan should be performed before puncturing the kidney.

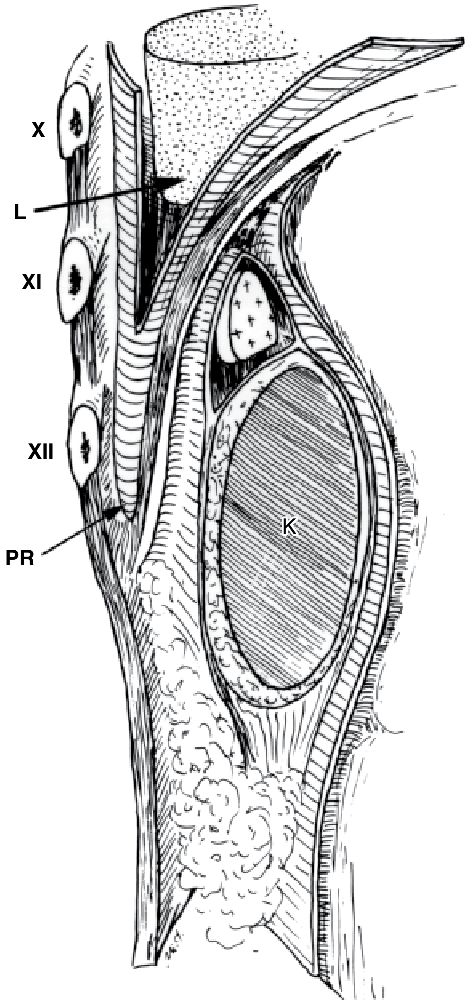

Figure 6.7 Schematic of a lateral view of the kidney and its relationships with the diaphragm, ribs, pleura, and lung. PR, posterior reflection of the pleura, L, lower edge of the lung; K, kidney; X, 10th rib; XI, 11th rib; XII, 12th rib.

## Relationship of kidneys to the ascending and descending colons

The ascending colon runs from the ileocolic valve to the right colic flexure (hepatic flexure), where it passes into the transverse colon. The hepatic colic flexure (hepatic angle) lies anteriorly to the inferior portion of the right kidney. The descending colon extends inferiorly from the left colic flexure (splenic flexure) to the level of the iliac crest. The left colic flexure lies anterolateral to the left kidney.

It is important to consider the position of the retroperitoneal ascending and descending colons. Occasionally, in the course of a routine abdominal CT scan, the retroperitoneal colon has been observed to lie in a posterolateral or even a retrorenal position [5], and in these cases, there is a great risk of kidney injury with the intrarenal percutaneous approach. A retrorenal colon is more common in the area of the inferior poles of the kidneys (Figure 6.9). Retrorenal colon was found on CT scan in 1.9% of patients in the supine position, but 10% when the prone position (the more commonly adopted position for percutaneous access to the kidney) was assumed [5]. Therefore, with the patient in the prone position and before any invasive percutaneous renal procedure, retrorenal colon should be looked for, especially around the inferior poles of the kidney, using fluoroscopy [5].

## Intrarenal vessels

### Intrarenal arteries

Generally, the main renal artery divides into an anterior and a posterior branch after giving off the inferior suprarenal artery. Whereas the posterior branch (retropelvic artery) proceeds as the posterior segmental artery to

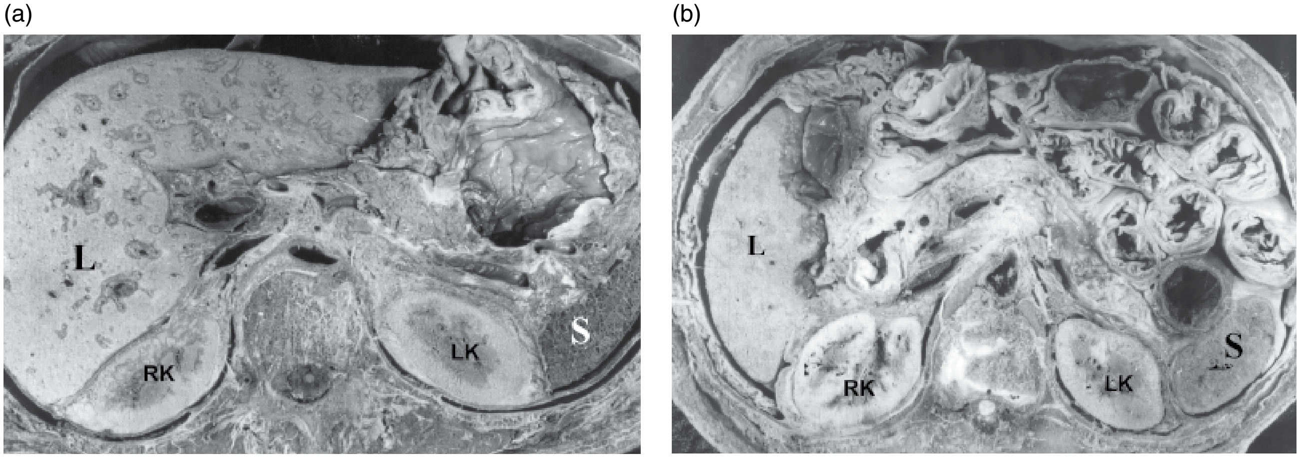

Figure 6.8 (a) Inferior view of a transverse section through a cooled cadaver at the level of the suprahilar region of the kidney. This shows that the liver (L) and spleen (S) are posterolaterally positioned in relation to the right (RK) and left (LK) kidneys. (b) Similar section to (a) at the level of the infrahilar region. This shows that inferiorly the liver (L) and spleen (S) are more laterally positioned in relation to the right (RK) and left (LK) kidneys.

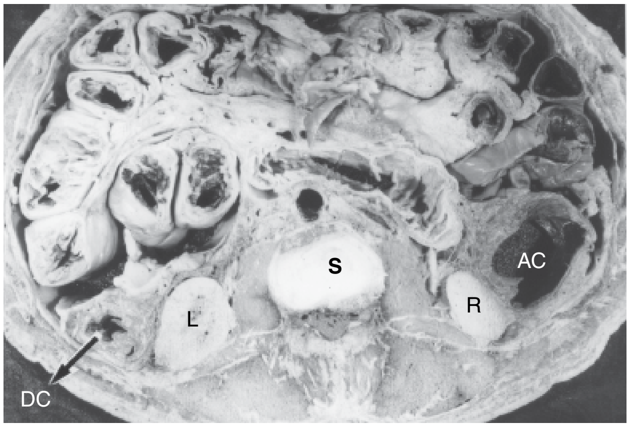

**Figure 6.9** Superior view of a transverse section through a cooled cadaver at the level of the inferior poles of the kidney. This shows the ascending (AC) and descending (DC) colons lying in a posterolateral position in relation to the right (R) and left (L) kidneys. S, spine.

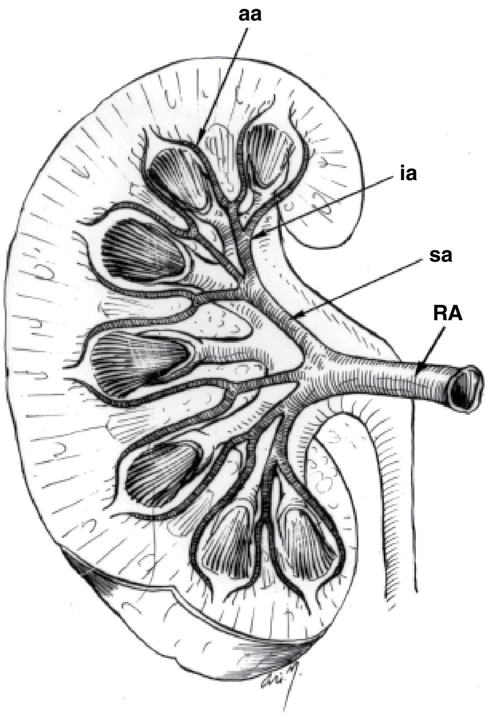

**Figure 6.10** Schematic of an anterior view of a right kidney. This shows the branching of the renal arteries and their official nomenclature according to kidney region. RA, renal artery; sa, segmental artery; ia, interlobar (infundibular) artery; aa, arcuate artery.

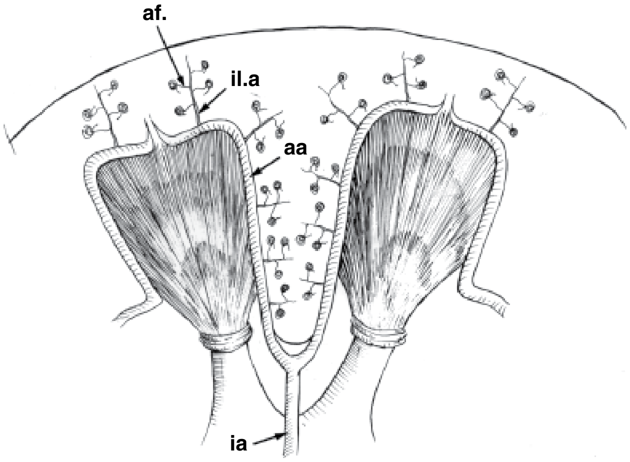

**Figure 6.11** Schematic of two adjacent pyramids and minor calyces. This shows the renal vasculature from the level of the interlobar arteries to the glomerular level. ia, interlobar (infundibular artery); aa, arcuate artery; il.a, interlobular artery; af., afferent arteriole of the glomerulus.

supply the homonymous segment without further significant branching, the anterior branch of the renal artery provides three or four segmental arteries. The segmental arteries divide before entering the renal parenchyma into the interlobar arteries (infundibular arteries), which progress adjacent to the calyceal infundibula and the minor calyces, entering the renal columns between the renal pyramids (Figures 6.10 and 6.11) [6]. As the interlobar arteries progress, near the base of the pyramids, they give origin (usually by dichotomous division) to the arcuate arteries (Figures 6.10 and 6.11). The arcuate arteries give off the interlobular arteries, which run to the periphery, giving off the afferent arterioles of the glomeruli (Figure 6.11) [6].

### Intrarenal veins

The intrarenal veins, unlike the arteries, do not have a segmental model. Moreover, in contrast to the arteries, there is free circulation throughout the venous system, with ample anastomoses between the veins. These anastomoses, therefore, prevent parenchymal congestion and ischemia in case of venous injury [7].

The small veins of the cortex, called stellate veins, drain into the interlobular veins that form a series of arches (Figure 6.12). Within the kidney substance, these arches are arranged in arcades, which lie mainly in the longitudinal axis. There are usually three systems of longitudinal anastomotic arcades and the anastomoses occur at different levels: between the stellate veins (more peripherally), between the arcuate veins (at the base of the pyramids), and between the interlobar (infundibular) veins (close to the renal sinus) (Figure 6.12). We have named these anastomoses as first order, second order, and third order, from periphery to center [7]. In early studies, we found three trunks (53.8%) and two trunks (28.8%) joining each other to form the main renal vein. Less frequently, we found four trunks (15.4%) and five trunks (1.9%) [7].

A detailed description of the kidney collecting system (the pelviocalyceal system), as well as the anatomic relationships between the intrarenal arteries and veins with

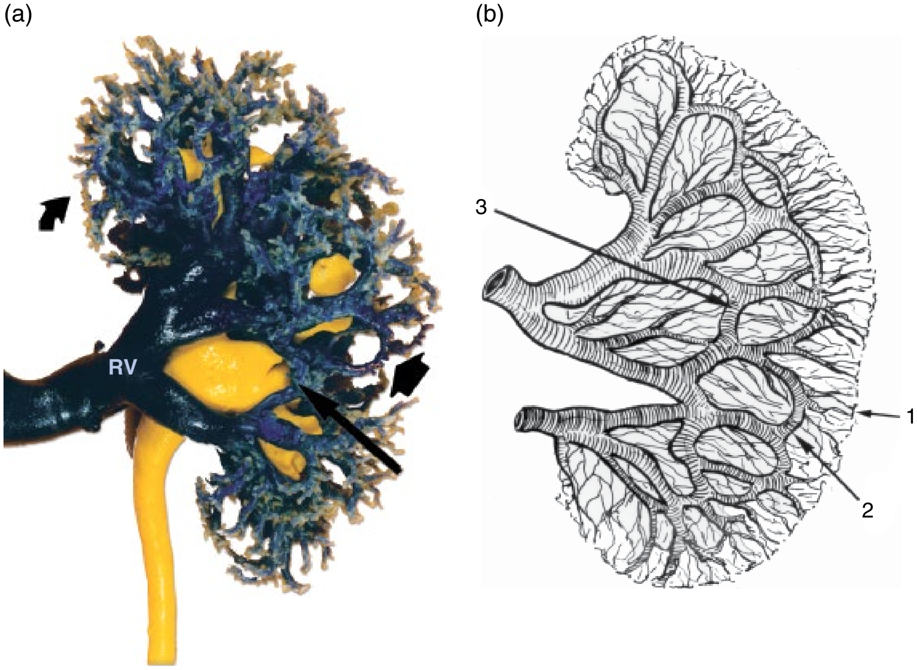

**Figure 6.12** (a) Anterior view of a left kidney endocast of the pelviocalyceal system together with the venous vascular tree. This shows the three systems of longitudinal anastomotic arcades; from lateral (periphery) to medial (hilar): stellate veins (curved arrow), arcuate veins (short arrow), and interlobar veins (long arrow). RV, renal vein. (b) Schematic showing the three orders of arcades: 1, first-order arcade; 2, second-order arcade; 3, third-order arcade.

the kidney collecting system, which are of utmost importance for endourology, is given below.

## Pelvicocalyceal system: endourologic implications

### Anatomic classification

Recent advances in endourology have revived interest in collecting system anatomy, since a full understanding of such anatomy is necessary to perform reliable endourologic procedures as well as uroradiologic analysis [8–10]. We have proposed a pelviocalyceal classification, including all morphologic types of collecting systems, which we believe is helpful for standardizing patients and procedures [9]. This classification was derived from the analysis of 140 three-dimensional (3D) polyester resin corrosion endocasts of the pelviocalyceal system (Figure 6.13), obtained from 70 fresh cadavers according to a technique described previously [8].

#### Basic intrarenal anatomy

The renal parenchyma basically consists of two kinds of tissue, the cortical tissue and medullar tissue. On a longitudinal section (Figure 6.14), the cortex forms the external layer of renal parenchyma. The renal medulla is formed by several inverted cones, surrounded by a layer of cortical tissue on all sides (except at the apices). As in longitudinal sections, a cone assumes the shape of a pyramid (Figure 6.14) and the established term for the medullar tissue is renal pyramid; the apex of this pyramid is termed the renal papilla. The layers of cortical tissue between adjacent pyramids are termed renal columns (cortical columns of Bertin; Figure 6.14) [8, 10].

The cortical tissue is made up of the glomeruli with proximal and distal convoluted tubules. The renal pyramids are made up of loops of Henle and collecting ducts; these ducts join to form the papillary ducts (about 20), which open at the papillary surface (area cribosa; Figure 6.15) and drain urine into the collecting system (into the fornix of a minor calyx).

A minor calyx is defined as the calyx that is in immediate apposition to a papilla (Figures 6.14 and 6.15). The renal minor calyces drain the renal papillae and range in number from 5 to 14 (mean, 8); we have found 70% of kidneys to have 7–9 minor calyces [8]. A minor calyx may be single (drains one papilla) or compound (drains two or three papillae) (Figures 6.13 and 6.15). The polar calyces are often compound, markedly in the superior pole (Figure 6.13). The minor calyces may drain straight into an infundibulum or join to form major calyces, which subsequently will drain into an infundibulum (Figures 6.13 and 6.15). Finally, the infundibula, which are considered the primary divisions of the pelviocalyceal system, drain into the renal pelvis.

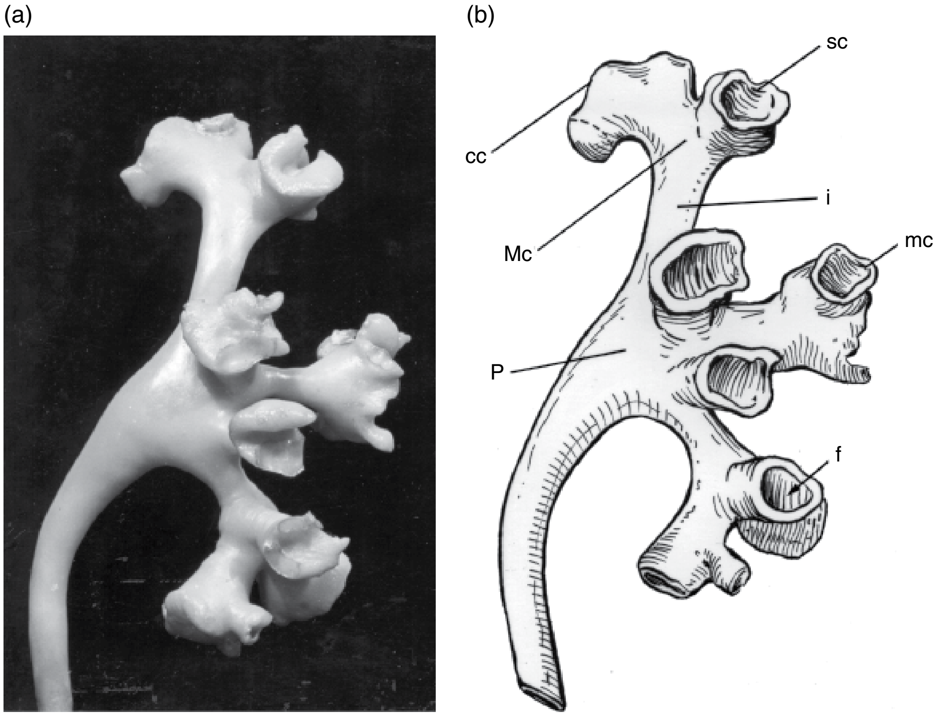

**Figure 6.13** (a) Anterior view of a pelviocalyceal endocast from a left kidney, obtained according to the injection–corrosion technique. (b) Schematic of the endocast shown in (a). This shows the essential elements of the kidney collecting system. cc, compound calyx; sc, single calyx; mc, minor calyx; Mc, major calyx; f, calyceal fornix; i, infundibulum; P, renal pelvis. Reproduced with permission of Georg Theim Verlag KG.

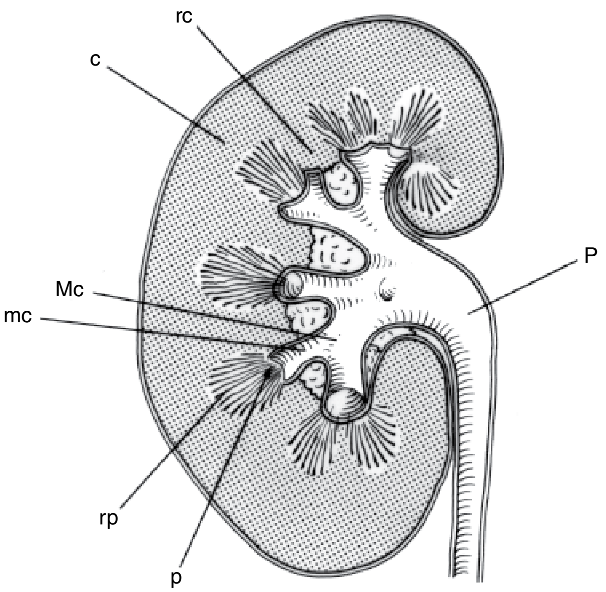

**Figure 6.14** Schematic of a longitudinal section of the kidney. This shows the intrarenal structures. c, renal cortex; rc, renal column (cortical column of Bertin); rp, renal pyramid; p, renal papilla; mc, minor calyx; Mc, major calyx; P, renal pelvis. Reproduced with permission of Georg Theim Verlag KG.

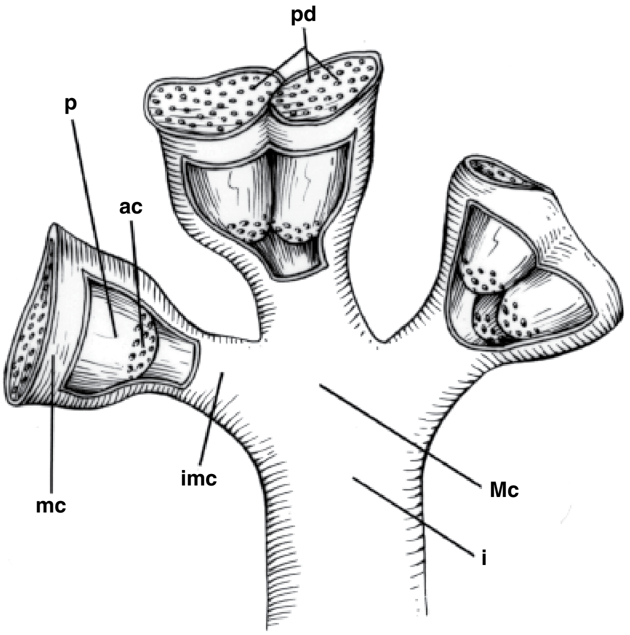

**Figure 6.15** Schematic representation of the possible minor calyx (mc) arrangements. A single mc drains only one papilla and a compound mc drains two or three papillae. p, renal papilla; pd, papillary ducts; ac, area cribosa; Mc, major calyx; imc, infundibulum of a mc (calyceal neck); i, infundibulum. Reproduced with permission of Georg Theim Verlag KG.

### Classification of the pelviocalyceal system

The analysis of 140 endocasts led us to a division into two major groups (with two intermediate varieties in each major group). This division was based on superior pole, inferior pole, and kidney midzone (hilar) calyceal drainage.

*Group A* is composed of pelviocalyceal systems that have two major calyceal groups (superior and inferior) as a primary division of the renal pelvis and a midzone calyceal drainage dependent on these two major groups (62.2%) (Figure 6.16). Group A includes two different types of pelviocalyceal system:

- Type A-I (45%): the kidney midzone is drained by minor calyces that are dependent on the superior and/or inferior calyceal groups (Figure 6.16a).
- Type A-II (17.2%): the kidney midzone is drained simultaneously by crossed calyces, one draining into the superior calyceal group and the other draining into the inferior calyceal group (Figure 6.16b). When we analyzed the endocasts with crossed calyces in the kidney midzone, we observed that the crossed calyces (laterally) and the renal pelvis (medially) bound a region (space) that we designated the "interpelviocalyceal" (IPC) region (space) (Figure 6.16b).

*Group B* is composed of pelviocalyceal systems with kidney midzone (hilar) calyceal drainage independent of both the superior and inferior calyceal groups (37.8%) (Figure 6.17). This group also includes two different types of pelviocalyceal system:

- Type B-I (21.4%): the kidney midzone is drained by a major calyceal group, independent of both the superior and the inferior groups (Figure 6.17a).
- Type B-II (16.4%): the kidney midzone is drained by minor calyces (one to four) entering directly into the renal pelvis (Figure 6.17b). Such calyces are independent of both the superior and inferior calyceal groups.

The kidney collecting system is very variable and is not symmetrical. We found pelviocalyceal systems with morphologic bilateral symmetry in the same individual in only 37.1% of the cases (26 pairs of kidneys).

Although our pelviocalyceal classification includes all morphologic types of calyces and renal pelvices, in performing endourologic procedures it is important to be aware that the collecting system anatomy is very variable. The endocast in Figure 6.18a, for example, reveals a very long and thin superior calyceal infundibulum; this anatomic formation will certainly cause difficulties in the introduction and manipulation of a nephroscope into the superior pole collecting system. The endocast in Figure 6.18b shows just the opposite aspect (both superior and inferior calyceal infundibula are short and thick); this anatomic formation will certainly make it easier to introduce and manipulate a nephroscope within the superior and inferior collecting systems.

## Comparative analysis between pyelograms and the corresponding 3D collecting system endocasts

Since standard urograms (pyelograms) show the collecting system in only one plane, it is extremely difficult for the practitioner to visualize and imagine this system in three dimensions. A full understanding of pelviocalyceal anatomy is a prerequisite for successful endourologic

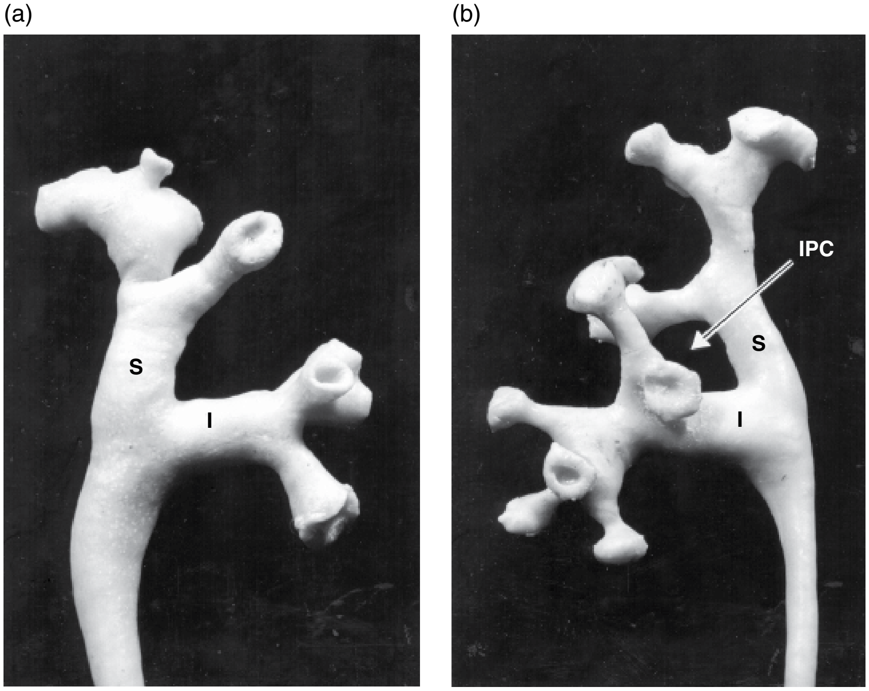

**Figure 6.16** View of the two morphologic types of pelviocalyceal systems that compose Group A. (a) Type A-I: anterior view of a left pelviocalyceal endocast shows the kidney midzone drained by calyces dependent on the superior (S) and inferior (I) calyceal groups. (b) Type A-II: anterior view of a right pelviocalyceal cast shows the kidney midzone drained by crossed calyces, dependent simultaneously on the superior (S) and inferior (I) calyceal group. This endocast shows the interpelviocalyceal (IPC) space. Reproduced with permission of Georg Theim Verlag KG.

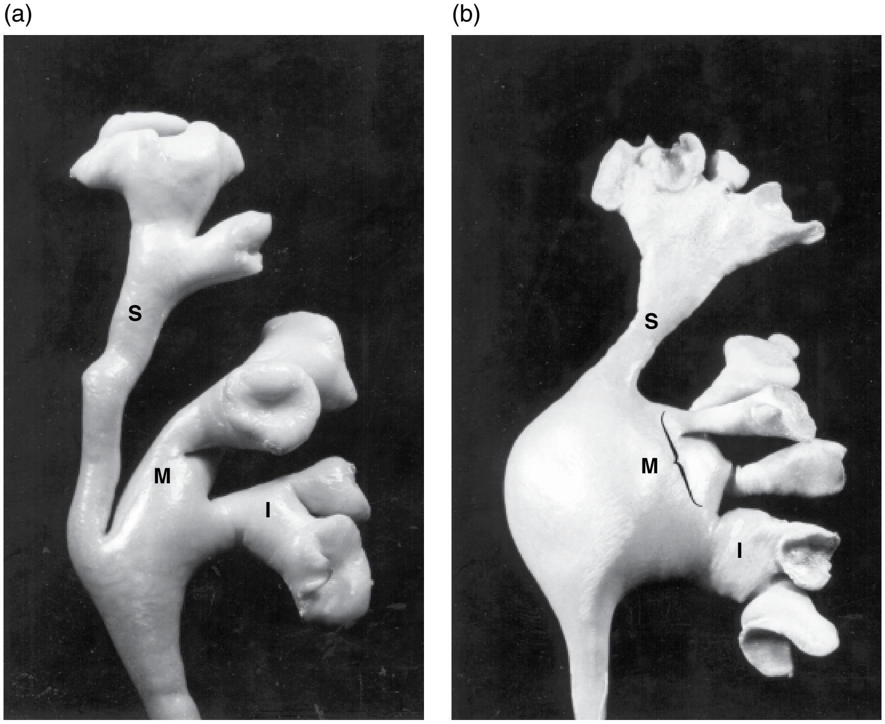

**Figure 6.17** View of the two morphologic types of pelviocalyceal systems that comprise Group B. (a) Type B-I: anterior view of a left pelviocalyceal endocast shows the kidney midzone drained by a hilar major calyx (M), independently of the superior (S) and inferior (I) major calyces. (b) Type B-II: anterior view of a left pelviocalyceal endocast shows the kidney midzone drained by minor calyces (M) entering directly into the renal pelvis, independently of both the superior (S) and inferior (I) calyceal groups. Reproduced with permission of Georg Theim Verlag KG.

interventions in the upper urinary tract, as well as for interpreting fluoroscopy pyelograms and other imaging examinations.

To assist endourologists in forming a mental image of the collecting system in three dimensions and learning the exact spatial position of the calyces, before obtaining the pelviocalyceal system endocast, iodinated contrast was injected into the ureter of 40 of our cases to opacify the collecting system to obtain a pyelogram. After radiography, the contrast was removed and the collecting system was filled with a polyester resin to obtain a 3D endocast. These 40 kidneys enabled a comparative study between the radiographic images and their corresponding 3D endocasts. This identified some remarkable anatomic aspects of the kidney collecting system that need to be considered during endourologic procedures.

### Presence of perpendicular minor calyces

In 11.4% of the endocasts (16 of 140) we found a perpendicular minor calyx draining directly into the renal pelvis or into a major calyx (Figure 6.19). The minor calyces perpendicular to the surface of the collecting system, which are seen in the endocasts, can be superimposed on other structures, which means their visualization radiographically can be difficult (Figure 6.20). Stones in such minor calyces viewed on standard anteroposterior radiographic images can appear as if they were placed in the pelvis or a major calyx. Thus, this anatomic detail must be considered in cases of stones that do not alter renal function and can appear as if they are in the renal pelvis or a major calyx. In this situation, a complementary radiologic study with lateral and oblique films must be performed to determine accurately the position and extent of the stones [11, 12].

When a stone is located in a perpendicular minor calyx (Figure 6.19), its removal presents additional difficulties for both extracorporeal shock-wave lithotripsy (ESWL) and percutaneous nephrolithotripsy (PCNL). Patients with stones in such calyces are not good candidates for ESWL because these calyces invariably present narrow infundibula (<4 mm in diameter); therefore, discharge of the disintegrated stone fragments will be difficult [13, 14]. Regarding percutaneous removal, direct access into the calyx containing the stone is easy; nevertheless, it involves a puncture without consideration of the arterial and venous anatomic relationships to the collecting system, which carries a high risk of injuring a vascular structure [12]. Therefore, in cases of stone in such calyces, safe access, techniques, and instruments should be used.

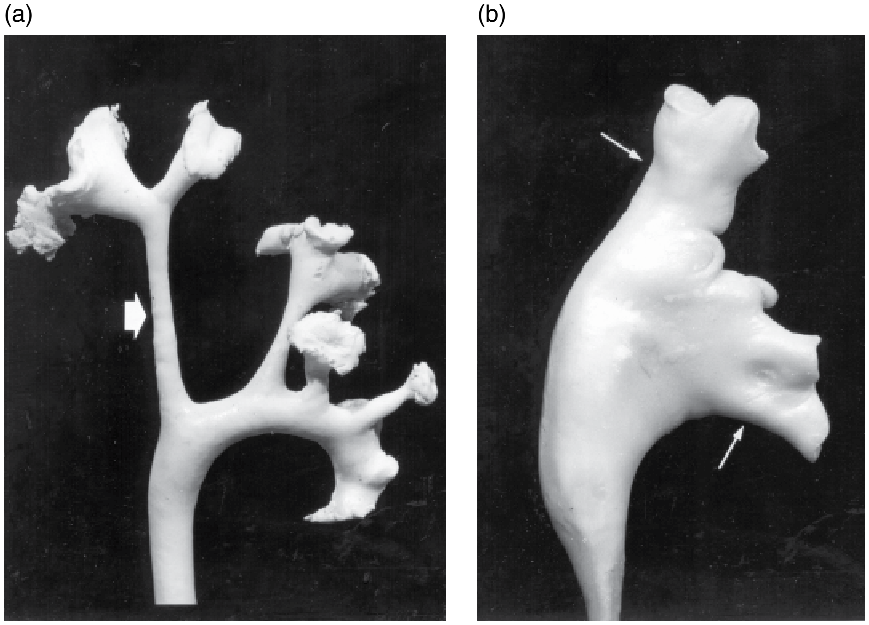

**Figure 6.18** Anterior view of two left pelviocalyceal endocasts, one showing a long and thin superior calyceal infundibulum (arrow) (a) and the other a short and thick superior and inferior calyceal infundibula (arrows) (b). Reproduced with permission of Georg Theim Verlag KG.

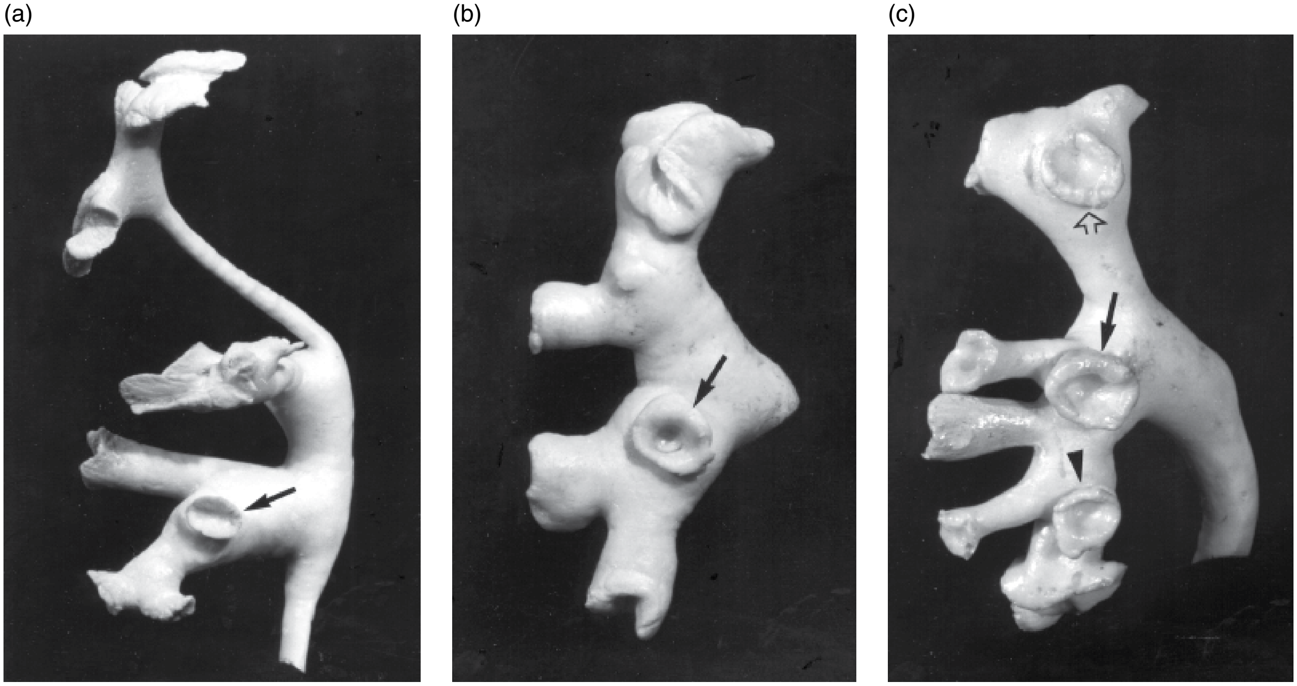

**Figure 6.19** Anterior views of a right pelviocalyceal endocast showing (a) a perpendicular minor calyx draining into the inferior calyceal group (arrow); (b) into the inferior calyceal group (arrow), very close to the renal pelvis; and (c) into the renal pelvis (arrow). This latter endocast also shows a perpendicular minor calyx draining into the superior calyceal group (open arrow) and a perpendicular minor calyx draining into the inferior calyceal group (arrowhead). Reproduced with permission of Georg Theim Verlag KG.

**Crossed calyces**

In 17.2% of the endocasts, the kidney midzone (hilar) was drained simultaneously by crossed calyces, one draining into the superior calyceal group and the other into the inferior calyceal group. On the pyelograms, the crossed calyces (laterally) and the renal pelvis (medially) outlined a radiotransparent region that we termed the interpelviocalyceal region (Figure 6.20a). In the 3D endocasts, that same region appeared as a space (Figure 6.20b) [9, 11, 12].

The interpelviocalyceal space may have different shapes: lozenge-like (the most common), long and narrow, and even small and round, depending on the shape of the

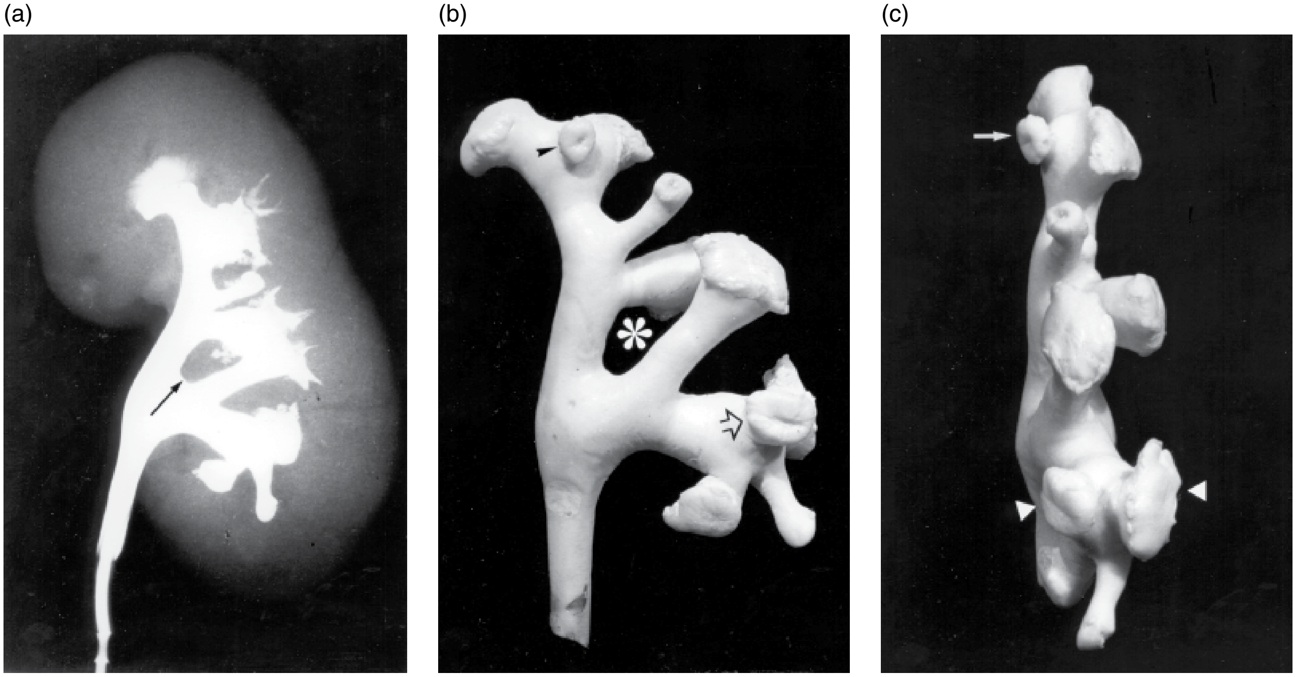

**Figure 6.20** Comparative study between radiographic view of a left kidney and its corresponding 3D endocast. (a) Anterior view of a retrograde pyelogram shows a radiographic image of the interpelviocalyceal region (arrow). (b) Anterior view of the corresponding 3D endocast. The asterisk denotes the interpelviocalyceal space; the arrowhead points to a minor calyx perpendicular to and superimposed on the surface of a superior major calyx, which cannot be seen on the pyelogram; and the open arrow points to an anterior minor calyx superimposed on the posterior minor calyx. It can be difficult to make the distinction between these features on a pyelogram. (c) Oblique view of the same endocast as in (b). The arrow points to a perpendicular minor calyx in the superior calyceal group; and arrowheads to the distinction between the anterior and posterior minor calyces, which are superimposed on the pyelogram. Reproduced with permission of Georg Theim Verlag KG.

calyces and the shape of the renal pelvis (Figure 6.21). Regardless of the form assumed by the interpelviocalyceal space, it is the result of crossed calyces in the mid kidney.

When the crossed calyces were in the mid kidney, the calyx draining into the inferior calyceal group was in the ventral position in 87.5% of the endocasts [9, 11, 12] (Figure 6.22). In some cases, even when radiographically the calyx draining into the inferior group was apparently in the dorsal position, we verified its ventral position on the endocast (Figure 6.22). This constant spatial arrangement is noteworthy for endourologic maneuvers. If the intention is to access the renal pelvis via a crossed calyx or to access a crossed calyx via the renal pelvis, it is useful to remember that the calyx draining into the inferior calyceal group is almost always in the ventral position. It is also worthy of remark that detection of an interpelviocalyceal region on the pyelograms is an indirect sign of crossed calyces in the kidney midzone.

### Position of the calyces relative to the lateral kidney margin

In 39 of the 140 endocasts (27.8%), the anterior calyces had a more lateral (peripheral) position than the posterior calyces (Figure 6.23). In 27 endocasts (19.3%), the posterior calyces were in a more lateral position than the anterior calyces (Figure 6.24). In the majority of the endocasts (74; 52.9%), the anterior and posterior calyces had varied positions: superimposed or alternately distributed (in one region the most lateral were the anterior calyces, and in another, the posterior calyces) (Figure 6.25).

Since the first choice of access to the collecting system is through a posterior calyx, much effort has been made to determine preoperatively which calyces are anterior and which posterior. Previous studies have presented contradictory results and lead to misunderstanding of this subject [15]. We have described the type of kidney collecting system found in the majority of the endocasts, in which the calyces are disposed in various positions (superimposed or alternately distributed), and can affirm that the position of the calyces cannot be defined as more lateral or more medial. Considering the large variation of position of the calyces (>50% in different positions), we believe that precise determination of calyceal position is difficult with the common radiologic methods, even using oblique and lateral views [9, 11]. To solve this problem quickly and inexpensively, during endourologic procedures, with the patient in the prone position, room air should be injected into the collecting system and this will rise to the more posterior portions of the collecting system, determining which calyces are located posteriorly (radiolucent contrast) [11, 12, 16].

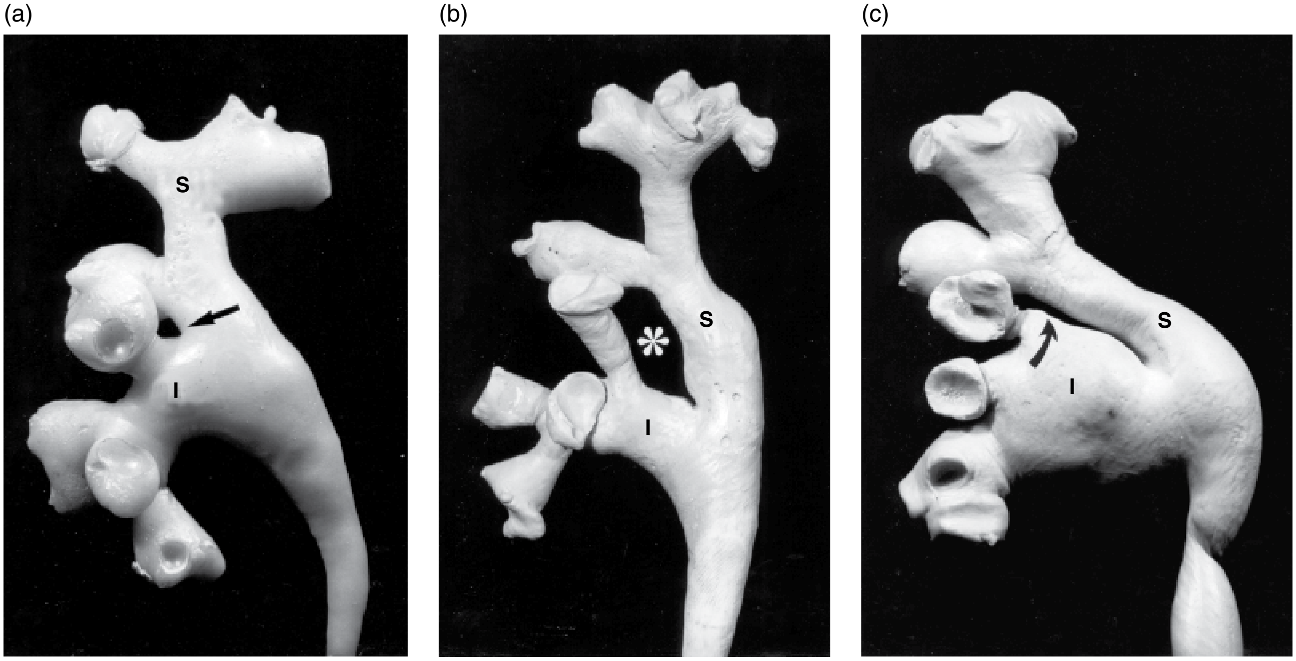

**Figure 6.21** Anterior view of right pelviocalyceal endocasts. This shows the different shapes that the interpelviocalyceal (IPC) space may assume: (a) small and round IPC space (arrow); (b) lozenge-like IPC space (most common shape) (asterisk); (c) long and narrow IPC space (curved arrow). S, superior calyceal group; I, inferior calyceal group. Reproduced with permission of Georg Theim Verlag KG.

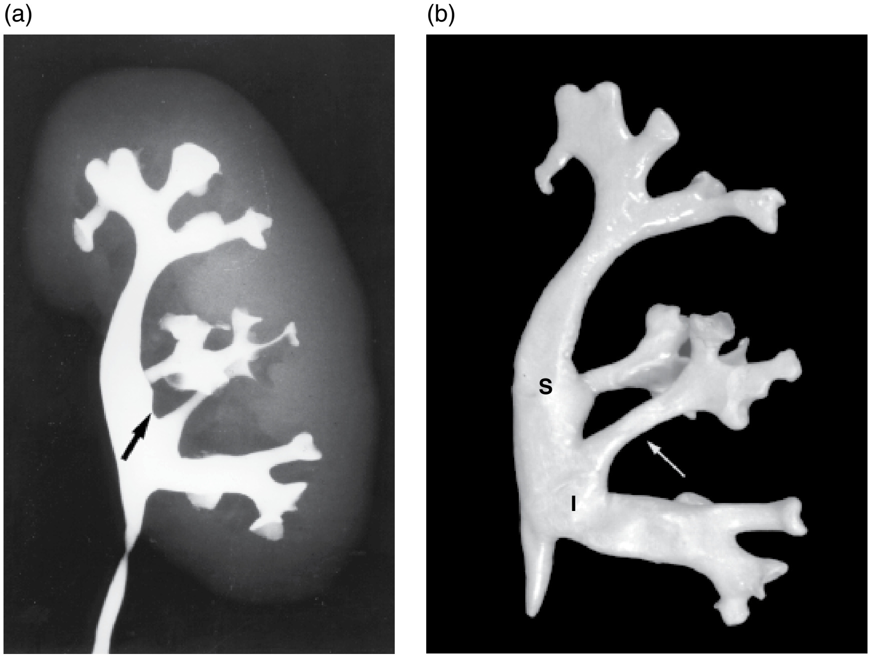

**Figure 6.22** Comparative study between a retrograde pyelogram of a left kidney and its corresponding 3D endocast of the pelviocalyceal system. (a) Anterior view of a retrograde pyelogram shows the radiographic image of the interpelviocalyceal (IPC) region (arrow). (b) Anterior view of the corresponding 3D endocast. The arrow points to the calyx which is draining into the inferior calyceal group in the ventral position (87.7% of the endocasts of the IPC space). S, superior calyceal group; I, inferior calyceal group. Reproduced with permission of Georg Theim Verlag KG.

### Position of the calyces relative to the polar regions and kidney midzone

The superior pole was drained by a midline calyceal infundibulum in 98.6% of the endocasts (Figure 6.26). The midzone (hilar) was drained by paired calyces that were arranged in two rows (anterior and posterior) in 95.7% of the endocasts (Figure 6.26). The inferior pole was drained by paired calyces arranged in two rows in 81 endocasts (57.9%) (Figure 6.26a) and by a single midline calyceal infundibulum in 59 endocasts (42.1%) (Figure 6.26b).

With regard to the calyceal drainage of the kidney polar regions, many investigators have affirmed that there usually is only one calyceal infundibulum draining

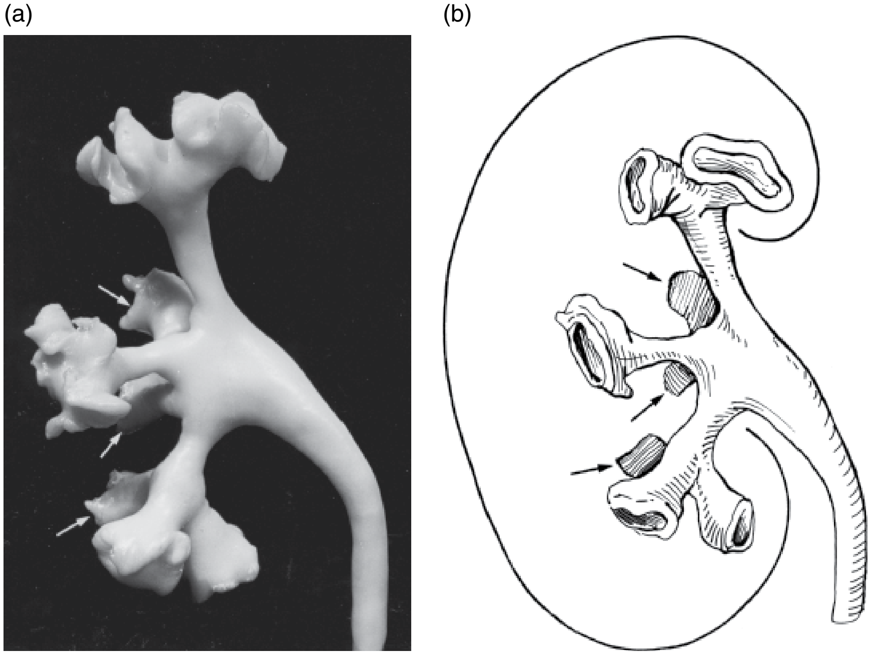

**Figure 6.23** Position of the calyces relative to the lateral margin of the kidney. (a) Anterior view of a right pelviocalyceal endocast, which shows the anterior calyces have a more lateral (peripheral) position than the posterior calyces (arrows). This means that the posterior calyces are located medially. (b) Schematic of the endocast shown in (a). This shows the peripheral calyces in the anterior plane and the medial calyces (arrows) in the posterior plane. Reproduced with permission of Georg Theim Verlag KG.

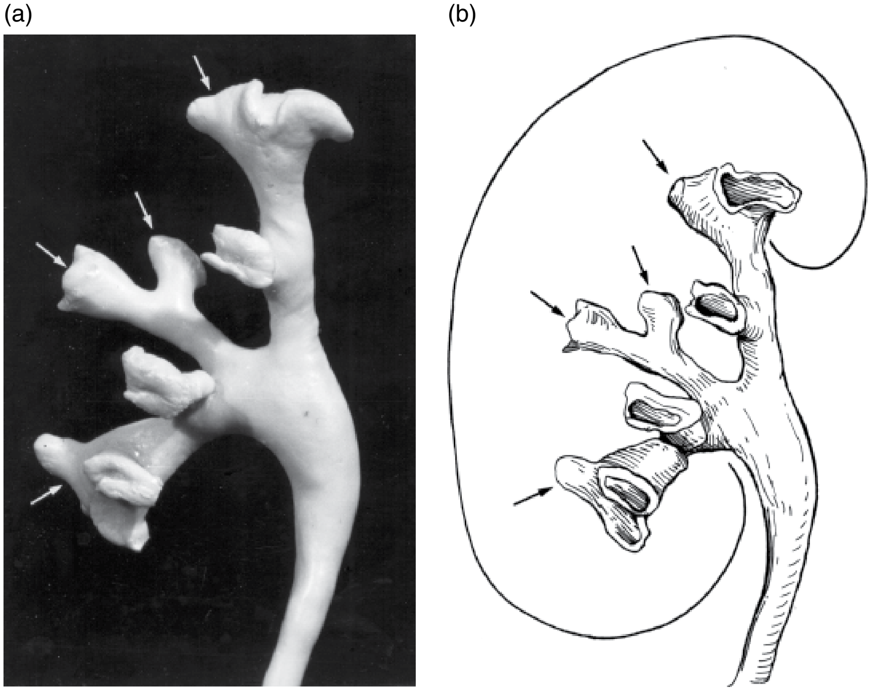

**Figure 6.24** Position of the calyces relative to the lateral margin of the kidney. (a) Anterior view of a right pelviocalyceal endocast. This shows that the posterior calyces (arrows) have a more lateral (peripheral) position than the anterior calyces. (b) Schematic of the endocast shown in (a). This shows the peripheral calyces in the posterior plane (arrows) and the medial calyces in the anterior plane. Reproduced with permission of Georg Theim Verlag KG.

each pole [3, 10, 14]. In our study, the superior pole was drained by only one midline calyceal infundibulum in 98.6% of the endocasts. However, the inferior pole was drained by paired calyces arranged in two rows in 81 of the 140 endocasts (57.9%) and by one midline calyceal infundibulum in 59 endocasts (42.1%) (Figure 6.26). These results are important in endourology; it will be easier to access endoscopically a polar region drained by a single infundibulum, which usually has a suitable diameter, rather than a polar region drained by paired calyces (Figure 6.26). Because the inferior pole is drained by paired calyces in 57.9% of the endocasts, this anatomic detail must be kept in mind, both to plan and perform the intrarenal access and endoscopic procedures in the inferior pole. The calyceal drainage of superior and inferior poles is also of utmost importance in ESWL [13, 17]. Concerning the kidney midzone (hilar) drainage, our results show that this region is drained by paired calyces

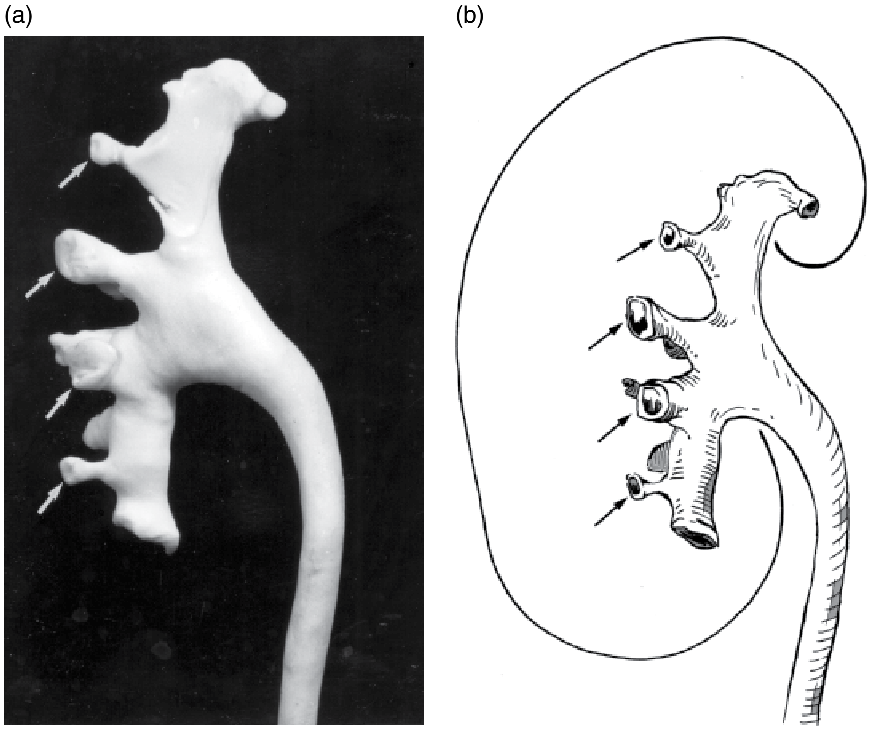

**Figure 6.25** Position of the calyces relative to the lateral margin of the kidney. (a) Anterior view of a right pelviocalyceal endocast, and (b) schematic of this endocast. The calyces in the anterior plane (arrows) are located alternately relative to the lateral margin of the kidney, i.e. in one region they are more lateral and in another they are more medial. Reproduced with permission of Georg Theim Verlag KG.

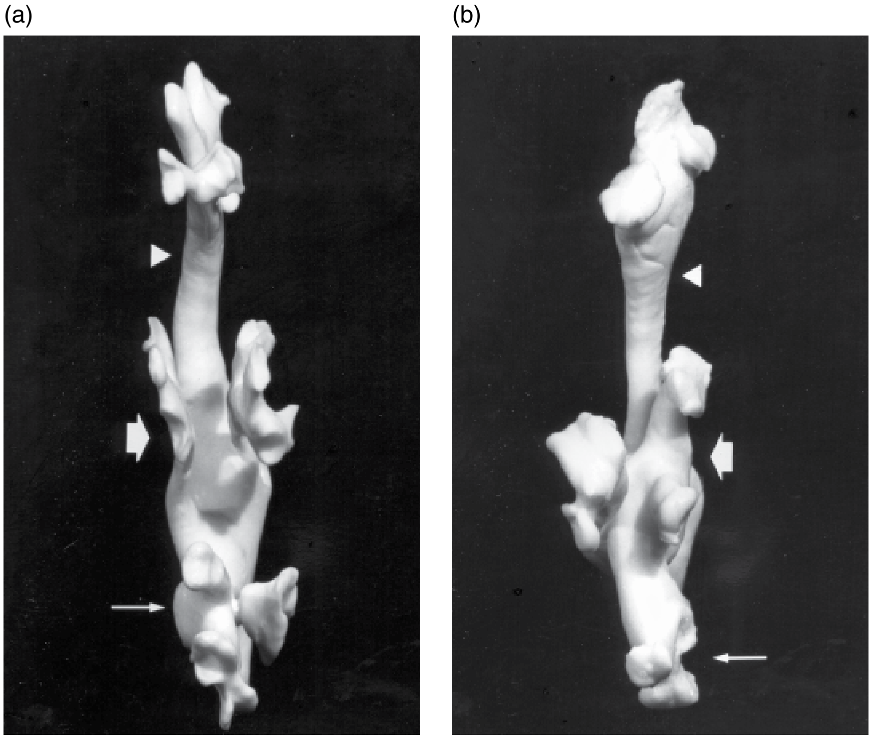

**Figure 6.26** Position of calyces relative to the polar regions and kidney midzone. (a) Lateral view of a left pelviocalyceal endocast. The superior pole is drained by a single midline calyceal infundibulum (arrowhead). The midzone (hilar) is drained by paired calyces arranged in two rows (short arrow); anterior and posterior. The inferior pole is drained by paired calyces arranged in two rows (long arrow). (b) Lateral view of a right pelviocalyceal endocast. The superior pole is drained by a single midline calyceal infundibulum (arrowhead). The midzone is drained by paired calyces arranged in two rows (short arrow); anterior and posterior. The inferior pole is drained by only one midline calyceal infundibulum (long arrow). Reproduced with permission of Georg Theim Verlag KG.

arranged in two rows (anterior and posterior) in 95.7% of the endocasts (Figure 6.26), which is of relevance to endourologists accessing and treating the mid kidney.

## Anatomic relationship of intrarenal vessels (arteries and veins) with the kidney collecting system: importance for puncture intrarenal access

Percutaneous nephrostomy is the procedure of choice for temporary drainage of urine and for gaining access to the kidney during numerous endourologic and interventional procedures. The development of new percutaneous techniques, as well as a variety of instruments, has enabled the replacement of several open surgeries by percutaneous therapy (renal abscess, calyceal diverticulum, infundibular stenosis, ureteropelvic junction obstruction, some cases of upper tract urothelial tumors, etc.) [18–20]. Percutaneous procedures are relatively invasive and complications may occur. One of the most significant complications is vascular injury that occurs when the urologist is obtaining intrarenal access. This problem may have several consequences, including intraoperative hemorrhage, hypotension, loss of functioning renal parenchyma, arteriovenous fistula, and pseudoaneurysm [21–25].

The goal of this section is to offer a detailed anatomic depiction of the intrarenal vessels and their relationships to the collecting system, and show how to perform safe percutaneous intrarenal access by keeping as many renal vessels as possible intact during puncture.

We analyzed 62 retrograde pyelograms and their corresponding 3D polyester resin corrosion endocasts of the kidney collecting system, together with the intrarenal arteries and veins, obtained from fresh cadavers.

The kidneys were punctured under fluoroscopic guidance and the endocasts obtained with needles positioned at the site of puncture (Figure 6.27). For comparative analysis, we studied kidneys that had been punctured through a calyceal infundibulum and kidneys punctured through a calyceal fornix.

### Intrarenal access through an infundibulum

Figure 6.13 shows the basic anatomy of the renal collecting system. Keeping those anatomic landmarks in mind, note that a puncture through an infundibulum (in any region of the kidney) presents clear hazards [26].

#### Superior pole

Puncture is most dangerous through the upper pole infundibulum because this region is surrounded almost completely by large vessels (Figure 6.28). Infundibular arteries and veins course parallel to the anterior and posterior aspects of the upper pole infundibulum. In our series, injury to an interlobar (infundibular) vessel was a common consequence of puncturing the upper pole infundibulum (67% of kidneys) (Figure 6.29); the injured vessel was an artery in 26% of those cases.

The most serious vascular accident in upper infundibulum puncture is lesion of the posterior segmental artery (retropelvic artery). This event may occur because this artery was crossed by and is related to the posterior surface of the upper infundibulum in 57% of the endocasts (Figure 6.30) [27]. Figure 6.31 shows an upper infundibulum puncture in which the needle tract produced complete laceration of the posterior segmental artery.

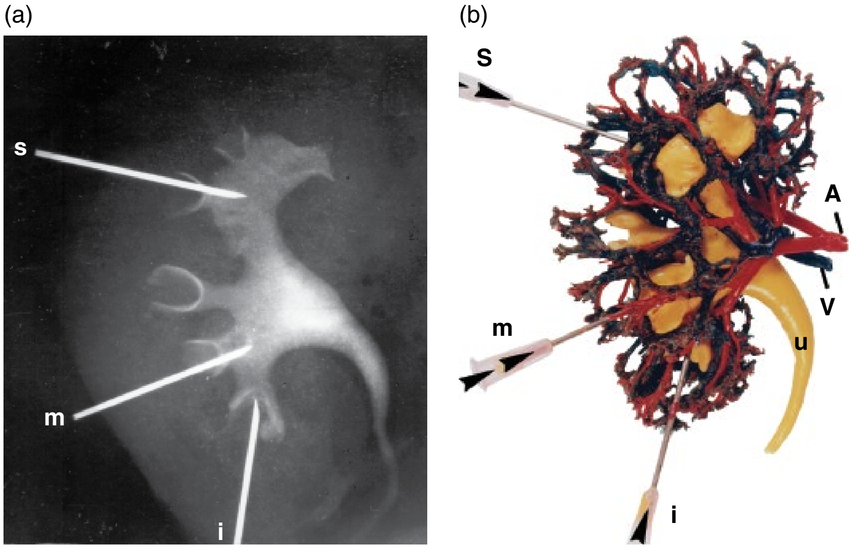

**Figure 6.27** (a) Anterior view of a retrograde pyelogram from a right kidney showing the superior pole (s), mid kidney (m), and inferior pole (i) punctures. These punctures were performed after polyester resin injections into the arterial and venous systems, while the resins were still in the gel state. Note that the injected resins are not opaque to X-rays. (b) Posterior view of the corresponding corrosion endocast obtained after contrast removal and pelviocalyceal system injection with resin. The needles are maintained in their original places. s, superior pole puncture; m, mid kidney puncture; i, inferior pole puncture. The arrowheads show the tracts of the needles. A, renal artery; V, renal vein; u, ureter. Reproduced with permission of Elsevier.

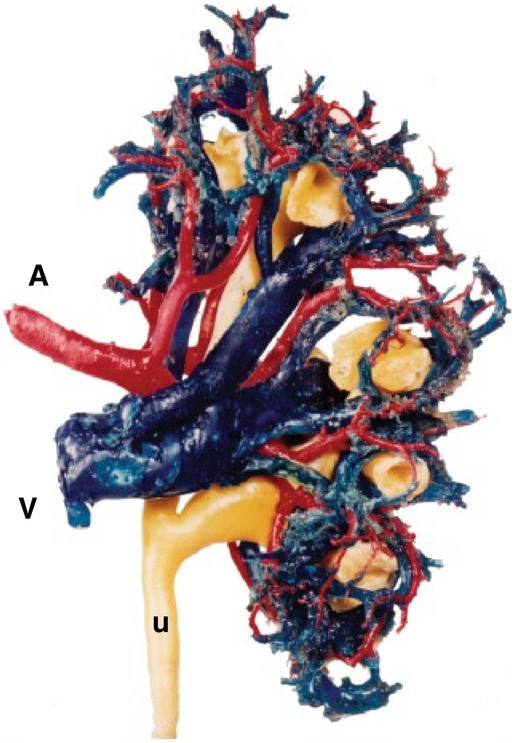

**Figure 6.28** Oblique medial view of an endocast of arterial (A), venous (V), and pelviocalyceal systems from a left kidney. This shows the upper infundibulum almost completely encircled by infundibular arteries and veins. This anatomic arrangement makes upper pole infundibular puncture especially dangerous. A, renal artery; V, renal vein; u, ureter. Reproduced with permission of Elsevier.

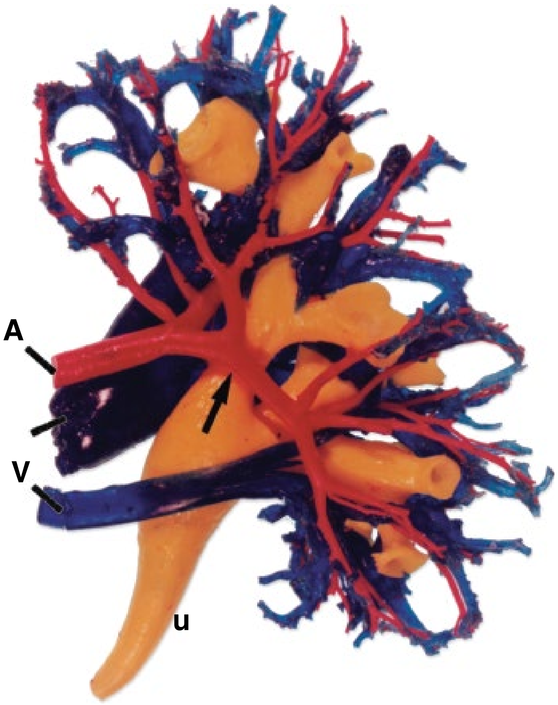

**Figure 6.30** Posterior view of an endocast from a right kidney. This shows the posterior segmental artery (retropelvic artery) crossing the posterior surface of the upper infundibulum (arrow). A, renal artery; V, renal vein; u, ureter. Reproduced with permission of Elsevier.

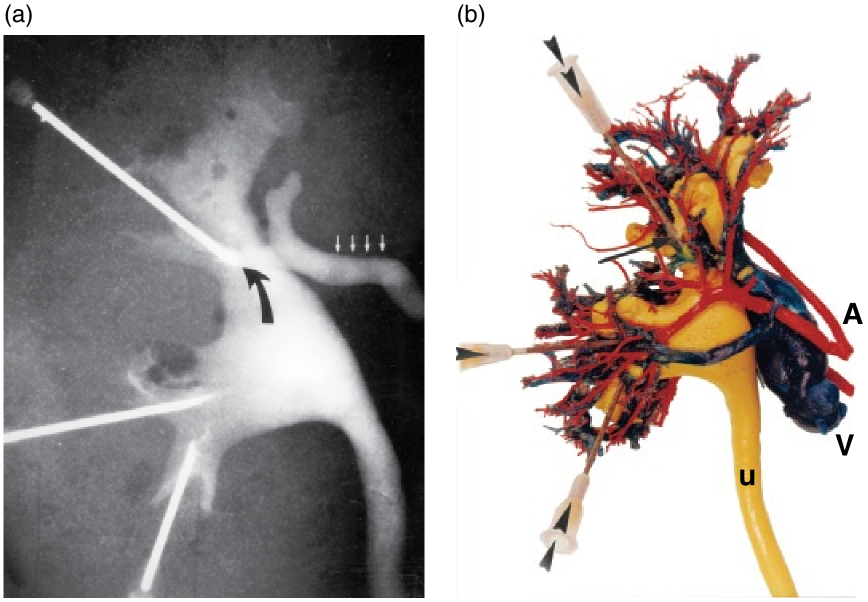

**Figure 6.29** (a) Posterior view of a retrograde pyelogram from a left kidney. Puncture performed through the upper infundibulum has injured an infundibular vein (curved arrow). Note the contrast in the retropelvic vein (short arrows).
(b) Posterior view of the corresponding endocast reveals the site of the lesion (arrow). Arrowheads show the needle tracts. A, renal artery; V, renal vein; u, ureter. Reproduced with permission of Elsevier.

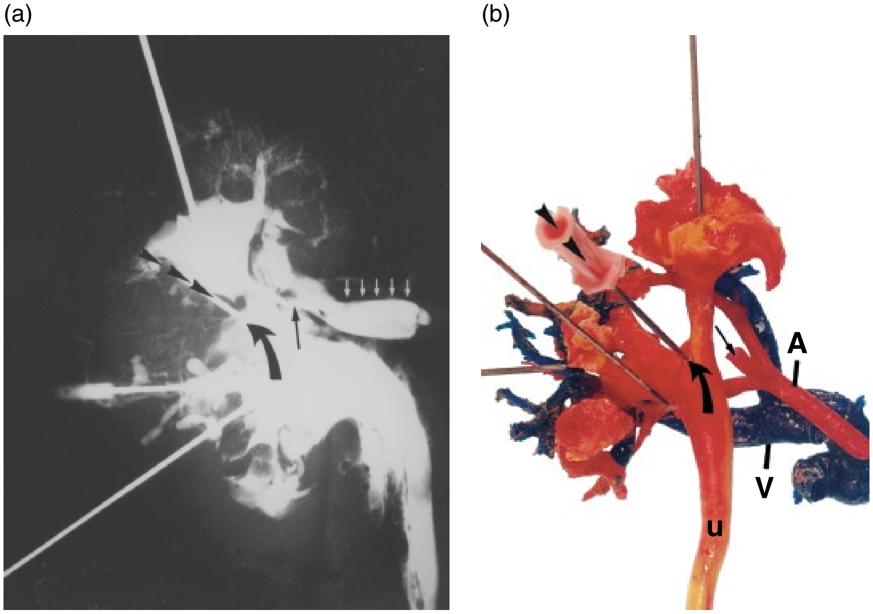

**Figure 6.31** (a) Posterior view of a retrograde pyelogram from a left kidney. This shows contrast extravasation, and contrast in the arterial system and main trunk of the renal artery (short arrows). The retropelvic artery was injured by the needle (needle tracts shown by the arrowheads). The curved arrow points to the site of the lesion; the long arrow points to the retropelvic artery filled with contrast extravasated from the collecting system. (b) Posterior view of the corresponding endocast. This shows the divided retropelvic artery (arrow) and the needle (arrowheads) responsible for the lesion (curved arrow). A, renal artery; V, renal vein; u, ureter. Reproduced with permission of Elsevier.

Because the posterior segmental artery (retropelvic artery) may supply up to 50% of the renal parenchyma, injury to it may result in significant loss of functioning renal tissue, as well as causing hemorrhage [28].

### Middle kidney

Intrarenal access through the mid kidney infundibulum caused arterial lesion in 23% of the kidneys studied. The middle branch of the posterior segmental artery was injured more often than any other vessel.

### Inferior pole

The posterior aspect of the lower pole infundibulum is widely presumed by endourologists and interventional radiologists to be free of arteries. It is considered, therefore, to be a safe region through which to gain access to the collecting system and to place a nephrostomy tube. In about 38% of the kidneys examined, however, an infundibular artery was found in this region [27]. Thus, significant complications may develop as a consequence of a posterior approach through the supposedly vessel-free lower infundibulum [22, 25, 26]. We found an arterial injury in 13% of kidneys we had punctured through the lower pole infundibulum.

Concerning the veins, we found large venous anastomoses, similar to collars, around the calyceal infundibula (the so-called calyceal necks) in many of the kidneys we studied [7]. Puncture through the lower pole infundibulum therefore also risks injury to a venous arcade (Figure 6.32). A venous lesion usually heals spontaneously, but consequent hemorrhage may be problematic during the procedure.

Our findings clearly demonstrate that percutaneous nephrostomy through an infundibulum of a calyx is not a safe route, because this type of access poses an important risk of significant bleeding from interlobar (infundibular) vessels.

Infundibular puncture also creates the hazard of through-and-through (two-wall) puncture of the collecting system (Figure 6.33). Because major segmental branches of the renal artery, as well as major tributaries of the renal vein, are positioned on the anterior surface of the renal pelvis, marked hemorrhage may occur as a result of an anterior through-and-through perforation. In addition, effective tamponade of injured anterior vessels is difficult because they lie distantly in the nephrostomy tract [24, 26, 29].

Although infundibular access is feasible in some circumstances and must be considered in specific situations (e.g. some difficult anatomic cases), the surgeon must evaluate the risk of an arterial lesion, primarily in the superior pole and in the mid kidney [24].

## Intrarenal access through the renal pelvis

Direct puncture of the renal pelvis for endourologic surgery should never be performed. Besides the fact that the nephrostomy tube inserted at this site is easily dislodged and difficult to reintroduce during the operative maneuvers, renal pelvis puncture has a prohibitive and unnecessary risk of injuring a retropelvic vessel (artery and/or vein) [7, 22, 27].

## Intrarenal access through a calyceal fornix

When we made a puncture through a fornix of a calyx, venous injury occurred in fewer than 8% of the kidneys. These injuries occurred indiscriminately in the upper

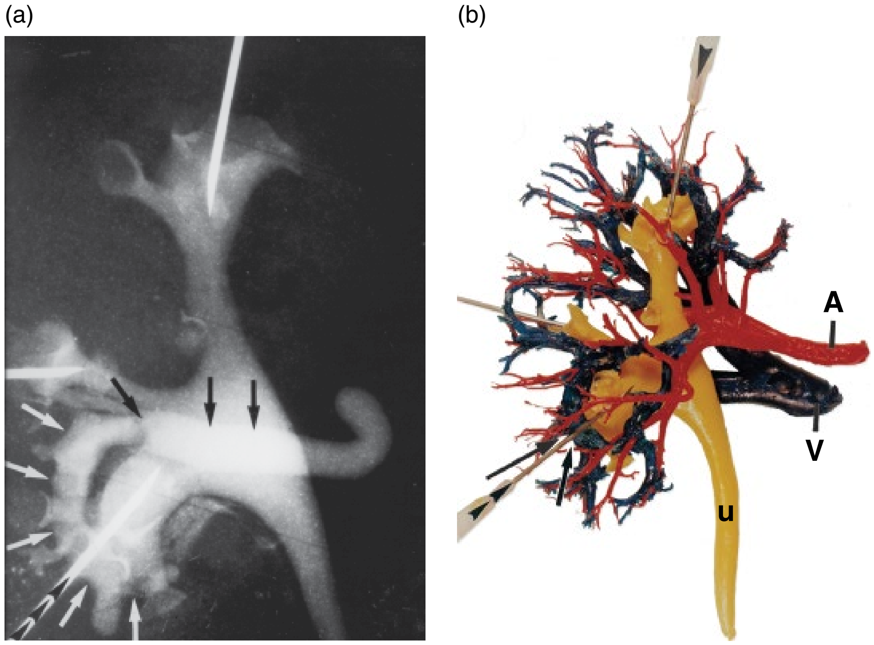

**Figure 6.32** (a) Posterior view of a retrograde pyelogram from a left kidney. This shows a puncture performed through the inferior infundibulum. A venous lesion and the contrast in a large venous arcade draining to the retropelvic vein (arrows) can be seen. The arrowheads show the tract of the needle. (b) Posterior view of the corresponding endocast reveals the site of the lesion in the venous arcade (arrows). The arrowheads show the tracts of the needles. A, renal artery; V, renal vein; u, ureter. Reproduced with permission of Elsevier.

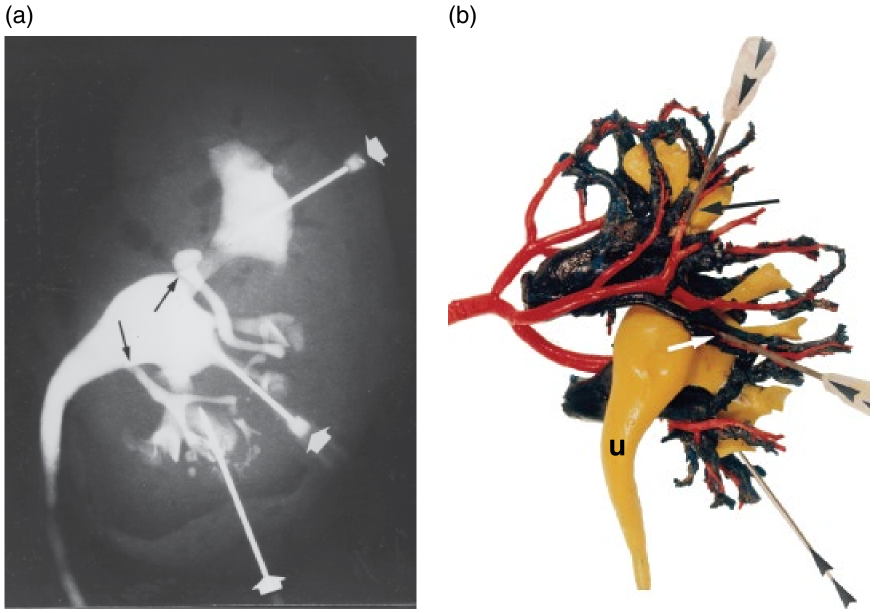

**Figure 6.33** (a) Posterior view of a retrograde pyelogram from a right kidney reveals superior, middle, and inferior punctures (short arrows) and contrast in the superior and inferior infundibular arteries (arrows). (b) Posterior view of the corresponding endocast reveals injury to an upper infundibular artery (black arrow). The mid kidney puncture (white arrow) was a through-and-through (two-wall) puncture and injured an anterior segmental artery. The injured vessel furnished the posteroinferior branch filled with contrast on the pyelogram. The arrowheads show the tracts of the needles. u, ureter. Reproduced from Sampaio et al. [24] with permission.

pole, mid pole, and lower pole calyces. We did not detect any arterial lesions as a consequence of a forniceal puncture [24].

## Where to puncture for intrarenal access

In conclusion, the high rate of vascular injury and the possibility of associated complications mean that *a nephrostomy tube should not be placed through an infundibulum of a calyx* (Figure 6.34). On the other hand, and regardless of the region of the kidney, *puncture and placement of a nephrostomy tube through a fornix of a calyx is safe* and should be the site chosen by the operator (Figure 6.35). Even in the superior pole, intrarenal puncture through a calyceal fornix is harmless (Figure 6.36). In addition, when puncturing through a fornix of a calyx, in case of lesion, injury is always to a peripheric vessel, such as a small venous arcade (Figure 6.37).

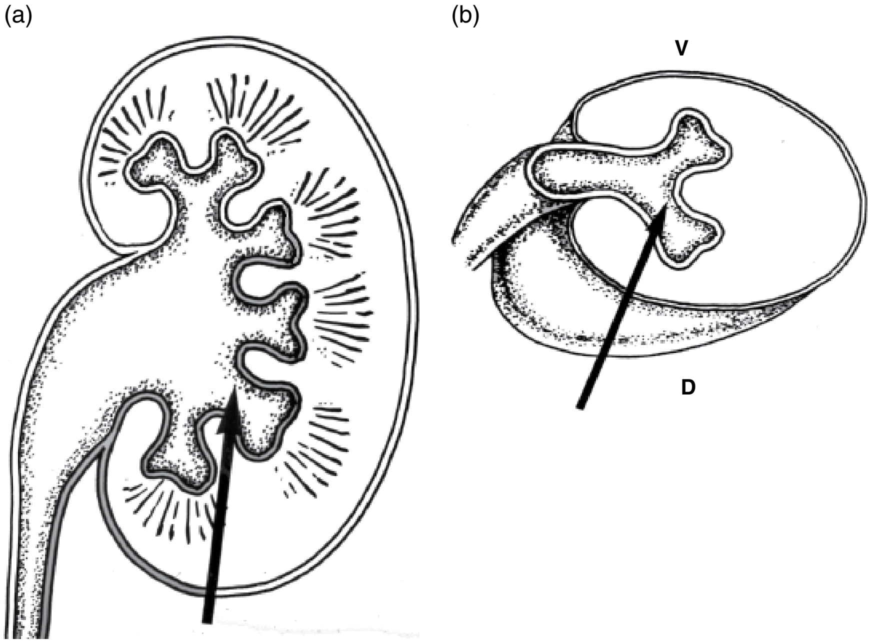

**Figure 6.34** (a) Schematic of a posterior view of a longitudinal section of a right kidney showing an intrarenal puncture performed through a calyceal infundibulum (arrow). This type of puncture should *not* be performed because it carries a high risk of vascular injury. (b) Schematic of a superior view of a transverse section of a kidney also shows an intrarenal puncture through a calyceal infundibulum (arrow); again this is *not* a recommended route. V, ventral region; D, dorsal region.

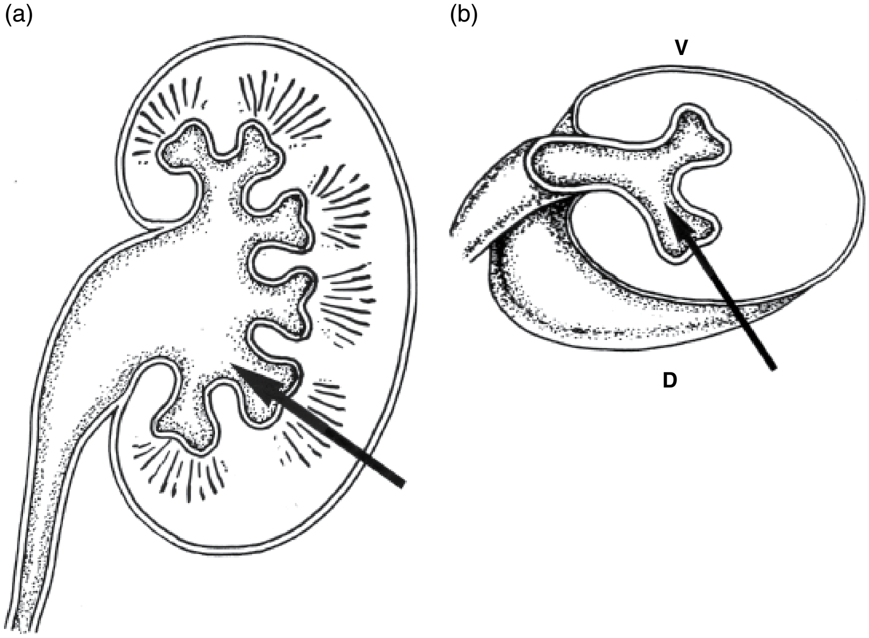

**Figure 6.35** (a) Schematic of a posterior view of a longitudinal section of a right kidney showing an intrarenal puncture performed through a calyceal fornix (arrow). This type of puncture is safe and is associated with a very low incidence of vascular injury. (b) Schematic of a superior view of a transverse section of the kidney shows an intrarenal puncture through a calyceal fornix (arrow), a route that is strongly recommended. V, ventral region; D, dorsal region.

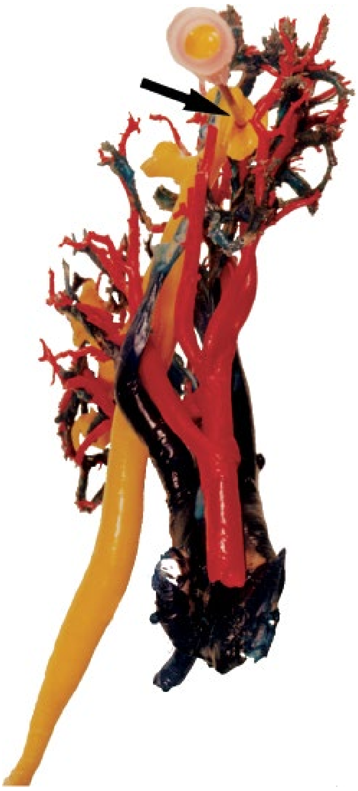

**Figure 6.36** Superior view of an endocast from a left kidney shows that, even in the superior pole, a puncture through the fornix of a calyx (arrow) is safe.

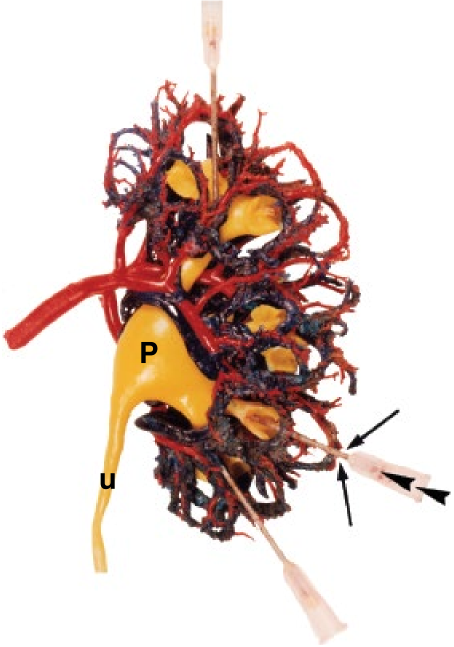

**Figure 6.37** Posterior view of an endocast from a right kidney with an inferior puncture performed through a fornix of a calyx. The arrows point to a lesion in a small peripheric venous arcade. The arrowheads show the needle tract. P, renal pelvis; u, ureter.

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## 7

# Nephrolithometric Scoring Systems for Percutaneous Nephrolithotomy

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## Introduction

Kidney stone disease is common and affects nearly 1 in 11 individuals in the United States [1]. The majority of stones pass spontaneously; however, up to 10–20% of stones require surgical intervention. Ureteroscopy and shock-wave lithotripsy are the primary surgical methods for treating small stones while percutaneous nephrolithotomy (PCNL) is the gold standard for stones larger than 2.0 cm [2]. There are several patient- and stone-related factors that dictate the feasibility of PCNL. Stone characteristics have a significant impact on surgical outcomes and features such as size, the extent of calyceal involvement, and stone density play an important role in the decision-making process. Additional factors that should be considered are the tract length, degree of obstruction of the collecting system, pelvicalyceal anatomy, and anatomical malformations [3–7]. Efforts have been made by several groups to characterize renal stones in a standard and reproducible fashion. The importance of establishing scorings systems is twofold. First, preoperative patient counseling necessitates the development of an integrated scoring system to assess and quantify stone complexity for optimal decision-making. Second, it allows a way to account for the methodological differences among studies reporting outcomes of PCNL.

Nephrolithometry scoring systems (NLSS) aim for preoperative prediction of stone-free status (SFS) and complications through assessment of the complexity of stones before performing a PCNL. The S.T.O.N.E. nephrolithometry, the Guy's stone score (GSS), the Clinical Research Office of the Endourology Society (CROES) nomogram, and the Seoul National University Renal Stone Complexity (S-ReSC) score are the four most common NLSS used today (Table 7.1) [8–11]. These NLSS not only consider imaging criteria of stones and renal anatomy but may also use relevant patient characteristics such as body mass index (BMI), previous renal surgery, and surgeon experience.

This chapter provides a comprehensive review of NLSS used today. Their individual advantages and disadvantages will be presented along with their commonalities. Despite validation of the NLSS discussed in this chapter over 10% of members of the Endourological Society were not aware of their existence and over 85% did not use them in clinical practice [12]. An understanding of the various NLSS is critical in overcoming the methodological differences among studies that look at outcomes of PCNL and the judicious use of such systems may improve stone-free rates and reduce morbidity associated with PCNL.

## Stone scoring tools: descriptions and assessments

### S.T.O.N.E. nephrolithometry: development, reproducibility, and validation

S.T.O.N.E. nephrolithometry was developed in 2013 as a means to quantitate kidney stone complexity in a standardized and reproducible manner. The scoring system consists of the five most reproducible variables obtained from preoperative imaging. These are Stone size, Tract length, Obstruction/hydronephrosis, Number of involved calyces, and Essence of stone density measured by Hounsfield units (Table 7.2). Stone size is determined by measuring and multiplying the vertical length by the greater of the two measurements, width or length, resulting in a size in square millimeters. The tract length is defined as the distance from the center of the stone to the surface of skin measured at a 45° angle on a supine

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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 7.1** The overview of most common NLSSs.

| Scoring system | Categorization | Method of derivation |
|---|---|---|
| Guy's stone score [11] | Grade I: a solitary stone in the mid/lower pole, or renal pelvis with simple anatomy<br>Grade II: a solitary stone in the upper pole with simple anatomy, multiple stones in a patient with simple anatomy, or any solitary stone in a patient with abnormal anatomy<br>Grade III: multiple stones in a patient with abnormal anatomy, stones in a caliceal diverticulum, or partial staghorn calculus<br>Grade IV: staghorn calculus or any stone in a patient with spina bifida or spinal injury | Literature review, expert opinion, iterative process |
| CROES nomogram [10] | A: stone burden, calculated as follows:<br>1) Measure the maximum length of each stone in millimeters<br>2) Measure the maximum width of each stone in millimeters<br>3) Calculate the stone burden for each stone = 0.785 × length × width<br>4) Add individual stone burdens if multiple stones<br>B: calyceal location: position in renal pelvis or multiple calyces involved, including staghorn calculi<br>C: stone count: single or multiple<br>D: case volume | Multiple logistic regression analysis |
| S.T.O.N.E. nephrolithometry | Scoring based on five variables from preoperative noncontrast computed tomography stone size:<br>S = stone size<br>1) 0–399 mm$^2$<br>2) 400–799 mm$^2$<br>3) 800–1599 mm$^2$<br>4) >1600 mm$^2$<br>T = tract length<br>1) <100 mm<br>2) >100 mm<br>O = obstruction<br>1) No or mild dilatation<br>2) Moderate to severe dilatation<br>N = number of involved calyces<br>1) 1 calyx involved<br>2) 2–3 calyces involve<br>3) Full staghorn calculus<br>E = essence (stone density)<br>1) <950 HU<br>2) >950 HU | Systematic review |
| Seoul National University Renal Stone Complexity (S-ReSC) score [8] | Identify number of preselected pelvicalyceal locations involved: each of the nine locations is worth 1 point; total score 5 cumulative number of locations involved | Not reported |

computed tomography (CT) film. The tract length is subdivided into two scores: ≤100 mm is one point and >100 mm is two points. The obstruction component of the scoring system evaluates the degree of hydronephrosis according to the dilation of the collecting system viewed on CT imaging. Assigning a score for this variable is dependent on the user's familiarity with recognizing hydronephrosis in axial imaging. None or mild hydronephrosis is given a score of 1 while moderate to severe hydronephrosis is scored as 2. The number of

**Table 7.2** The overview of the S.T.O.N.E. nephrolithometry [9].

| | Score | | | |
|---|---|---|---|---|
| **Variable** | **1** | **2** | **3** | **4** |
| Stone size ($mm^2$) | 0–399 | 400–799 | 800–1599 | >1600 |
| Tract length (mm) | <100 | >100 | | |
| Obstruction | None | Severe | | |
| Calyces | 1–2 | 3 | Staghorn | |
| Essence | <950 HU | >950 HU | | |

calyces evaluates the extent of calyces infiltrated by the stone. This component is highly dependent on the user's understanding of renal cross-sectional anatomy [2]. If one or two calyces are involved the score of 1 is given, if three calyces are involved the score is 2, and if it is a staghorn stone the highest score of 3 is assigned. The essence component of the scoring system evaluates the stone density measured in Hounsfield units (HU) for a circular region of interest (ROI). Due to the heterogeneity of stone shape, this measurement is made by creating a circular ROI that encompasses the most stone possible while minimizing adjacent soft tissue. It is important to capture as large an area of the stone as possible in order to appreciate the average density of the stone. As most stones are lamellate in their composition, density will vary considerably from the center to the outer edges of the stone. It is important to evaluate the average density of the entire stone for the sake of reproducibility. This variable is scored based on radiodensity threshold of 950 HU. Stones greater than 950 HU are scored 2 and those less than 950 HU are scored 1.

The parameters used for the S.T.O.N.E. score are easy to calculate, do not require specialized software, and are derived from noncontrast-enhanced CT images. The methodology for choosing the associated variables were identified via a literature review of English language studies from 1976 to 2012 on MedLine to identify the most clinically relevant and reproducible variables that had been shown to impact outcomes following PCNL. The scoring system was subsequently validated in a cohort of 117 PCNL patients to evaluate the predictive value of the S.T.O.N.E. nephrolithometry. A "low" score of 4–5 demonstrated a correlation with SFS of 94–100%, a "moderate" score of 6–8 correlated with a SFS of 83–92%, and "high" scores of 9–13 correlated with SFS ranging from 27 to 64% [9]. A subsequent study demonstrated interobserver reliability, although the degree of training and levels of expertise with CT imaging clearly impacted the accuracy of grading and assessment of stone complexity. The authors found that quantifying the stone size and number of involved of calyces were least reproducible overall [13].

S.T.O.N.E. nephrolithometry has been externally validated in a number of studies. Akhavein and colleagues validated the system as a reproducible and predictive model for treatment success in 122 patients [14]. A multi-institutional study of 850 patients confirmed that the model was significantly associated with SFS, overall complications, estimated blood loss (EBL), operation time, and length of stay [15]. Studies by Labadie and Noureldin showed that the system was correlated with EBL, operative time, and length of hospital stay [16–18]. A study by Kumsar and colleagues showed that this system is effective in predicting postoperative complications [19]. This NLSS when compared to the Guy's and CROES nomogram also had more predictive ability in a retrospective review of 217 patients at a single institution [20]. S.T.O.N.E. has also been validated among a pediatric population, correlating with SFS, length of hospitalization, and complications [21].

### Strengths and weaknesses

The GSS and CROES nomograms, which are discussed later in this chapter, were initially developed using abdominal plain films, whereas S.T.O.N.E. nephrolithometry was developed on the basis of CT findings. Furthermore, because it stratifies patients into low-, moderate-, and high-risk groups, it is clinically practical for decision-making and surgical planning. Notably, S.T.O.N.E. can be calculated using only a preoperative CT, making it ideal for building a retrospective database with limited clinical information.

Additionally, the score would benefit from greater refinement of the methods used to score each of the factors to take into account their relative predictive power. It is not clear that the cutoffs used for tract length and stone density are optimal. Furthermore, the authors acknowledge the need for a standardized method to measure stone size and number of calyces involved in order to improve predictive value. A standardized definition of calyx as well as the imaging plane used to enumerate calyceal involvement would improve reproducibility. Additionally, the score assigned by degree of hydronephrosis is subjective and would benefit from stricter criteria.

## Guy's stone score: development, reproducibility, and validation

The GSS was developed to be quick, simple, and reproducible with good correlation with SFS and complication rates so that it could be used in everyday practice. An analogy might be the use of the American Society of Anesthesiologists score, which is widespread in clinical practice [22]. It was created using evidence from published data combined with knowledge and experience of senior endourologists at a single institution [11]. It consists of four grades based on stone burden and patient anatomy (Figure 7.1). The score was refined using an iterative process after evaluating 10 consecutive cases. The score was prospectively validated in 100 patients who underwent PCNL procedures in a tertiary stone center. The authors used abdominal radiography preoperatively and CT and abdominal radiography to determine SFS as defined as no stones visible or presence of clinically insignificant residual fragments <4 mm 6-weeks post-PCNL. A multivariate analysis showed that the GSS was the only predictive factor of SFS as compared to stone burden, operating surgeon, weight, age, comorbidity, and urine culture. Moreover, SFS correlated with increasing grade of GSS: grade I, 81% stone-free, II 74.2%, III 35%, and IV 29%. A higher grade correlated with the need for ancillary procedures. The authors did not find any correlation between the stone score and postoperative complications [11].

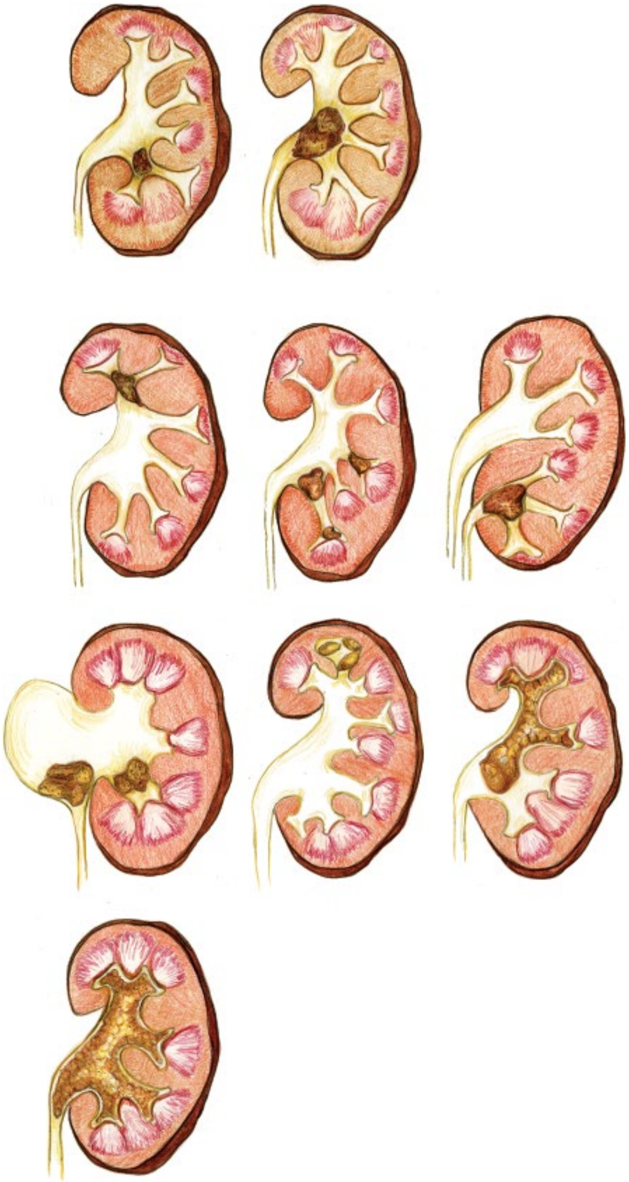

**Figure 7.1** Illustration of the Guy's stone score [11]. (Top row, left to right) Grade I: solitary stone in the mid/lower pole with simple anatomy; solitary stone in the pelvis with simple anatomy. (Second row, left to right) Grade II: solitary stone in the upper pole with simple anatomy; multiple stones in a patient with simple anatomy; any solitary stone in a patient with abnormal anatomy. (Third row, left to right) Grade III: multiple stones in a patient with abnormal anatomy; stones in a calyceal diverticulum; partial staghorn calculus. (Bottom row, left to right) Grade IV: staghorn calculus; any stone in a patient with spina bifida or spinal injury.

External validation in several series demonstrated that GSS effectively predicted SFS [15–17, 20, 23–29]. Importantly, Ingimarsson et al. and Vicentini et al. used preoperative CT to validate the GSS. Additionally, Ingimarsson et al. used a more stringent SF measurement, < 2 mm fragment, to determine SFS and confirmed a good interrater reliability [24]. Vicentini et al. also found a positive correlation between GSS and other operative outcomes such as operative time and blood transfusion rates, as well as postoperative complications [27]. A large, multicenter cohort study confirmed that the GSS score was an independent predictor of residual fragments after PCNL [15].

### Strengths and weaknesses

The GSS provides a simple, intuitive, and reproducible tool for predicting SFS following PCNL and it allows for stratifying cases between surgeons of different experience and reporting results. This NLSS has been validated in numerous studies and use of multiple imaging modalities, including abdominal radiography and CT, broadens its universal appeal and integration across varying guidelines for postoperative imaging. In addition, it takes into account patient variables, which are not included in other NLSS.

However, there are a number of key limitations to this system. First, important considerations such as stone size, calyceal involvement, density, and composition are not accounted for in this NLSS. These variables determine technical difficulty of PCNL, which have important implications for procedural success [3, 30, 31]. Second, the GSS was based on published literature and expert opinion, which are arbitrary and assume different radiological findings have the same influence on PCNL outcome. Data-driven models such as the CROES nomogram have been found to have superior predictability for SFS and also predict certain postoperative complications while the GSS does not [10]. Third, the simplicity of assigning a GSS does not account for clinical variability. For example, a patient with spina bifida and a full staghorn stone would receive the same grade IV rating even if they had just a 2 cm pelvic stone. The use of just four categories may underestimate the complexity of large kidney stones and affect the tool's ability to predict outcomes. Lastly, the overall SFS of 62% was relatively low in comparison to global overall SFS [10], raising the question of generalizability [32].

## CROES nomogram: development, reproducibility, and validation

In 2013, Smith and associates, on behalf of the Clinical and Research Office of Endourology Society (CROES) PCNL study group, proposed an alternative to the GSS. This NLSS is a statistically derived data-driven risk estimator model based on regression modeling derived from multiple institutions [10]. A total of 2806 patients from 96 centers worldwide were included in the development of the nomogram. Stone burden was the most influential patient factor that influenced stone-free rates (SFR). Additional factors that were strongly associated with SFR were case volume, prior stone treatment, staghorn stone, stone location, and stone count. Each variable is associated with the score of 0–100 and the sum of the individual scores are used to predict the SFS, defined as no visible stones or residual fragments <4 mm on abdominal X-ray 30 days following PCNL (Figure 7.2). An interpretation scale was created to associate the total score with the percentage chance of achieving SFS and bootstrapping techniques were used with 1000 cases to validate the model. Additionally, the nomogram proved clinically useful for directing treatment strategy at a threshold of 60% or more estimated SFS using a decision analysis curve [10].

The CROES nomogram was externally validated by a number of studies [15, 16, 23, 25, 28]. Specifically, Bozkurt found that the CROES nomogram correlated with SFR using CT as well as operative time, EBL, length of hospital stay, and complications [23].

### Strengths and weaknesses

The CROES nomogram is unique in that it incorporates case volume per year as a continuous variable in its calculation. This is based on outcomes of a previous study of the relationships between case volume, PCNL efficacy, and safety outcomes [33]. Moreover, the nomogram uniquely grades risk across a continuous scale rather than dividing stones of varying complexity into discrete groups.

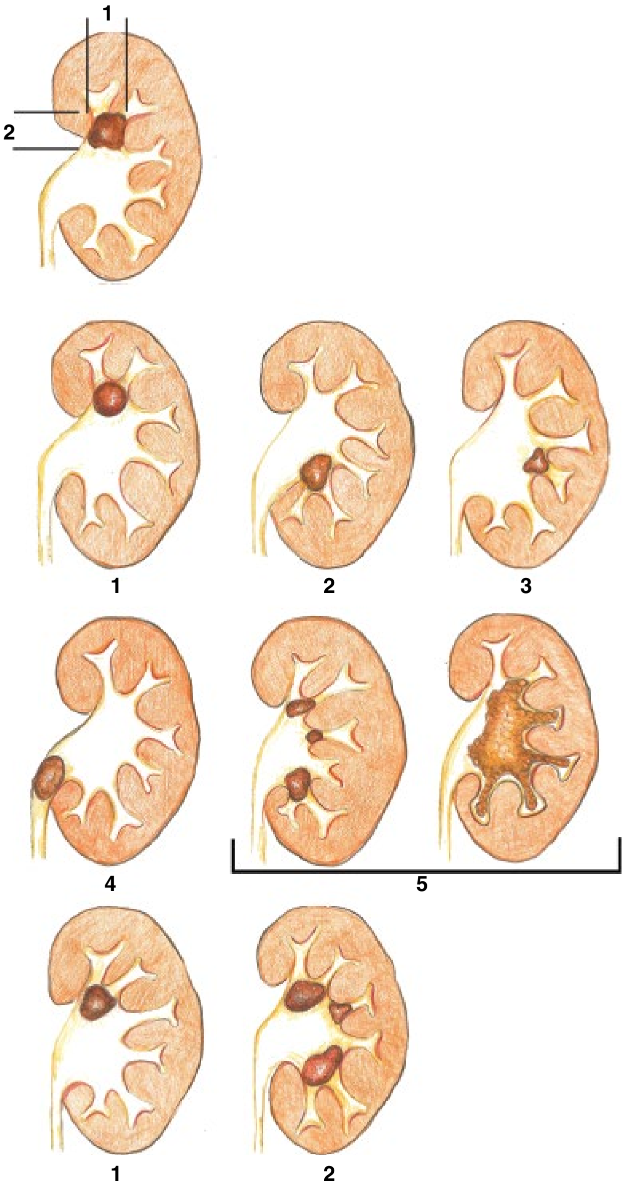

**Figure 7.2** Illustration of CROES nomogram [10]. (Top row) Stone burden. Calculate as follows: (1) measure maximum length of each stone in millimeters, (2) measure the maximum width of each stone in millimeters; (3) calculate stone burden for each stone (stone burden = 0.785 × $\text{Length}_{\max}$ × $\text{width}_{\max}$; (4) add individual stone burdens. (Second and third rows) Stone location: (1) upper calyx; (2) lower calyx; (3) middle calyx; (4) renal pelvis; (5) multiple renal locations (includes staghorn stone). (Bottom row) Stone count: (1) single; (2) multiple.

There are, however, important limitations. First, the CROES regression coefficients are derived to predict SFS and as such cannot be used to give a similar continuous predictive score for any other outcome. All that can be proved is whether scores are significantly higher or lower for outcomes other than SFS [25]. Second, the database was not created specifically for the development of a predictive model for classification of stone disease prior to PCNL and therefore lacks important variables affecting the outcomes. Third, the authors acknowledge that the study lacked radiological data on hydronephrosis and other pelvicalyceal abnormalities, each of which may influence outcomes. Fourth, the stone density and composition were not accounted for and this is known to affect the outcome of stone fragmentation and clearance [34, 35]. Lastly, the CROES design is more complicated than other available nomograms, making its everyday application challenging.

### S-ReSC score: development, reproducibility, and validation

The S-ReSC score was developed based on the assertion that the distributional complexity of stones is the most important factor that determines PCNL treatment success. A nine-point system was devised with 1 point assigned to nine specific pelvic and calyceal locations (Figure 7.3). A score of 1–2 is considered low, 3–4 is medium, and >5 is high. The score is assigned by adding the cumulative sites involved. The authors evaluated 155 consecutive cases at their center to retrospectively validate S-ReSC. The SFS for low scores was 96.0%, for medium it was 69.0%, and for high it was 28.9%. Logistic regression showed that S-ReSC significantly predicted SFS. Additionally, multiple regression analyses showed that the S-ReSC score was associated with stone number, burden, and renometry, variables that are commonly accepted as being predictive of postoperative success. It also showed that the S-ReSC score had comparatively higher predictive value than any variable alone [8].

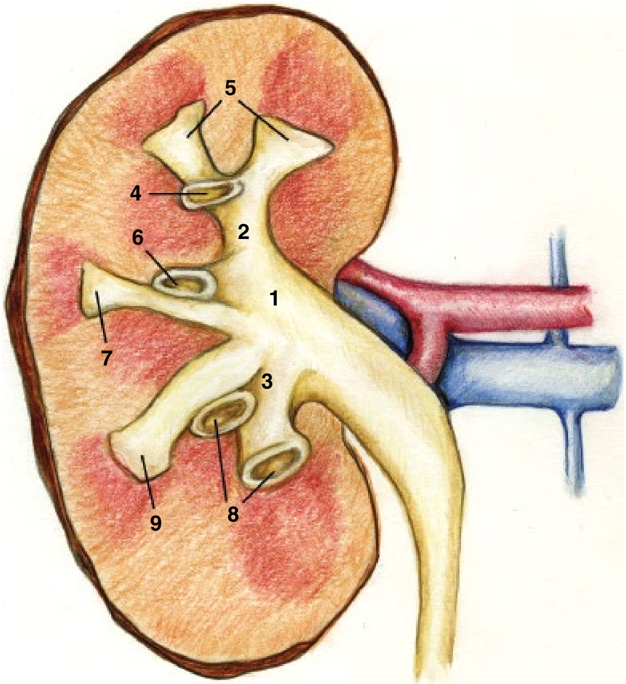

**Figure 7.3** Illustration of S-ReSC [8]. The score is calculated by counting the number of sites involved, regardless of the size and number of the stones. The sites were as follows: (1) renal pelvis; (2, 3) superior and inferior major calyceal groups (major calyx and infundibulum); and anterior and posterior minor calyceal groups of the (4, 5) superior, (6, 7) middle, and (8, 9) inferior calyx.

Studies by Choo, Park, and Jung and coworkers each externally validated the S-ReSC score. In a 327 patient cohort at two tertiary centers, Choo et al. demonstrated that it predicted SFS as defined by <4 mm [36]. Park et al. validated the S-ReSC score for retrograde intrarenal surgery (RIRS), rather than PCNL. The S-ReSC score was found to be predictive of SFS with low (1–2), intermediate (3–4), and high (5–12) scores correlated with 86.7, 70.2, and 48.6% SFS, respectively [37]. Similarly, Jung et al. validated a modified S-ReSC score for prediction of SFS after RIRS by adding additional points for hard-to-reach stones in the lower poles [38].

#### Strengths and weaknesses

The S-ReSC score is a simple, easily applicable scoring tool that predicts SFS. It is based on just a single variable, stone location, which is determined with preoperative CT and demonstrates high reproducibility as a result of this simplicity.

Importantly, the S-ReSC score relies on the hypothesis that the single variable of stone location is the ultimate predictive indicator of SFS. However, it is clear from the literature that there are many variables that have important influence on outcomes. Additionally, the score was created and validated initially with a cohort at a single center. Factors that may influence success rates in the larger Western patient population (i.e. skin-to-stone distance, a surrogate for BMI) may prove useful in broadening its application.

The four tools discussed here are summarized in Table 7.3.

## Common variables in NLSS

Stone burden and location are common variables associated with all of the scoring systems mentioned in this chapter. There are individual variables that distinguish the NLSS from one another, and this may influence surgical complexity and outcomes.

### Stone burden

It is well documented that the most important variable to predict outcomes of PCNL is stone burden [3, 16, 30, 31, 39, 40]. In the first study providing a head-to-head comparison of three nephrolithometry systems – GSS, CROES nomogram, and S.T.O.N.E. – Labadie et al. [16] found that stone burden alone had the same predictive value for SFR as did each of the scoring systems. Most urologists currently utilize stone size to estimate the complexity of the procedure and surgical outcomes;

**Table 7.3** A review of the literature on validating all currently existing scoring systems.

| Study | Country | *n* | Preop imaging | Postop imaging | Definition of stone-free | Clearance by stone complexity | Complications by stone complexity | Statistical method |
|---|---|---|---|---|---|---|---|---|
| **Guy's stone score** | | | | | | | | |
| Thomas et al. 2011 [11] | UK | 100 | CT, X-ray, IVU | KUB radiograph | <4 mm fragments | **Overall 62%**<br>Grade I 81%<br>Grade II 72.4%<br>Grade III 35%<br>Grade IV 29% | Not reported: no significant correlation only | Multivariate linear regression analysis |
| Mandal et al. 2012 [26] | India | 278 | X-ray, IVU, ultrasound, noncontrast CT | KUB radiograph | Complete absence of stones | **Overall 76.1%**<br>Grade I 100%<br>Grade II 74%<br>Grade III 56%<br>Grade IV 0% | **Overall 41.7%**<br>Grade I 4.8%<br>Grade II 9.1%<br>Grade III 26.2%<br>Grade IV 44.4% | Univariate analysis |
| Vicentini et al. 2014 [17] | Brazil | 147 | CT scan | | Asymptomatic fragments <4 mm | **Overall 71.6%**<br>Grade I 95.2%<br>Grade II 79.5%<br>Grade III 59.5%<br>Grade IV 40.7% | **Overall 18.7%**<br>Grade I 4.8%<br>Grade II 9.1%<br>Grade III 26.2%<br>Grade IV 44.4% | Univariate analysis |
| Ingimarsson et al. 2014 [24] | Lebanon | 66 | CT scan | | No fragments/No fragments >2 mm/No fragments >4 mm | **Overall 90%**<br>Grade I 95%<br>Grade II 97%<br>Grade III 95%<br>Grade IV 75% | Not reported – no significant correlation only | Univariate analysis |
| Kumsar et al. 2015 [19] | Turkey | 102 | CT scan | KUB radiograph | Complete absence of stones | **Overall 10.8%**<br>Grade I 10%<br>Grade II 4%<br>Grade III 66%<br>Grade IV --- | **Overall 19.6%** | Chi square test |
| Labadie et al. 2015 [16] | USA | 246 | CT scan | Unclear | Not defined | **Overall 56%**<br>Grade I 70.2%<br>Grade II 65.4%<br>Grade III 48.1%<br>Grade IV 35.9% | **Overall 17%** | Logistic regression analysis |
| Noureldin et al. 2015 [17] | Canada | 185 | Unclear | Plain radiographs or noncontrast CT | Asymptomatic residual fragments <4 mm | **Overall 71.9%**<br>Grade I 91.5%<br>Grade II 80%<br>Grade III 47.6%<br>Grade IV 43.2% | **Overall 16.2%**<br>Grade I 17%<br>Grade II 15%<br>Grade III 9.5%<br>Grade IV 21.6% | Logistic regression analysis |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Bozkurt et al. 2015 [23] | Turkey | 437 | CT scans | X-ray KUB (unless CT; which is reserved for only symptomatic patients) | Asymptomatic residual fragments <4 mm | **Overall 75%**<br>Grade I 92.8%<br>Grade II 72.4%<br>Grade III 68.5%<br>Grade IV 47.4% | **Overall 35.0%**<br>Grade I 13.0%<br>Grade II 2.5%<br>Grade III 8.7%<br>Grade IV 10.3% | Linear and logistic regression analyses |
| Sfoungaristos et al. 2015 [29] | Isreal | 261 | CT scan | KUB radiograph | <4 mm fragments | **Overall: 84.7**<br>Grade I 96.8%<br>Grade II 91.0%<br>Grade III 71.7%<br>Grade IV 46.2% | **Overall 37.9%**<br>Grade I 25.8%<br>Grade II 46.1%<br>Grade III 41.5%<br>Grade IV 46.2% | Logistic regression analysis |
| Choi et al. 2016 [20] | Korea | 217 | KUB radiograph, CT scan | KUB radiograph or CT scan | <4 mm fragments | **Overall 53.9%** | **Overall 32.7%** | Logistic regression analysis |
| Jaipuria et al. 2016 [25] | India | 606 | CT scan | KUB radiograph, ultrasound | <4 mm fragments | **Overall 81.5%**<br>Grade I 96.5%<br>Grade II 81.4%<br>Grade III 77.2%<br>Grade IV 59% | **Overall 29.0%**<br>Grade I3.5%<br>Grade II 28.8%<br>Grade III 27.8%<br>Grade IV 67% | Logistic regression analysis |
| Tailly et al. 2016 [15] | Canada, USA | 586 | CT scan | Ct scan, KUB radiograph, ultrasound | <2 mm fragments | **Overall 67.4%**<br>Grade I 80.3%<br>Grade II 73.8%<br>Grade III 60.5%<br>Grade IV 52.3 | **Overall 29.2%** | Logistic regression analysis |
| **CROES nomogram** | | | | | | | | |
| Smith et al. 2013 [10] | International (CROES PCNL Group) | 2806 | Unclear | X-ray KUB | No fragments >4 mm | **Overall 82%**<br>Odds ratios and nomogram reported<br>ROC AUC: 0.76 | Not reported | Multivariate logistic regression |
| Labadie et al. 2015 [16] | USA | 246 | CT scan | Unclear | Not defined | **Overall 56%**<br>80–129: 22.7%<br>130–169: 46.4%<br>170–219: 45.5%<br>≥220: 72.7% | **Overall 17%** | Logistic regression |
| Bozkurt et al. 2015 [23] | Turkey | 437 | CT scans | X-ray KUB (unless CT; which is reserved for only symptomatic patients) | Asymptomatic residual fragments <4 mm | **Overall 75%**<br>Grade 1 48.5%<br>Grade 2 51.4%<br>Grade 3 69.1%<br>Grade 4 92.8% | **Overall 35%**<br>Grade 1 4.8%<br>Grade 2 8.0%<br>Grade 3 7.5%<br>Grade 4 14.2% | Linear and logistic regression analyses |
| Choi et al. 2016 [20] | Korea | 217 | KUB radiograph, CT scan | KUB radiograph or CT scan | <4 mm fragments | **Overall 53.9%** | **Overall 32.7%** | Logistic regression analysis |

(*Continued*)

**Table 7.3** (Continued)

| Study | Country | *n* | Preop imaging | Postop imaging | Definition of stone-free | Clearance by stone complexity | Complications by stone complexity | Statistical method |
|---|---|---|---|---|---|---|---|---|
| Sfoungaristos et al. 2015 [29] | Isreal | 176 | CT scan, KUB radiograph | CT scan | <4 mm fragments | **Overall: 85.8%** | **Overall 42.6%** | Logistic regression analysis |
| Tailly et al. 2016 [15] | Canada, USA | 586 | CT scan | CT scan, KUB radiograph, ultrasound | <2 mm fragments | **Overall 67.4%**<br>Grade 1 84.2%<br>Grade 2 71.8%<br>Grade 3 58.6%<br>Grade 4 44.4% | **Overall 29.2%** | Logistic regression analysis |
| **S.T.O.N.E. nephrolithometry** | | | | | | | | |
| Okhunov et al. 2013 [9] | USA | 117 | Noncontrast CT | Fluoro ± CT | Complete absence of stones on CT | **Overall 80%**<br>Low (4–5) 94–100%<br>Medium (6–8) 83–92%<br>High (9–11) 27–64%<br>ROC AUC: 0.83 | Not reported | Multivariate logistic regression |
| Okhunov et al. 2013 [13] | USA | 58 | Noncontrast CT | Fluoro ± CT | N/A* | N/A* | N/A* | Cohen's Kappa coefficient |
| Okhunov et al. 2014 [60] | USA | 706 | CT scans | Unclear | Not defined | **Overall 67%**<br>STONE score significantly associated with postop SFS | STONE score significantly associated with overall complication rate | Univariate analysis |
| Labadie et al. 2015 [46] | USA | 246 | CT scan | Unclear | Not defined | **Overall 56%**<br>5–6: 70.6%<br>7–8: 66.3%<br>9–13: 46.2%<br>ROC AUC: 0.67 | **Overall 17%** | Logistic regression |
| Akhavein et al. 2015 [14] | USA | 122 | CT scans | | Residual fragments <4 mm | Score vs. clearance %:<br>5–7: 100%<br>8: 80%<br>9: 94.1%<br>10: 79.2%<br>11: 66.7%<br>12: 45% | Score vs. complication %:<br>5: 0%<br>6: 1.6%%<br>7–8: 0%<br>9: 0.8%<br>10: 6.6%<br>11–12: 0% | Univariate analysis and logistic regression |
| Farhan et al. 2015 [61] | Pakistan | 107 | CT scan | | <2 mm | **Overall 80.0%** | **Overall 18%** | Univariate analysis |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Noureldin et al. 2015 [17] | Canada | 185 | Unclear | Plain radiographs or noncontrast CT | Asymptomatic residual fragments <4 mm | **Overall 71.9%**<br>5: 100%<br>6: 75%<br>7: 77.3%<br>8: 67.6%<br>9: 79.3%<br>10: 58.3%<br>11: 42.9%<br>12–13: 0% | **Overall 16.2%**<br>5: 20%<br>6: 18.2%<br>7: 11.4%<br>8: 20.6%<br>9: 20.7%<br>10: 8.3%<br>11: 0%<br>12: 25%<br>13: 0% | Logistic regression analysis |
| Noureldin et al. 2015 [18] | Canada | 155 | Noncontrast CT | KUB and/or Noncontrast CT | Residual stones ≥4 mm considered as non-stone-free | **Overall 71.6%**<br>Significant inverse association between S.T.O.N.E. score and clearance<br>AUC: 0.63 | **Overall 15.5%**<br>No correlation between S.T.O.N.E. score and complications | Multivariate logistic regression |
| Choi et al. 2016 [20] | Korea | 217 | KUB radiograph, CT scan | KUB radiograph or CT scan | <4 mm fragments | **Overall 53.9%** | **Overall 32.7%** | Logistic regression analysis |
| Jaipuria et al. 2016 [25] | India | 606 | CT scan | KUB radiograph, ultrasound | <4 mm fragments | **Overall 81.5%**<br>5–6: 94.7%<br>7–8: 76.5%<br>9–13: 70.6% | **Overall 29.0%**<br>5–6: 11.9%<br>7–8: 29.5%<br>9–13: 50% | Logistic regression analysis |
| Tailly et al. 2016 [15] | Canada, USA | 586 | CT scan | Ct scan, KUB radiograph, ultrasound | <2 mm fragments | **Overall 67.4%**<br>5–6: 82.1%<br>7–8: 72.7%<br>9–10: 58.6%<br>11–13: 39.2% | **Overall 29.2%** | Logistic regression analysis |
| **S-ReSC score** | | | | | | | | |
| Jeong et al. 2013 [8] | S Korea | 155 | Noncontrast CT | | No evidence of residual stones on postop images after 1 month | **Overall 72.3%**<br>Low (1–2) 96%<br>Medium (3–4) 69%<br>High (5–9) 28% | **Overall 25.2%**<br>Low (1–2) 1.9%<br>Med (3–4) 28.6%<br>High (5–9) 34.2% | Univariate analysis; ROCs |
| Jung et al. 2014 [38] | S Korea | 88 | Noncontrast CT | | No evidence of residual stone at 1 month | **Overall** 85.2%<br>Low (1–2) 94.2%<br>Medium (2–4) 84.0%<br>High (>4) 45.5% | Not invesitgated | Logistic regression analysis |

(*Continued*)

**Table 7.3** (Continued)

| Study | Country | *n* | Preop imaging | Postop imaging | Definition of stone-free | Clearance by stone complexity | Complications by stone complexity | Statistical method |
|---|---|---|---|---|---|---|---|---|
| Choo et al. 2014 [36] | S Korea | 327 | Noncontrast CT | | Complete clearance/clearance with clinically insignificant residual fragments (4 mm) at 1 month follow-up imaging | **Overall 65.4%**<br>Low (1–2) 83.9%<br>Medium (3–4) 47.6%<br>High (5–9) 21.4% | Not investigated | Univariate and multivariate regression analyses; ROCs |
| Park et al. 2015 [37] | S Korea | 159 | Unclear | | No evidence of a stone or with clinically insignificant residual fragment stones <2 mm | **Overall 73.0%**<br>Low (1–2) 86.7%<br>Medium (3–4) 70.2%<br>High (5–12) 48.6% | Not investigated | Uni- and multivariate linear regression |
| Jaipuria et al. 2016 [25] | India | 606 | CT scan | KUB radiograph, ultrasound | <4 mm fragments | **Overall 81.5%**<br>Low (1–2) 96.6%<br>Medium (3–4) 81.6%<br>High (5–9) 61% | **Overall 29.0%**<br>Low (1–2) 12.9%<br>Medium (3–4) 28.6%<br>High (5–9) 51.3% | Logistic regression analysis |

AUC, area under the curve; IVU, intravenous urography; KUB, kidney–ureter–bladder imaging; ROC, receiver operating characteristic.

however, there is a lack of uniformity in the literature with regards to calculating stone burden [16, 41, 42]. Each of the described models uses a different algorithm for calculating the stone burden. None of these methods has been shown to be superior and so the most reproducible method that accurately reflects clinically significant stone burden should be utilized.

### Location

Stone location and distribution have a substantial impact on SFR [43]. The GSS grade is largely based on location as single stones in the lower or middle poles or renal pelvis are assigned the lowest grade while single stones in the upper pole are assigned a higher grade. The CROES nomogram goes further, assigning a different score for the renal pelvis, and lower, middle, and upper poles. S.T.O.N.E. nephrolithometry accounts for the number of calyces occupied by the stone but does not specify stone location in determining the overall score. The S-ReSC score is solely based on stone distribution as determined by the cumulative number of calyces involved but does not consider their location. The relative weight that each scoring system places on the stone location is a key determinant of how it influences the score.

### Staghorn stones

Staghorn stones are particularly challenging, requiring more complex procedures, multiple tracts and, sometimes, multistaged or multimodal treatments [41]. There is no precise definition for staghorn calculi, leading to interobserver inconsistencies [41, 42]. Mishra and colleagues created the Staghorn Morphometry, a system by which the volume and distribution of staghorn stones can be evaluated to predict the requirement for number of tracts and stages for PCNL procedures. They proposed a scoring system that classifies each stone into one of three types [44]. Mishra provides a sophisticated method to predict the number of tracts and stages required for PCNL for staghorn renal calculi; however, it only applies to one type of stone and requires complex imaging software for calculation. Whether specifying staghorn status specifically or accounting for it by proxy via stone burden is necessary for the best predictive outcome remains to be studied.

### Anatomical malformations

The influence of anatomic abnormalities on PCNL outcomes has been previously evaluated and discussed in several studies [4, 6]. However, there is no consensus on their relevance given that a number of studies have demonstrated that abnormal renal anatomy is not associated with inferior surgical outcomes [6, 45, 46]. Although anatomical variables such as duplicated collecting system, horseshoe kidneys, and calyceal diverticulum were evaluated, during the literature review in the development of S.T.O.N.E., due to the low incidence of these conditions the study was not powered sufficiently to detect a difference and therefore they were not included in the resulting scoring system. These parameters should be evaluated using a larger cohort to elucidate their impact role in the scoring system.

### Previous surgery and experience of surgeon

Only the CROES nomogram takes previous surgical intervention and caseload or experience of the surgeon into consideration, having found that both significantly impact treatment success. Previous stone treatment has a twofold informational yield. Firstly, it indicates prior therapy failure, demonstrating the complexity of the stone. Secondly, case volume and experience clearly impact surgical outcomes.

### Tract length

Skin-to-stone distance is an important parameter to predict success in PCNL. Particularly, in obese patients tract length dictates the difficulty of obtaining surgical access. Additionally, skin-to-stone distance alters the effectiveness of real-time fluoroscopy necessary for proper access. The increased skin-to-stone distance makes puncture, dilation, and securing a tract more difficult. Finally, challenges related to initial access adds difficulty to the limitations on the length of working sheaths, nephroscopes, and working instruments [47]. A longer nephrostomy tract decreases maneuverability of the nephroscope and may result in longer procedures with a lower SFR and increased complications [5, 48]. The S.T.O.N.E. nephrolithometry is the only scoring system that includes tract length. CROES included BMI, a possible correlate, in the initial analysis during the development of the system but ultimately did not find it to be predictive and therefore excluded it from the nomogram.

## Surgical complications

Risk of surgical complications is an important variable that should guide clinical decision-making. In their comparative study, Labadie et al. found that while the GSS and S.T.O.N.E. successfully predicted the length of stay and EBL, none of the three scoring systems, GSS, CROES nomogram or S.T.O.N.E., predicted surgical complications [16]. Patient factors unrelated to the stone may be more indicative of the postoperative complication risk. Borrowing from the surgical oncology literature and the concept of patient frailty, Leavitt et al. have illustrated that a patient's inability to independently perform activities of daily living is a strong predictor of complications and length of stay following PCNL [49].

## Predicting radiation time

A recent multicenter study found that patients with greater stone size, BMI, number of involved calyces, skin-to-stone distance, and S.T.O.N.E. nephrolithometry score experience increased radiation exposure during PCNL [50]. In their multivariate regression, Thomas et al. showed that patient weight, not individual GSS, was correlated with radiation time and exposure [11]. Sfoungoristos et al. found that GSS, CROES score, and S.T.O.N.E. are significantly associated with fluoroscopy time [51]. With a predictive classification system, benefits and risks of using alternative imaging modalities during evaluation of disease as well as during stone removal may be weighed against increased radiation exposure.

## Quality of life

A recent survey of the literature found health-related outcomes for stone management has revolved around the quality of life outcomes, suggesting that quality of life should play an important role in clinical decision-making. Patients with recurrent urinary tract stones report more bodily pain, depression, and lower general health scores than the general American public [52–57]. Simply measuring physiologic and biologic outcomes is not ideal. A comprehensive universal tool should not only consider procedural complexity and outcomes, but also meaningful measures for patients such as quality of life. A patient may prefer a staged ureteroscopic approach over a single-setting PCNL; these preferences should be considered.

## Applicability to multiple procedures

Finally, each system above was developed as a way of quantifying stone complexity and predicting surgical outcomes. A system which can be adapted to and therefore descriptive of multiple surgical procedures is ideal as it would allow for outcome comparisons and individualized surgical planning encompassing all available modalities. There are a number of additional systems that predict outcomes following other procedures such as RIRS and extracorporeal shock-wave lithotripsy [7, 58] but, so far, only the S.T.O.N.E. and the S-ReSC scores have been studied for its applicability to an alternate procedures [37, 59]. Understanding the relative predictive value of a universal tool for multiple treatment modalities will broaden its applicability to stone disease and allow for effective comparison between treatment options, informing clinical decision-making.

## Conclusions

Prior to surgery, patients should be provided with the most accurate information about their estimated SFS and risk of complications. Categorizing patients into low-, intermediate-, high-risk surgical groups helps surgeons to appropriately counsel patients regarding their likely postoperative clinical course and, in complex scenarios, refer patients to tertiary centers. To date, there are four NLSS that have been independently validated and each has their own strength and weaknesses. The current existing data is insufficient to state which scoring system is best.

While further research to prospectively validate these scoring systems is necessary, a NLSS should be incorporated into common practice, as this would greatly improve patient counseling, surgical planning, evaluation of outcomes, and academic reporting. It would allow reliable and accurate comparisons of treatment efficacy and quality of surgical care and facilitate the meaningful comparison of clinical studies. Furthermore, it would facilitate risk adjustment, enabling physicians to better define the nephrolithiasis disease continuum and identify patients who should be referred out to tertiary centers.

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# 8

# Pathophysiology of Urinary Tract Obstruction

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## Introduction

There are a host of diseases that can cause either unilateral or bilateral ureteral obstruction (UUO and BUO; Table 8.1). Most are well known to the urologist. In this chapter we will review patient presentation and the tools available for diagnosis. Following this, we will present data from experimental studies on both UUO and BUO.

We have been involved with research on the pathophysiology of UUO and BUO for the last 30 years. When we first began in this field the literature on the effects of UUO and BUO on the kidney focused mainly on the glomerulus and tubular function. The progression of the vasodilation and subsequent vasoconstriction of the afferent and efferent glomerular arterioles and the ultimate effect this had on renal blood flow, the glomerular filtration rate (GFR), and tubular function were initially reported. At that time, measuring effective renal blood flow (RBF) and inulin clearance, along with the usual parameters of tubular function, would be ample information to report. This progressed to reporting more information on the hormones, peptides, eicosanoids, and other vasoactive mediators that were circulating, and the effect they had on the intraglomerular vasculature and overall RBF, glomerular filtration, and tubular function.

The focus now is the interstitium, the space between the tubules. UUO is accompanied by changes in the architecture of the kidney. The most prominent interstitial change is fibrosis, and the accumulation of collagens and other extracellular matrix components. Interstitial fibrosis is characteristic of many clinical entities, including diabetes, ureteral obstruction, transplant rejection, renal ischemia, and glomerulonephritis. It has been shown in a variety of chronic renal diseases that the presence of interstitial fibrosis is a major determinant of GFR. Therefore, an understanding of the processes leading to fibrosis could eventually lead to targeted antifibrotic strategies that could allow patients to maintain, or possibly regain, renal function.

In this chapter, we will explore some of the time-tested and older information on the effects of UUO and BUO on the renal glomerulus and tubule. We will present some of the newer concepts regarding the cellular and molecular mechanisms in the development of renal fibrosis. While the information presented will expose the reader to the basics of this information, it will not be a comprehensive review of the subject (for reviews, see [1, 2]).

## Patient presentation

### Symptoms

Urinary tract obstruction can result in a wide range of symptoms, from asymptomatic (incidentally discovered) to the classic picture of renal colic. The symptom complex varies according to (i) the time interval over which the obstruction occurs (i.e. acute or chronic); (ii) whether the obstruction is unilateral or bilateral; (iii) the etiology of the obstruction (i.e. intrinsic vs. extrinsic); and (iv) whether the obstruction is complete or partial.

Acute obstruction is usually associated with flank pain that may radiate into the groin and/or ipsilateral thigh. Patients commonly experience nausea, vomiting, and chills. If the renal unit is infected, high fevers may also be present. A patient with high fever, above 38.3 °C, requires emergent urologic intervention and relief of the obstruction. It is more common to have acute UUO than BUO; however, if acute BUO occurs, the patient also may experience a sudden onset of anuria. UUO and BUO can develop over long periods of time, in which case patients are usually asymptomatic, making the diagnosis of obstruction more difficult and, in many

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**Table 8.1** Possible causes of obstructive nephropathy.

| | |
|---|---|
| **Renal** | |
| Congenital | Polycystic kidney<br>Renal cyst<br>Fibrous obstruction at uteropelvic junction<br>Peripelvic cyst<br>Aberrant vessel at uteropelvic junction |
| Neoplastic | Wilms' tumor<br>Renal cell carcinoma<br>Transitional cell carcinoma of the renal pelvis<br>Multiple myeloma |
| Inflammatory | Tuberculosis<br>Echinococcus |
| Metabolic | Calculi |
| Miscellaneous | Sloughed papillae<br>Trauma<br>Renal artery aneurysm |
| **Ureter** | |
| Congenital | Stricture<br>Ureterocele<br>Ureterovesical reflux<br>Ureteral valve<br>Ectopic kidney<br>Retrocaval ureter<br>Prune belly syndrome |
| Neoplastic | Primary carcinoma of ureter<br>Metastatic carcinoma |
| Inflammatory | Tuberculosis<br>Schistosomiasis<br>Abscess<br>Ureteritis cystica<br>Endometriosis |
| Miscellaneous | Retroperitoneal fibrosis<br>Pelvic lipomatosis<br>Aortic aneurysm<br>Radiation therapy<br>Lymphocele<br>Trauma<br>Urinoma<br>Pregnancy |
| **Bladder and urethra** | |
| Congenital | Posterior urethral valve<br>Phimosis<br>Urethral stricture<br>Hypospadias and epispadias<br>Hydrocolpos |
| Neoplastic | Bladder carcinoma<br>Prostate carcinoma<br>Carcinoma or urethra<br>Carcinoma of penis |
| Inflammatory | Prostatitis<br>Paraurethral abscess |
| Miscellaneous | Benign prostatic hypertrophy<br>Neurogenic bladder |

cases, incidental. When the obstruction is bilateral and chronic, patients may present with nonspecific complaints of an increase in abdominal girth (legwear does not fit), ankle edema, malaise, anorexia, headaches, weight gain, fatigue, and shortness of breath. They may also have symptoms reflective of uremia, such as mental status changes, tremors, and gastrointestinal bleeding. Patients with either a solitary kidney or a nonfunctioning contralateral renal unit can present with UUO and symptoms of uremia.

When the obstruction is unilateral and chronic, the patient may complain of intermittent flank pain during periods of forced diuresis, such as after the consumption of alcohol, a known diuretic. This has been referred to as a Dietls crisis, after the Polish physician, Joseph Dietl. Classically, the pain is described as a sudden excruciating pain in the kidney caused by distention of the renal pelvis, rapid ingestion of large amounts of liquid, or kinking of a ureter that produces temporary occlusion of the flow of urine from the kidney. If there is hydronephrosis associated with blunt trauma, the presenting symptom can also be gross hematuria. The extrinsic causes of obstruction usually have a more insidious and hence symptom-free presentation, whether they are unilateral or bilateral. These obstructions are usually detected incidentally during the routine clinical workup of the primary disease process. A history of the patient's voiding habits is also significant. These can vary from symptoms of a weak and intermittent urine stream, urgency, urgency incontinence, overflow incontinence, and nocturia, to barely any urination at all (i.e. complete obstruction). Finally, patients may also notice rather profound increases in their urine output, out of proportion to their fluid intake, which results from poor renal concentrating ability.

### Clinical signs and biochemical findings

The clinical signs of urinary tract obstruction are somewhat nonspecific. Obstruction is occasionally associated with an abdominal mass, usually suprapubic, but it may also be a large flank mass, palpable during physical examination, which on rare occasions can be visible. The patient may also have signs of volume overload, such as bipedal edema, pulmonary congestion, and hypertension. Laboratory data may include hematuria (microscopic and/or gross), proteinuria, crystalluria, pyuria, and urinary casts. When chronic obstruction is the predominant clinical picture, the urinary diagnostic indices are most often similar to those seen with acute tubular necrosis: an elevated urinary sodium concentration, a decreased urine osmolality, and a decreased urine-to-plasma creatinine ratio. If the obstruction is more acute and not accompanied by renal failure, the urinary indices can resemble those of prerenal azotemia: a low urinary sodium concentration and an increased urine osmolality [3]. The serum chemistry studies may demonstrate elevations of serum blood urea nitrogen (BUN) and creatinine, hyperkalemia, and acidosis.

When patients experience acute obstruction in the presence of bacterial urinary tract infection, they may present with signs and symptoms of pyelonephritis or systemic sepsis. Obstruction coexisting with infection is a true urologic emergency, and appropriate imaging studies (computed tomography [CT] scan, renal ultrasonography, or retrograde ureteropyelography) must be performed on an emergency basis. The obstruction must be relieved by either percutaneous nephrostomy or a ureteral stent.

The rationale for immediate relief of obstruction is based upon the physiology of fluid reabsorption during obstruction. After the onset of obstruction there is increased intrapelvic pressure, resulting in pyelolymphatic and pyelovenous urine back flow as well as possible forniceal rupture and extravasation [4, 5]. Accordingly, there is direct movement of urine and bacteria into the vascular tree during obstruction, resulting in a life-threatening situation. In chronic obstruction, despite a marked reduction in GFR and RBF [6], urine continues to move into the vascular system [7].

## Diagnosis

### Excretory urography

For the urologist, the intravenous urogram (IVU) has been the gold standard for the detection of ureteral obstruction in patients with normal renal function and who have no allergies to contrast material and are not pregnant. The urogram can provide both functional and anatomic details of the obstruction, as opposed to ultrasonography, which provides more anatomic detail.

Acute urinary obstruction is visualized on the IVU by (i) the obstructive nephrogram; (ii) a delay in filling of the collecting system with contrast material; (iii) dilation of the collecting system, possibly with an increase in renal size; and (iv) possible forniceal rupture with urinary extravasation [8]. Chronic cases of ureteral obstruction are usually visualized by ureteral dilation, tortuosity, and a standing column of contrast in the ureter to the point of obstruction. The kidney may demonstrate marked parenchymal thinning (either segmental or complete), calyceal crescents, and the soap bubble nephrogram [8]. *However, the IVP is rarely performed today in radiology departments.* It has essentially been replaced by the unenhanced CT scan (see below).

## Ultrasonography

The renal sonogram is a good starting point for evaluating renal units of patients who have azotemia, contrast-induced allergy, are pregnant, or are in the pediatric age group. Significant information can be obtained about both the renal parenchyma and the collecting system with no exposure to radiation, and no contrast-induced nephrotoxicity or anaphylaxis.

Hydronephrosis will appear as a dilated collecting system separating the normally echogenic renal sinus, creating an anechoic central area surrounded by parenchyma. Echoes within the collecting system may indicate an infection (pyonephrosis), hemorrhage, or a lesion of the transitional mucosa, among other diagnoses. The thickness of the renal parenchyma can be measured as an indicator of the duration of the obstruction; the degree of hydronephrosis should not be equated with the duration of the obstruction.

There are several pitfalls to the use of ultrasonography for diagnosing obstruction. Both the underdiagnosis of hydronephrosis, i.e. missing an obstruction (false negative), and overdiagnosis of obstruction due to the presence of hydronephrosis (false positive) are possible. Sonograms can be false negative as a result of an acute onset of obstruction, an intrarenal collecting system, dehydration, and the misinterpretation of caliectasis for renal cortical cysts. Sonograms can be false positive for obstruction as a result of a capacious extrarenal pelvis, parapelvic cysts, vesicoureteral reflux, and a high urine flow state [8]. Therefore, although an excellent tool for the initial evaluation of selected patients with suspected renal obstruction, the sonogram should be interpreted carefully and must be consistent with the overall clinical picture.

## Diuretic renography

The diuretic renogram is becoming more widely utilized than excretory urography for evaluation of the dilated collecting system. It provides a noninvasive measure of the relative renal function and has the ability to wash out the radiopharmaceutical agent from the dilated collecting system. There is a marked reduction in radiation dose in comparison with excretory urography, and there is no potential for contrast-induced nephrotoxicity [9].

The most widely used radiopharmaceutical agents are: (i) tubular tracers such as $^{131}$I-*ortho*-iodohippurate (OIH) and $^{99m}$Tc-mercaptoacetyltriglycine (MAG3); and (ii) glomerular tracers, namely $^{99m}$Tc-diethylene triaminepentaacetic acid (DTPA). For evaluating obstruction, the radiopharmaceutical agent of choice today is MAG3, because it is more efficiently extracted by the kidney than is DTPA, delivers a lower dose of radiation to the obstructed kidney than does OIH, and is excreted by the same portion of the tubule that responds to furosemide [9, 10]. MAG3 has been shown to provide better counting statistics and visualization of the anatomy of obstruction than do OIH and other radiopharmaceutical agents [11].

The technique of patient preparation and the timing of the administration of the diuretic, when diuretic renography is performed, are extremely important. The patients should be well hydrated before the procedure. An intravenous line may be started before the procedure [9, 12]. Patients who can void spontaneously do not require bladder catheterization. Those who cannot void spontaneously do require bladder catheterization to: (i) ensure adequate bladder drainage; (ii) reduce false-positive results; and (iii) decrease the radiation dose to the bladder and gonads. The patient's renal function is extremely important when the results from a diuretic renogram are interpreted. In the presence of a reduced creatinine clearance, it may be necessary to increase the diuretic dose to achieve an adequate flow rate and reduce the possibility of a false-negative result [13].

The timing of the administration of the diuretic after the administration of the radiopharmaceutical agent has been carefully worked out. Brown et al. determined that the urinary flow rate is 3.5 ml/minute greater at 15–18 minutes after intravenous furosemide than at 3–6 minutes after a diuretic (Figure 8.1) [14]. The traditional diuretic renogram is performed by administering the radiopharmaceutical agent and obtaining images, followed 20 minutes later by intravenous administration of the diuretic, and then measuring the half-life for the clearance of the tracer from the collecting system. O'Reilly et al. referred to this technique as the F + 20 diuretic renogram [15, 16]. Figure 8.2 depicts the various outcomes from the F + 20 diuretic renogram. Diagnostic dilemma arises with patients who show a partial

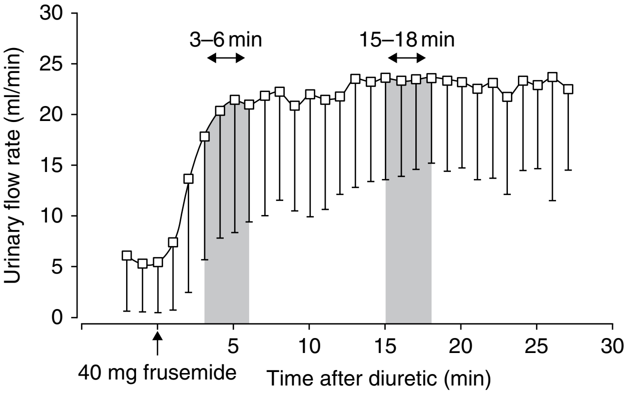

**Figure 8.1** Mean urinary flow rates following diuretic injection (error bars indicate standard deviation). Reproduced with permission of John Wiley and Sons.

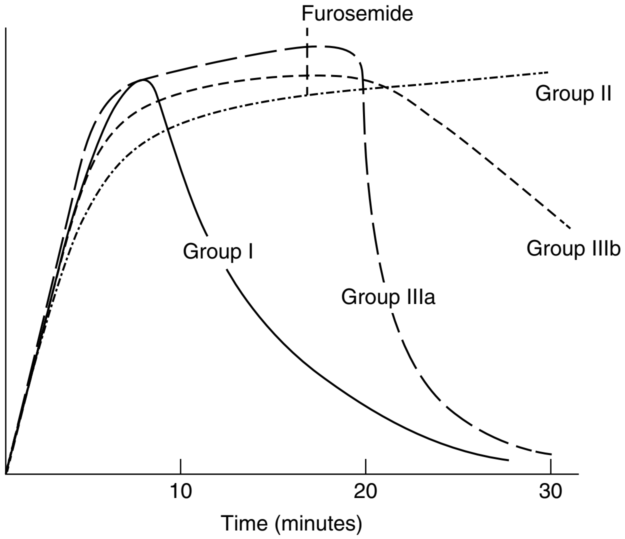

**Figure 8.2** Gamma camera renograms obtained from computer-generated regions of interest using OIH demonstrate four responses. Group I is a normal renogram. Since obstruction is sometimes unmasked by diuretic administration, O'Reilly et al. recommend a repeat renogram 15 minutes after diuretic administration. A second group I normal renogram excludes obstruction. Progressive accumulation (group II), despite administration of furosemide at about 20 minutes after tracer injection, confirms obstruction. On the other hand, rapid emptying following diuretic administration (group IIIA) despite an initial rise in the renogram curve indicates dilation without obstruction. Finally, an increasing curve with a partial excretory response may indicate either partial obstruction or renal dysfunction with an inability to respond to the diuretic (group IIIB). Reproduced with permission of Elsevier.

excretory response; this indicates either an inability to excrete the radioisotope because of poor renal function or a truly partially obstructed system (Group IIIa in Figure 8.2). Upsdell et al. were able to convert this equivocal response to the diuretic into a wash-out response by administering the diuretic 15 minutes before administering the radiopharmaceutical agent, i.e. F−15 [13]. This is the time it takes for Lasix to reach its maximal diuretic effect and thus eliminates "lag-time" as a false positive for obstruction. Some centers routinely use the F−15 technique for diuretic renography when renal obstruction is suspected. Others use the F + 20 technique for their routine diuretic renograms, reserving the F−15 technique for use when the F + 20 method demonstrates partial obstruction.

Data from the diuretic renogram can be interpreted either visually or by quantitative measurements of the half-life of the diuretic response [12]. There are many factors that influence the half-life, including: (i) renal function, which includes the level of renal maturity; (ii) compliance of the collecting system; (iii) volume of the collecting system; (iv) hydration of the patient; (v) presence or absence of a bladder catheter; (vi) radiopharmaceutical agent; and (vii) dose of the diuretic [9, 17]. It is generally accepted that a clearance of the radiopharmaceutical agent from the renal pelvis with a half-life of less than 10 minutes is normal; some experts consider a half-life of less than 15 minutes to be normal. Clearance of tracer with a half-life between 15 and 20 minutes is considered equivocal and a half-life greater than 20 minutes indicates an obstruction [9, 18].

## Whitaker test

The Whitaker test was considered the gold standard for the evaluation of upper urinary tract dilation. It provided urodynamic evidence of a mechanical obstruction of the upper urinary tract at a given flow rate. With the advent of the diuretic renogram and some of the newer radiopharmaceutical agents, the Whitaker test is not often utilized clinically. The Whitaker test is performed with the patient placed on a fluoroscopy table in the prone position. Before the patient is positioned prone, a bladder catheter is placed and connected to a pressure transducer for continuous monitoring of intravesical pressures with changes in renal pressure. A renal cannula (18G) is then inserted and connected to a pressure transducer. A combination of saline and contrast is administered via the renal cannula at a rate of 10 ml/minute. Bladder pressure is monitored throughout the procedure and its relationship to changes in renal pressure can be significant. Contrast is given along with the saline, making fluoroscopic monitoring of the anatomic site of the obstruction possible [19].

Results are separated into three categories [20]:

1) Pressure less than 15 $cmH_2O$ = nonobstructed
2) Pressures of 15–22 $cmH_2O$ = equivocal
3) Pressures greater than 22 $cmH_2O$ = obstructed.

Because the diuretic renogram is noninvasive and easily reproducible, and provides quantitative evaluation of the split and total renal function with minimal radiation exposure, it is clinically utilized more today than the Whitaker test. However, when there is extreme upper tract dilation and/or poor renal function precluding an adequate diuretic response, the pressure flow study may still have clinical utility.

## Duplex Doppler ultrasonography and renal resistive index

The use of duplex Doppler during ultrasonographic evaluation of the kidney allows the determination of the renal resistive index (RI) where [21, 22]:

$$\mathrm{RI} = ([\text{peak systolic velocity}] - [\text{lowest diastolic velocity}]) / [\text{peak systolic velocity}]$$

A value of 0.70 has been taken as the upper limit of normal [23]. RIs above 0.70 are used for the diagnosis of obstruction, although this diagnosis is not exclusive for obstruction, in as much as medical renal diseases alone can also cause the RI to exceed 0.70. An RI in the obstructed kidney that is 0.1 greater than the RI in the contralateral kidney is considered to be significant enough to indicate obstruction [24].

There is much controversy in the literature regarding the use of the RI in obstruction. Platt et al. presented data on 23 patients with acute UUO of 36 hours duration or less, measuring the RI index in the "obstructed" and the contralateral renal units [25]. The mean RI in the obstructed kidney was 0.77, as opposed to 0.60 for the normal contralateral kidney. In three obstructed kidneys with an RI of less than 0.70, two had pyelosinus extravasation and one had obstruction for less than 4–5 hours. Because the vasoconstriction of UUO occurs after 5–6 h, the RI may not rise until renal obstruction has been present for at least 5–6 hours. Platt et al. concluded that Doppler determination of renal RIs is a valuable addition for improving the accuracy of routine renal ultrasonography in the diagnosis of renal obstruction in patients presenting with acute renal colic and for whom an IVU is not desirable, e.g. pregnant patients and patients with a history of contrast-induced allergy or renal failure.

Other investigators believe there is no role for duplex Doppler sonography in the detection of acute renal obstruction [22, 26]. Tublin et al. evaluated 32 patients with acute renal colic [26]. Twelve of the obstructed kidneys had a mean RI of less than 0.70, and seven of the nonobstructed kidneys had a mean RI of greater than 0.70. Using an RI of greater than 0.70 as diagnostic of acute renal obstruction, they determined that the sensitivity and specificity of duplex Doppler sonography were 37 and 84%, respectively. When using a difference in the RI of greater than 0.10 between the ipsilateral and contralateral renal units to diagnose obstruction, they determined that the sensitivity and specificity were 37 and 100%, respectively.

The difference in clinical findings between the two studies described above may result from several factors, including: (i) the quality of the examination and the Doppler waveform analysis; (ii) the duration of obstruction; (iii) the presence of a fornix rupture and extravasation; and (iv) the degree of obstruction. Finally, Tublin et al. pointed out that the initial management of the acute renal colic with nonsteroidal anti-inflammatory drugs (NSAIDs) could alter the intrarenal vascular tone and hence affect the RI [26].

## CT and magnetic resonance imaging

Smith et al. investigated the use of noncontrast-enhanced CT in the diagnosis of acute flank pain [27]. They compared the findings in 20 patients with acute flank pain on both noncontrast-enhanced CT and IVU. CT and IVU demonstrated ureteric obstruction in 12 patients. In five of the 12, a stone was demonstrated on both studies. Six patients had a stone that was seen on noncontrast-enhanced CT and not on IVU. In one patient, a stone could not be visualized on either study, and no obstruction was demonstrated with either investigation in eight patients. Noncontrast-enhanced CT was performed at either 5 or 10 mm cuts, and all studies were completed within 5 minutes. Noncontrast-enhanced CT is more sensitive than IVU in the detection of ureteric stones in acute flank pain ($P < 0.01$). In addition, CT can provide information about extrinsic causes of ureteral obstruction, as well as nonurinary causes for the acute flank pain. CT is currently the accepted alternative to IVU especially for patients in whom the immediate use of intravenous contrast without steroid preparation is contraindicated, e.g. patients with asthma or in patients with elevations in serum BUN and/or creatinine.

Today, unenhanced helical CT is gaining widespread acceptance in many institutions over conventional CT imaging. The images are obtained faster than conventional CT scanning, often in one breath hold. The axial images can be used to create sagittal and/or coronal reformations, adding to the anatomic detail of the urinary tract and the potential for stone passage. The secondary signs of obstruction on helical CT include: (i) hydroureter; (ii) perinephric stranding; (iii) hydronephrosis; (iv) periureteral edema; and (v) renal swelling [28]. Unenhanced helical CT and conventional CT may not differentiate a uric acid from a calcium stone, necessitating a kidney–ureter–bladder (KUB) X-ray study to differentiate the stone type. However, it has been described that uric acid calculi have lower attenuation values than calcium oxalate calculi, which have very high attenuation values (1000–1570 Hounsfield units). Therefore, the differentiation of stone type is possible on the CT images [28]. It should be noted that stones formed following administration of indinavir (Crixivan) are not detectable on CT [29].

Rothpearl et al. investigated the use of magnetic resonance imaging (MRI) for the simultaneous visualization of the entire urinary tract without the use of intravenous contrast or ionizing radiation [30]. For all patients with urinary tract obstruction, a diagnosis of obstruction was made on the MR urogram. However, in eight patients in whom ureteral calculi was the source of obstruction, there was no visualization of calculi on the MR urogram. This was accomplished by comparing the urogram with a scout radiograph of the kidneys, ureter, and bladder. The point of obstruction was identified in all patients, and other etiologies for obstruction, e.g. intraluminal ureteral neoplasm and ureteral stricture disease, were well visualized. Some of the disadvantages of this technique, in addition to the inability to identify the ureteral calculus, are the image acquisition time of 34 minutes and the cost of the procedure. Additional studies comparing MRU to CT also reveal that MRU misses small calculi and mild dilatation. In addition, it is time-consuming and expensive and is limited to special situations, such as pregnant patients [31]. Again, for patients with allergies to iodinated contrast and renal failure, this technique may have its place.

## Experimental ureteral obstruction

The experimental models for ureteral obstruction include: (i) unilateral or bilateral ureteral ligation; (ii) burying the mid ureter within the psoas muscle; and (iii) placing silastic plastic tubing around the ureter to constrict the ureteral lumen.

### Unilateral ureteral obstruction

**RBF, GFR, and ureteral pressure**

The acute unilateral occlusion of a ureter will result in a characteristic triphasic relationship between RBF and ureteral pressure [32]. The first phase is characterized by a rise in both ureteral pressure and RBF lasting approximately 1–1.5 hours. This is followed in phase 2 by a decline in RBF and a continued increase in ureteral pressure lasting until the fifth hour of occlusion. The final phase ensues with a further decline in RBF accompanied by a progressive decrease in ureteral pressure (Figure 8.3). Hemodynamically, phase I is characterized by an initial afferent arteriole vasodilation [6] followed by an efferent arteriole vasoconstriction in phase II and afferent arteriole vasoconstriction in phase III [33]. The third phase of UUO, the vasoconstrictive phase, is characterized by both pre- and postglomerular vasoconstriction that reduces both RBF and ureteral pressure [32]. Yarger et al. demonstrated a marked decrease in the perfusion of the superficial cortical tissue and an increase in the perfusion of juxtamedullary glomeruli after 24 hours of UUO [34]. In addition, effective renal plasma flow (eRPF) was shown to be 55% of control values in the obstructed kidney after 24 hours of UUO [35]. Utilizing the injection of microspheres during ureteral occlusion, they also demonstrated an increase in intrarenal blood flow to the juxtamedullary nephrons, with a corresponding decrease in blood flow to the outer cortical nephrons. They believed that an increase in renin in the outer cortex relative to the inner medulla may explain the shift in intrarenal blood flow [35]. Glomerular cast studies show the poor glomerular perfusion that accompanies UUO (Figure 8.4). Arendshorst et al. confirmed with micropuncture studies that changes seen in the whole kidney by 24 hours of UUO are found at the single nephron level in association with afferent arteriolar vasoconstriction [36]. Studies using a continuous infusion of $^{51}$Cr-ethylenediamnietetra-acetic acid ($^{51}$Cr-EDTA), which allow direct measurement of GFR during obstruction, show a 75% decrease in GFR after the onset of UUO [37].

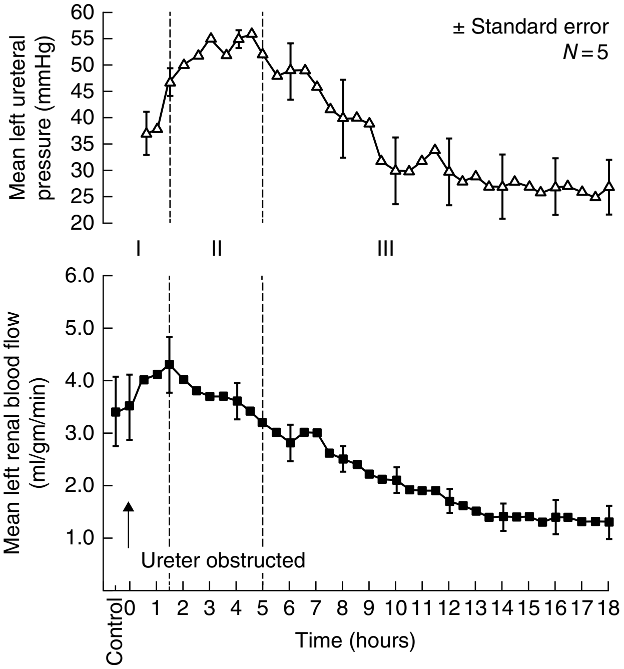

**Figure 8.3** Triphasic relationship between ipsilateral renal blood flow and left ureteral pressure during 18 hours of left occlusion. The three phases are designated by roman numerals and divided by vertical dashed lines. In phase I, RBF and ureteral pressure rise together. In phase II, the left RBF begins to decline; ureteral pressure remains elevated and, in fact, continues to rise. Phase III shows the left RBF and pressure declining together. Reproduced with permission of Elsevier.

The initial increase in RBF, which has been well characterized in the dog and rat [38], may not occur in all species. In studies in the pig, which has a multicalyceal kidney similar to humans, there is a continuing decline in RBF after onset of UUO [37]. In baboons, 12 hours of UUO was not accompanied by a significant change in RBF [39]. In the 4-week-old lamb, RBF was stable for 5 hours after onset of UUO, and declined to 71% of baseline at 5 days [40]. It is not known if the difference in the RBF response is due to the presence of a multicalyceal kidney or other factors.

Although the physiologic changes characteristic of phase I and III of UUO have been known for some time,

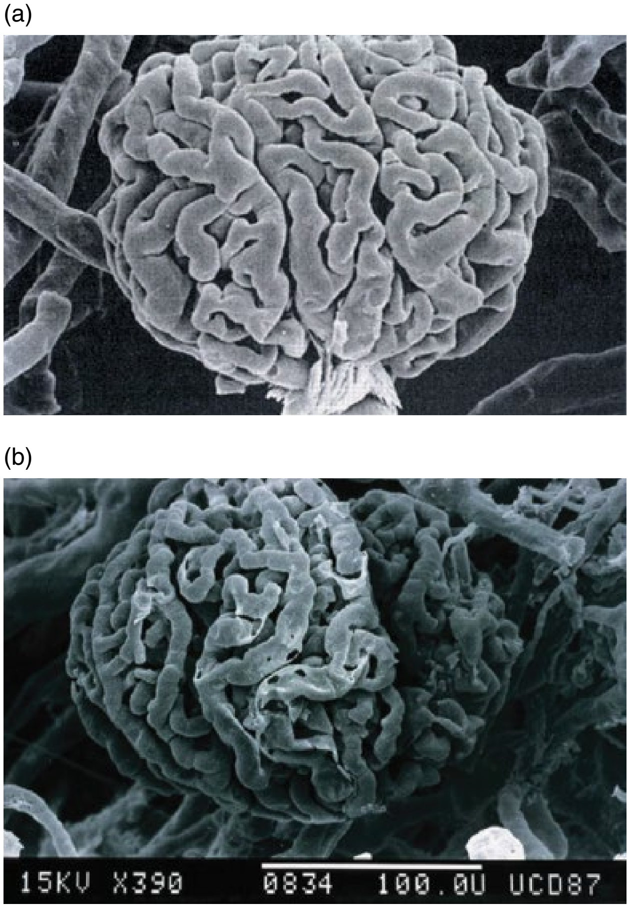

**Figure 8.4** (a) Scanning electron microscopic appearance of normal glomerular cast (magnification ×390). (b) Appearance of glomerular microvascular cast after obstruction showing capillary collapse and irregularity (magnification ×390). Reproduced with permission of Elsevier.

studies are still underway to understand the underlying cellular and molecular changes. Early studies invoked local physical interactions to explain changes in afferent and efferent arteriolar tone. Table 8.2 summarizes the effects of the various mediators on afferent and efferent glomerular arteriolar tone. However, it soon became clear that biochemical mediators were responsible for a substantial portion of these changes. Numerous studies have been carried out to determine the role of eicosanoids (prostaglandins and thromboxane), angiotensin II, nitric oxide, and endothelin in the acute and chronic changes in RBF.

## Bilateral ureteral obstruction

### RBF, GFR, and ureteral pressure

The triphasic pattern of RBF and ureteral pressure changes that characterizes UUO is not seen after BUO or unilateral obstruction of a solitary kidney. RBF increases after the first 90 minutes of BUO, as it does with UUO [41]. However, between 90 minutes and 7 hours of BUO, the RBF is significantly lower than the RBF during the same time interval of UUO (Figure 8.5a). The decrease in RBF is accompanied by an increase in renal vascular resistance during BUO to a greater level than with UUO (Figure 8.5b). However, by 24 hours of BUO, the RBF is as low and renal vascular resistance as high as with 24 hours of UUO (Figure 8.5a, b). However, ureteral pressure is higher than in UUO (Figure 8.5c). Gulmi et al. found effective RBF to be markedly decreased even at 48 hours of BUO [42]. After release of BUO, the RBF remained significantly decreased in comparison with preobstruction values for 11 hours of the study. Jaenike showed that the distribution of RBF after BUO is much different from that in the UUO model [43]. Using radioactive microspheres, he showed that 55% of RBF remains in the cortical nephrons and only 14% is shifted to the innermost renal zones. Yarger et al. used micropuncture studies to demonstrate a decrease in both whole kidney as well as single nephron clearance of *para*-aminohippurate (PAH) (17 and 55%, respectively) [44]. Solez et al., using intravenous [$^{125}$I]albumin infusion, showed a marked decrease in inner medullary plasma flow to 8% of normal by 18 hours of BUO [45].

Ureteral pressure follows a similar pattern for the first 4.5 hours of both BUO and UUO, i.e. a progressive rise in pressure (Figure 8.5c). However, after 4.5 hours of BUO,

**Table 8.2** Vasoactive mediator involvement in the hemodynamic changes of unilateral ureteral obstruction.

| | Afferent arteriole | Efferent arteriole |
|---|---|---|
| Vasodilation | Prostaglandin E2 (PGE2)<br>Prostaglandin I2 (PGI2)<br>Nitric oxide (NO)<br>Atrial natriuretic peptide (ANP) | PGI2<br>NO |
| Vasoconstriction | Angiotensin II (AII)<br>Endothelin (ET)<br>Platelet activating factor (PAF) | AII<br>ET<br>PAF<br>ANP |

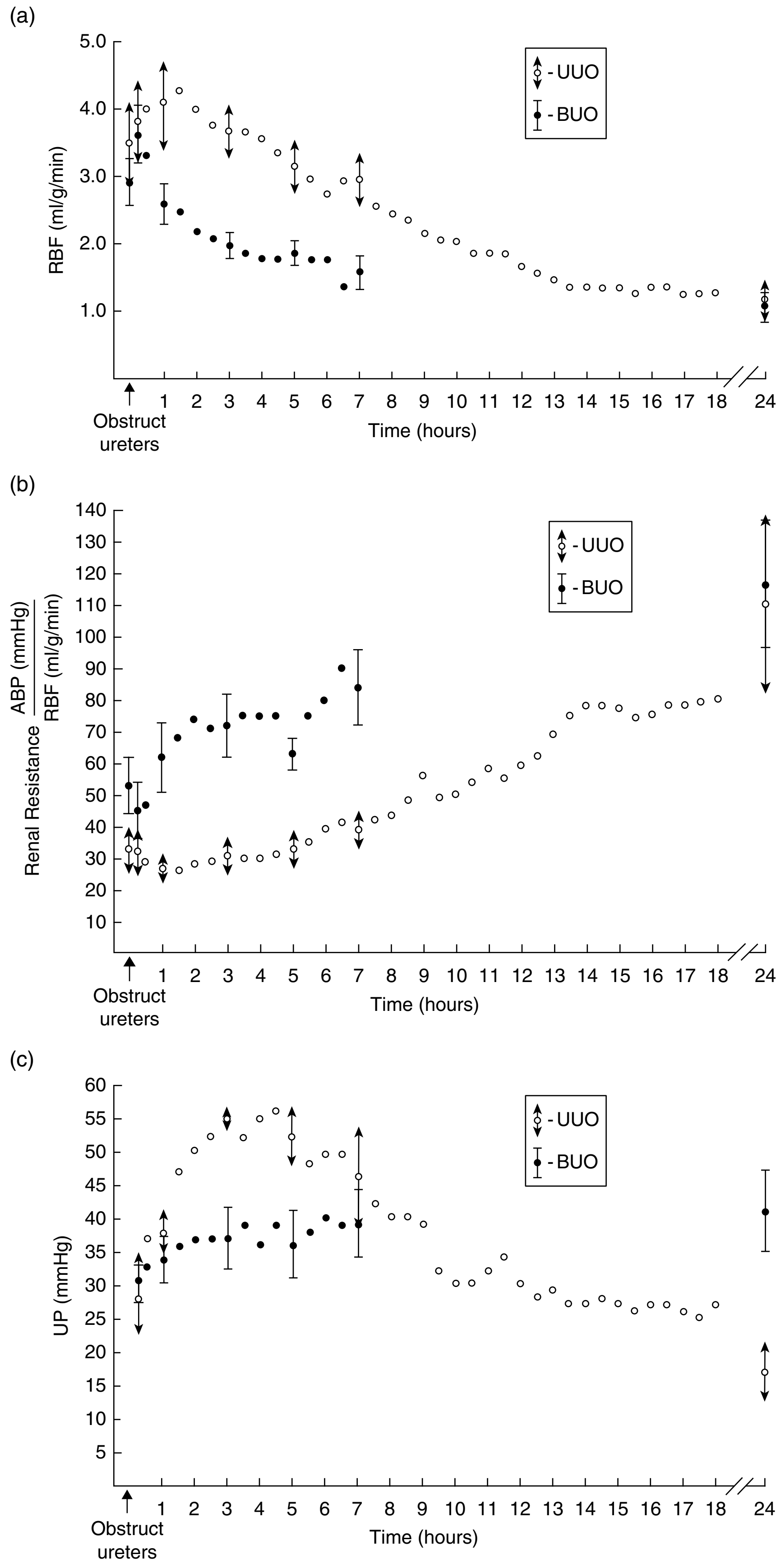

**Figure 8.5** (a) Comparison of RBF in UUO and BUO, demonstrating a similar pattern of change over the 24 hour period, although the RBF in the BUO model is below that of the UUO model from 1.5 to 7 hours postobstruction. (b) Comparison of the renal resistance (RR) in UUO and BUO demonstrating similar changes over the 24 hours period with the RR in the BUO model being higher than in the UUO model in the early hours, corresponding to the lower RBF at that time in BUO. ABP, arterial blood pressure. (c) Comparison of ureteral pressure (UP) in UUO and BUO demonstrating significant difference in the UP at 24 hours postobstruction.

the ureteral pressure remains elevated until 24 hours, whereas in UUO, ureteral pressure begins to progressively decline to control levels by 24 hours of ureteral occlusion (Figure 8.5c). This increase in ureteral pressure has been documented to at least 48 hours after BUO [42]. Dal Canton et al. demonstrated an increase in intratubular pressure from 14.1 to 28.9 mmHg ($P < 0.005$) with micropuncture studies in rats after 24 hours of BUO [46]. This change in intratubular pressure caused a decrease in the hydrostatic pressure gradient from 31.7 to 20.0 mmHg and a decrease in the effective filtration pressure at the afferent end of the glomerulus from 16.6 to 5.4 mmHg ($P < 0.001$). Yarger et al. also measured both proximal and distal tubular pressures during micropuncture studies of rats after 24 hours of BUO and found the pressures to be 30 and 27.7 mmHg, respectively, in comparison with 9.2 and 6.5 mmHg, respectively, in UUO rats ($P < 0.001$). The micropuncture studies of both groups have confirmed what other investigators have observed from the monitoring of ureteral pressure, a rise after 24 hours of BUO. Therein lies one of the differences between BUO and UUO. BUO passes through a phase of preglomerular vasodilation and then a postglomerular vasoconstriction and remains in this state. This explains the progressive and persistent rise in ureteral pressure despite a decrease in RBF and an increase in renal vascular resistance. In contrast, during UUO, the kidney passes through three phases: preglomerular vasodilation, postglomerular vasoconstriction and, finally, preglomerular vasoconstriction (see above).

The GFR after 48 hours of BUO is significantly decreased (22% of control values) in comparison with preobstruction GFR [42]. This decrease was also seen by Jaenike in rats after 24 hours of BUO; the GFR was reduced to 20% of the control value [43]. With micropuncture studies, Jaenike also found single nephron GFR (SNGFR) to be 34% of normal [43]. However, Yarger and Harris showed that the number of functioning nephrons, as well as the GFR of those functioning nephrons, is higher for kidneys after BUO than after UUO [47]. Harris and Yarger also demonstrated that 84% of superficial and 49% of juxtamedullary nephrons filter after 24 hours of BUO, as opposed to 40% of superficial and 12% of juxtamedullary nephrons after 24 hours of UUO [33].

Dal Canton et al. performed micropuncture studies on rats after 24 hours of BUO [46]. They observed a decrease in SNGFR after release of BUO to 40% of normal, secondary to an increase in intratubular pressure from 14 to 30 mm Hg. There was little change in glomerular capillary pressure (46 and 50 mmHg, pre- and postobstruction, respectively). With relief of obstruction, there was a 52% increase in afferent arteriole resistance, resulting in a low SNGFR in the postrelief period. Therefore, in both BUO and UUO, there is a decline in SNGFR after 24 hours of ureteral occlusion. In UUO this is secondary to an increase in afferent arteriolar resistance, whereas in BUO it is secondary to a rise in intratubular pressure with little change in afferent arteriolar resistance (Table 8.3).

**Table 8.3** Comparison of the effects of UUO and BUO in glomerular hemodynamics. Reproduced with permission of Elsevier.

| | $P_T$ | $P_G$ | AAPF | $R_a$ | SNGFR |
|---|---|---|---|---|---|
| 24 hours UUO | = = = | ↓ | ↓↓ | ↑↑ | ↓↓ |
| 24 hours BUO | ↑↑ | = = = | = = = | = = = | ↓↓ |

AAPF, afferent arteriole plasma flow; $P_T$, intratubular pressure; $P_G$, hydrostatic pressure across glomerular capillaries; $R_a$, resistance of single afferent arteriole; SNGFR, single nephron GFR.

### Involvement of atrial natriuretic peptide

Several investigators have postulated the accumulation of a "substance" during BUO that would affect the glomerular hemodynamics in such a way that there would be preglomerular vasodilation and postglomerular vasoconstriction, as seen with late-phase BUO. This substance would not accumulate during UUO, because it could be excreted by the contralateral kidney. Wilson and Honrath demonstrated such a substance with cross-circulation studies in rats [48]. When the cross-circulation was between a donor rat with 24 hours of BUO and a normal recipient rat, there was an immediate increase in both sodium and water excretion. This did not occur when the donor rat was subjected to 24 hours of UUO.

Harris and Yarger also postulated the existence of a circulating diuretic factor that accumulated only during BUO [49]. They observed an increase in urine flow and sodium excretion after relief of BUO, UUO with contralateral nephrectomy, or UUO with the continuous intravenous reinfusion of urine from the contralateral kidney. In contrast, the UUO-alone animals did not have postobstructive diuresis and natriuresis.

The discovery of atrial natriuretic peptide (ANP) paved the way for studies on the role of ANP in BUO. ANP has several physiologic effects, including vascular smooth muscle relaxation, i.e. vasodilation, natriuresis, and diuresis. The natriuretic and diuretic actions of ANP have been shown to be caused by: (i) an increase in GFR through afferent arteriole vasodilation and efferent arteriole vasoconstriction; (ii) an increase in glomerular capillary ultrafiltration coefficient (Kf); and (iii) inhibition of the glomerular–tubular feedback mechanism [50]. These glomerular hemodynamic effects point to ANP as the circulating diuretic and natriuretic substance postulated by previous investigators to explain the observed changes in RBF, ureteral pressure, and glomerular filtration during BUO.

**Table 8.4** Differences in tubular function after release of unilateral and bilateral ureteral obstruction (24 h).

| | Control | Unilateral | Bilateral |
|---|---|---|---|
| Postobstructive diuresis | | Absent | Present |
| Percent of filtration excreted (V/GFR) | 1% | Decreased to 0.5% | Increased to 18% |
| $Na^+$ excretion fraction filtered | | | |
| Proximal tubular reabsorption | | Decreased | Decreased |
| Distal tubular reabsorption | | | Decreased |
| Proximal fraction reabsorption | 58% | 74% | 46% |
| Distal fraction reabsorption | 12% | | 34% |
| Fraction $K^+$ excreted | 12.3% | Decreased to 7% | Increased to 90% |
| Concentration U:P | 7.6 | 1.35 | 1.47 |

Fried et al. demonstrated an elevated level of plasma ANP in rats after 24 hours of BUO, but not after 24 hours of UUO (393 vs. 261 pg/ml;, $P < 0.01$) [51]. Purkerson et al. have shown plasma ANP levels of 400 pg/ml in rats with 24 hours of BUO, in comparison with 71 pg/ml in rats with UUO ($P < 0.01$) and 81 pg/ml in controls ($P < 0.01$) [52]. Elevated ANP has also been demonstrated in patients with either BUO or UUO of a solitary kidney, or in volume-replete dogs after 48 hours of BUO [42, 53].

With the demonstration of elevated levels of ANP in BUO, it became clear that ANP was likely the factor previously postulated by Wilson and Honrath [48] and Harris and Yarger [49]. The stimulus for the elevated plasma ANP seems to be an increase in intravascular volume, as determined by an elevation in pulmonary capillary wedge pressure and body weight in volume-replete dogs with BUO [42]. In support, clinical studies in patients on chronic hemodialysis show that intravascular volume, and not the degree of renal failure, is the stimulus for an elevation in their plasma ANP levels.

### Other mediators

Reyes et al. have examined the role of NO in BUO [54]. When N-NAME, an L-arginine antagonist, was infused, there was a further decrease in GFR and eRPF compared to controls, suggesting that NO was maintaining GFR and eRPF during BUO. This was confirmed by showing that there was an improvement in GFR and eRPF, as well as a decrease in renal vascular resistance with the infusion of L-arginine into rats with unilateral release of 24 hours of BUO. Other factors may also be involved in BUO. Reyes and Klahr demonstrated that antibodies to either platelet activating factor, endothelin, or vasopressin can ameliorate changes in GFR and eRPF either during or after release of BUO [55–57].

### Tubular changes in BUO

There are differences between tubular function after release of BUO and UUO (Table 8.4). Several investigators have described marked diuresis and natriuresis after the relief of either BUO or UUO of a solitary kidney in humans [53, 58–61]. Maher et al. described a significant increase in urine volume and sodium excretion after relief of obstructive uropathy [57]. The urinary flow more closely followed the osmolar excretion than the sodium excretion in this patient study. The predominant urine solute during this osmotic diuresis was urea, accounting for 37–68% of the total urine osmolality. When serum urea returned to normal, the diuresis ceased. Maher et al. therefore postulated that the physiologic diuresis was caused by a high serum urea concentration, which ceased when the BUN returned to normal.

Muldowney et al. measured total exchangeable sodium to determine whether the postrelease natriuresis of BUO is pathologic or merely a physiologic elimination of excess body sodium [62]. They found that patients with chronic obstructive uropathy had an increase in total exchangeable body sodium before release of obstruction. After relief of the obstructive uropathy, total exchangeable body sodium levels returned to normal within 2–3 weeks. The loss of sodium in the urine did not result in clinical sodium depletion in any of the patients. Muldowney et al. concluded that the increased loss of sodium in the urine upon release of chronic obstructive uropathy is a physiologic reduction of excess body sodium to normal levels.

Gulmi et al. described nine patients with obstructive uropathy and postobstructive diuresis and natriuresis [53]. Patients with obstruction had a significantly elevated plasma ANP, in comparison with the control group of patients (Figure 8.6). There was an increase in both absolute and fractional excretion of sodium that subsided with improvement in renal function.

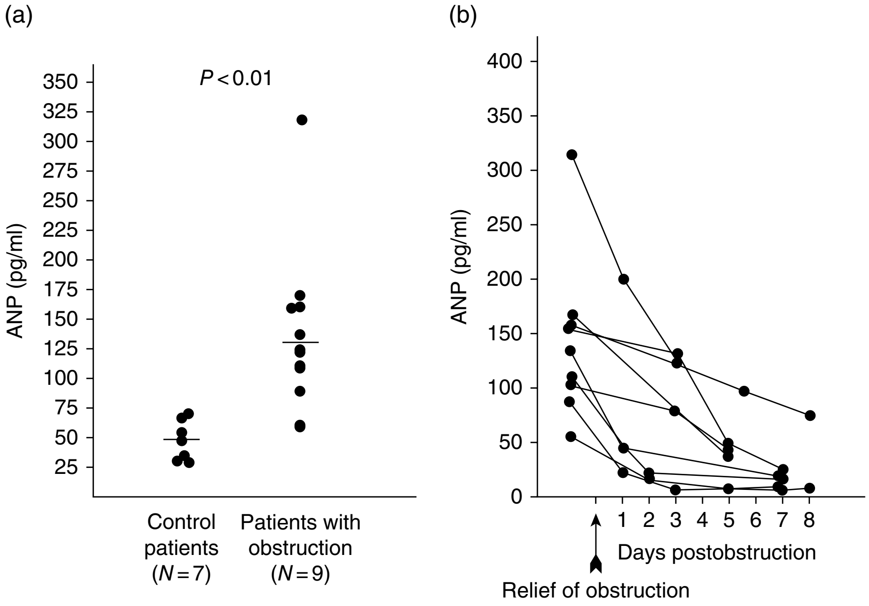

**Figure 8.6** Plasma ANP levels in (a) control group and patients with obstruction, and (b) before and after relief of obstruction. Reproduced with permission of Elsevier.

This natriuresis and diuresis was associated with an elevation of serum ANP in all patients, which decreased as water and salt excretion decreased (Figure 8.6). Because ANP is a known diuretic and natriuretic, it may be one of the main factors causing the loss of water and salt in the postobstructive state.

## Fibrosis in ureteral obstruction

The obstructed kidney is characterized by accumulation of collagen-rich scar tissue, the most common feature of fibrotic organs. Most of the microscopic changes are confined to the tubules with little effect on the glomeruli. Fibrosis is a rapid occurrence in the experimentally obstructed kidney, with studies demonstrating the accumulation of collagens I, III, and IV, fibronectin, and laminin in the interstitium [63–65].

Despite the relative sparing of the glomerulus from fibrosis, there is a clear decline in GFR in the obstructed kidney. This is consistent with the finding in a variety of chronic renal diseases, that the presence of interstitial fibrosis is a major determinant of GFR [66]. There are several possible reasons for this: tubular atrophy can result in atubular glomeruli, which detached from their corresponding proximal tubules, are unable to filter properly [67]. The accumulation of extracellular matrix can isolate tubules from their oxygen supply and may also result in obliteration of peritubular capillaries, which can also result in decreased GFR [68].

Fibrosis is a complex process, and the mechanisms which initiate and sustain it are both the subject of much investigation and controversy. As more is understood about this process, the prospect of developing targeted therapies to attenuate this process becomes likely. Both the renal epithelium and fibroblasts have long been studied in the obstructed kidney. A review of fibrosis [69] presented five different ways in which epithelial injury can result in tissue fibrosis (Figure 8.7). The first is epithelial cell death, either apoptosis or necrosis. The second is dysregulation of metabolic pathways, resulting in cell stress. The third is epithelial-mesenchymal transition (EMT), in which there is a decreased expression of important epithelial surface proteins. The fourth involves interactions between the profibrotic cytokine transforming growth factor-β (TGF-β) and integrins, proteins that function mechanically by attaching the cell cytoskeleton to the extracellular matrix. And finally, injured epithelial cells initiate innate and adaptive immune responses. Each of these processes has been studied in the UUO model, and a summary of the most pertinent data is presented below.

### Tubular apoptosis

Truong et al. provided the first detailed analysis of apoptosis in UUO [70]. They studied the tubular and interstitial components from 0 to 90 days of UUO. There was virtually no change in glomerular apoptosis throughout the period examined. There was a sharp peak in tubular apoptosis at day 25, whereas interstitial apoptosis peaked at day 75. The apoptotic rate was twofold higher in tubular cells than in interstitial cells. Choi et al. demonstrated similar findings in mice studied from 4 to 45 days of

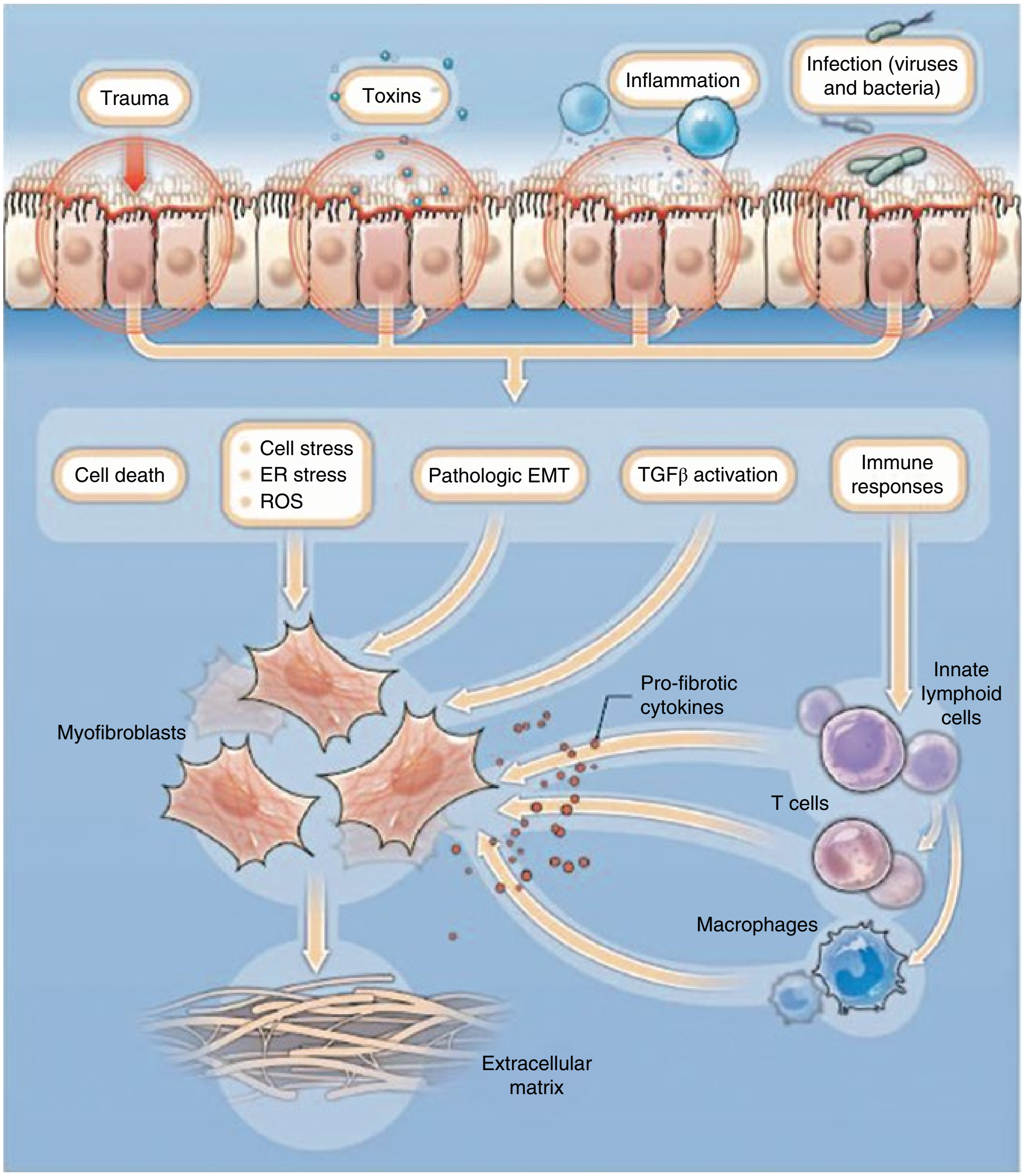
Trauma
Toxins
Inflammation
Infection (viruses and bacteria)
Cell death
Cell stress
ER stress
ROS
Pathologic EMT
TGFβ activation
Immune responses
Myofibroblasts
Pro-fibrotic cytokines
Innate lymphoid cells
T cells
Macrophages
Extracellular matrix

**Figure 8.7** Mechanisms by which epithelial injury can lead to organ fibrosis. A wide range of injurious stimuli initiate several distinct profibrotic programs in epithelial cells. In the most extreme case, injury induces cell death, which is sufficient to initiate fibrosis in a variety of fibrotic disease models. Injured epithelial cells can undergo dysregulated metabolism, leading to production of reactive oxygen species (ROS) and endoplasmic reticulum (ER) stress, or they can be reprogrammed toward a mesenchymal-like phenotype (pathologic EMT). In response to danger signals that are released or activated in response to injury, epithelial cells use cell-surface integrins to activate latent TGF-β, a well-characterized central mediator of tissue fibrosis. Finally, injured epithelial cells recruit and activate a variety of immune cells, which, in turn release profibrotic cytokines along with innate lymphoid cells, T cells, and macrophages (for example interleukins IL-13 and IL-17 among many others). Each of these perturbations of epithelial cells ultimately leads to expansion, recruitment, and/or activation of tissue myofibroblasts, the principal source of pathologic extracellular matrix that characterizes organ fibrosis.

UUO [71]. Tubular apoptosis was maximal at day 15, whereas interstitial apoptosis was still increasing at day 45. Docherty et al. suggested that tubular apoptosis is a major contributor to fibrosis in UUO, and conversely that inhibiting apoptosis decreases fibrosis in UUO [72]. In many experimental studies demonstrating effectiveness of various antifibrotic strategies tubular apoptosis was decreased along with decreases in fibrosis. However, whether this is causative or merely a response to the treatments remains to be determined.

### Dysregulation of metabolic processes and changes in cellular metabolism

Tissue injury can lead to disruption of the local environment. The cell stress response involves mechanisms by which cells cope with these disruptions. A significant participant in the stress response is the endoplasmic reticulum (ER), the cell organelle responsible for synthesis, folding, modification, and assembly of proteins. Although ER stress [73] can function to re-establish the normal environment, excess ER stress can damage cells, perhaps through inducing cell apoptosis and release of inflammatory mediators. Recent studies targeting different proteins involved in the ER stress response implicate this process in fibrosis. Metformin reduced renal fibrosis in UUO, along with expression of GRP78, a modulator of ER stress [74]. The reticulon family of proteins has been shown to be involved in apoptosis and the ER stress response. Reticulon 1 was found to be increased in UUO, and reduction of reticulon 1A expression in UUO both attenuated fibrosis and decreased ER stress markers [75].

ATP, the source of cellular energy, is made in mitochondria via the electron transport chain. Injury and aging may be characterized by a decrease in cellular ATP. A new class of compounds, the SS-peptides, have been shown to be remarkably effective in decreasing and preventing tissue injury in response to a variety of insults [76]. SS-31, a prototype of this group, has been shown to interact with and stabilize cardiolipin in the inner mitochondrial membrane [77]. This prevents mitochondrial damage and maintains ATP levels. Mitochondrial dysfunction in UUO has been shown in studies demonstrating increased cytosolic cytochrome *c* [78]. Using the mitochondrial targeted SS-31 in UUO, we demonstrated its efficacy in deceasing fibrosis, apoptosis and oxidative stress [79].

### Epithelial-mesenchymal transition

*In vitro*, it has been shown that tubules can be transformed into cells with a myofibroblastic phenotype. Many studies have demonstrated that incubation of renal tubular epithelial cells with varying doses of the TGF-β causes changes [80, 81] including: (i) the typical cobblestone appearance of cells in culture is replaced by the elongated spindle shape associated with fibroblasts and (ii) loss of apical–basal polarity and cell surface microvilli: the apical–basal polarity is replaced by a front end/back end fibroblast-like polarity; (iii) using electron microscopy, large bundles of actin microfilaments and dense bodies are seen; (iv) the expression of either α-smooth muscle actin (α-SMA) or fibroblast-specific protein-1 (FSP-1); and (v) loss of the epithelial antigen, E-cadherin. The effects of TGF-β are blocked by a neutralizing antibody to TGF-β. The loss of cell adhesion, expression of the mesenchymal markers, and subsequent degradation of the basement membrane allows for changes in shape and motility. Many studies have demonstrated that epithelial-mesenchymal transition (EMT) occurs in UUO and have suggested that this is a major contributor to fibrosis. Yang and Liu showed a marked decrease in E-cadherin and a marked increase in α- SMA in UUO [82]. There was also an increase in TGF-β receptors in renal tubules. When hepatocyte growth factor was administered, interstitial fibrosis was decreased, as well as the expression of α-SMA. Iwano et al. used a combination of bone marrow chimeras and transgenic reporter mice, and studied the expression of FSP+ cells in UUO [83]. They determined that a small population of FSP+ cells derived from bone marrow, but a larger proportion arose from local EMT of proximal tubular cells. Both FSP+ cell populations were able to synthesize collagen and to proliferate. Conversely, when they used methods to selectively remove the FSP+ cell population in the kidney and the mice then underwent UUO, both type I collagen deposition and fibrosis were reduced. These results demonstrate that FSP+ fibroblasts are at least partially responsible for the fibrosis of UUO [83]. Sato et al. have also demonstrated decreased E-cadherin and increased α-SMA expression in UUO [84]. Using Smad-3 knockouts (a downstream effector of TGF-β), they demonstrated that the decrease in E-cadherin and the increase in α-SMA can be reversed. Furthermore, Smad-3 knockouts exhibit less fibrosis than their wild-type counterparts. In a recent review of the role of EMT in fibrosis, Zeisberg [85] notes that, in mice, transgenic expression of snail, a protein induced in epithelial cells by EMT, recapitulates all stages of renal fibrosis in mice. Despite all the previous studies, there has recently emerged evidence that challenges the role of EMT; this has been reviewed recently by Duffield [85, 86], who suggests that some of the data implicating EMT represent artifacts and have therefore led to erroneous conclusions. One study used fate mapping of mesenchyme-derived stromal cells of the developing kidney that mature into perivascular pericytes (perivascular cells that wrap around blood capillaries) in the adult kidney; this study showed that pericyte precursors are the primary and only source of myofibroblasts in the UUO model [87]. The other used an epithelial-specific transgene Ksp-Cadherin-Cre to activate the heritable marker yellow fluorescent protein (YFP). In the UUO model, the authors detected neither epithelial cells that migrated out of the epithelial compartment nor any epithelial cells that became myofibroblasts [88].

### Interactions of TGF-β and integrins

TGF-β has long been implicated in the fibrosis of UUO. Studies from our laboratory as early as 2000 demonstrated that 1D11, a monoclonal antibody to TGF-β, decreased fibrosis, apoptosis, and macrophage infiltration in UUO [89]. Similar results were found with antisense to TGF-β [90]. Subsequently many other studies confirmed these findings using other strategies to decrease fibrosis [1, 2, 91]. TGF-β exists as a latent form, and when epithelial cells contract, bound integrins lead to local TGF-β activation, potentially at a high local concentration [92]. This could lead to EMT, as described above, or to activation of other cells in the vicinity, including fibroblasts. Interestingly, inducible deletion of the TGF-β type II receptor in matrix-producing interstitial cells in the UUO model did not abrogate fibrosis in the UUO model; thus, despite showing decreased collagen in interstitial cells which were of mesenchymal origin, fibrosis was not affected. Thus, although TGF-β is clearly an important mediator in UUO, other cytokines may be able to replace it in its absence [93].

### Activation of immune responses

Secretion of inflammatory cytokines from epithelial cells leads to the recruitment of different immune cells into the local environment. In UUO, the macrophage has been studied most thoroughly. As early as 1994, an increase in macrophages in interstitial tissue by 12 hours after UUO was demonstrated [94]. There was a continued increase through 96 hours. We and others have confirmed the presence of interstitial macrophages in UUO [65, 95, 96]. Recent attention has focused on macrophage sub-types in UUO. The two broad sub-categories of macrophages are M1 (activation associated with inflammation) and M2 (dampen inflammation; reviewed in [97]). An early increase in expression of M1 macrophages was shown by Tian et al. [98], in association with high-mobility group box 1 protein. Markers for both M1 and M2 macrophages were upregulated in a vitamin D3 model of increased fibrosis in UUO [99]. Several inflammatory cytokines have also been studied. Both interleukins IL-18 and IL-1β have been shown to be upregulated in the UUO model [100, 101]; neutralization of IL-18 reduces interstitial fibrosis [101]. Interestingly, a recent study using the SS-31 peptide (see above) in a renal ischemia/reperfusion model, has shown its effectiveness in preserving mitochondrial integrity, ameliorating expression of inflammatory markers (including IL-18 and IL-1β) and halting progression of interstitial fibrosis; this was remarkable, considering that SS-31 was administered 1 month after the initial ischemic insult [102]. Activation of IL-1β and IL-18 is under the control of immune receptors which form large multiprotein signaling complexes, known as inflammasomes [103]. Since mitochondria play an integral role in the assembly and activation of the inflammasome, Szeto and colleagues suggest that protection of mitochondria during ischemia and inflammation results in reduced inflammation and fibrosis.

### Strategies to decrease fibrosis

Over the last 30 years, investigators have attempted to decrease the fibrosis of UUO through either drug treatments or genetic manipulation. Many of these have targeted single mediators (TGF-β or angiotensin II for example), which had been implicated in the fibrosis of UUO (for reviews see [1, 2, 91]). However, virtually none of the treatments aimed at a single target have produced treatments ready for use in patients. Our recent understanding of the complexity of the fibrotic process suggests that while there are new pathways to target, the multiple factors responsible for fibrosis may lead to strategies requiring intervention in more than one pathway. Alternatively, protection of mitochondria, which has been shown to prevent acute and chronic injury in several models [76, 102], may prove to be a unique and effective antifibrotic strategy.

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# 9

# Organizing the Endourological Operating Room

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## Introduction

To work effectively an operating room (OR) needs specialized planning and execution. A combined "civil–mechanical–electrical–electronic–biomedical" effort is required, coordinated by the needs, preferences, and safety of the medical/surgical team. Apart from the scarcity of practical publications and details in this area, the highly technical nature of many of the issues, and the difficulty of communicating them, often result in planning mistakes being made at a very simple level.

OR complexes are designed and built to carry out investigative, diagnostic, therapeutic, and palliative procedures of varying degrees of invasiveness. Since the introduction and widespread application of minimally invasive surgery, the design of the modern OR has changed dramatically. Adapting the modern OR for endourology is a challenge that begins with the more general problem of designing the OR. There is a need for safety, convenience, and economy in planning a dedicated endourology fluoroscopy-compatible OR complex. It is necessary that planning is perfect, keeping in mind future needs, as subsequent changes or renovations are tedious and pose tremendous economic burden [1].

In the current era of information technology, audiovisual (AV) recording and telementoring have become a frequently used teaching and training aid in operative surgery (see Chapter 3 in this volume). Most surgical meetings today devote a major session to the live operative workshop. Unfortunately, many video recordings are of poor quality and often, because of the constraints of the equipment and the operating environment, do not demonstrate the principles of the technique as well as the presenter intended. The other problem is economic restriction, especially in semi-government-aided or private hospitals. These shortcomings are severely felt, especially in a tertiary care teaching hospital, as surgical workshops are held quite regularly and AV transmission consumes a large chunk of the investment. In addition to being used to relay the operation, the teacher can access the video display to monitor the progress of the operation, and it can be used to teach residents in the OR about the procedure.

In this chapter we present a comprehensive description of the planning of a state-of-the-art endourology-dedicated OR, with both high-class OR equipment and technology-driven OR data management.

## Designing and planning a dedicated OR

The design and layout of the OR is extremely important. The state-of-the-art design enables hassle-free movement of equipment, surgeon ease in viewing multiple screens, and efficient data archiving, management, and relay systems. It is necessary to anticipate the average number of procedures that will be carried out. It is better to plan with the next 10 years in mind.

Meeting these challenges requires a multidisciplinary team and a well-planned process that addresses all aspects from long-term goals to exacting details. Design and construction firms apply experience and expertise to handle the intricacies of the dedicated OR. Select an architect and construction manager with considerable healthcare experience, including of surgical suites and ORs. Architect, engineer, equipment planner, construction manager, and key equipment vendors should all be included in the team [2]. Strategic equipment placement is essential to increase efficiency and safety within the surgical space. Equipment booms and other ceiling- supported equipment are used increasingly in ORs because of the advantages they offer [3]. Equipment booms are ceiling-mounted, articulated arms that support much of the OR equipment, like

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Companion website: www.wiley.com/go/smith/textbookofendourology

lithotripters, light sources, endocameras, electrocautery equipment, anesthetic gas connections, and electric plug points. The booms, which can move in every direction, significantly reduce clutter and interconnect equipment, freeing floor space and simplifying cleaning. They utilize the space above the false ceiling, thereby enhancing sterile setup and reducing maintenance as a result of cable breakage. Booms, however, require a significant amount of structural support, which must be coordinated with the lighting, mechanical, and electrical systems above the false ceiling.

## General principles of OR construction

In general any OR is divided into four zones:

Zone 1. Protective zone: the administrative area of the OR that houses changing rooms, store and record rooms, etc.
Zone 2. Clean area: such as pre- and postoperative rooms
Zone 3. Sterile area: OR, anesthesia room, scrub room
Zone 4. Disposal area: housing waste from all the ORs.

The OR should have a unidirectional flow of movement: there should be one entry and one exit. Pre- and postoperative rooms should be separate. There should be no toilets in the clean area. Scrub room should be in between the ORs. ORs should have automatic sliding doors or double swing doors with a vision panel. ORs should have one door for patient entry and another for surgeons' entry from scrub room. The OR should have 30 air changes per hour, a positive pressure of 15 Pa, a temperature of 21 ± 3 °C degrees, and a relative humidity of 55%.

## General design for a fluoroscopy-compatible endoscopic OR

### Size

The size of a general OR should be a floor area of 6 × 6 m with a height of 3 m. Since endourologic procedures use large equipment, like a C-arm, laser, ultrasound machine, and workstation, the recommended size of a dedicated endoscopic OR is 7 × 7 × 3.5 m.

### Ceiling

The floor-to-false-ceiling height should be around 3.5 m. The overall height of the OR should be around 4.2 m to give an over-ceiling space of 70 cm. Individual cassettes made of painted sheet steel are clipped into the grid to form a suspended metal ceiling. The individual cassettes can be removed and reinstalled to permit maintenance and refitting work.

The over-ceiling plan is an important feature. This space includes:

- Cables for various multiple equipment booms, such as oxygen, nitrous oxide, compressed air, vacuum, and electrical wires.
- Air conditioning pipelines.
- Data-relay wires in various hanging arms.

The ceiling air supply with a sterile-air distributor is one of the most important elements for hygiene in the OR. Bacteria, viruses, and dust particles are trapped immediately before the air enters the room. The sterile-air distributor generates a homogenous and low-turbulence displacement flow. The inner air supply area remains free from contaminants drawn in from the room environment. In this way the area around the operating table is kept in a high state of cleanliness during operations, with an extremely low pathogen level of less than 10 colony-forming units per cubic meter. Sterile-air distributors can be easily detached or swung away for quick and economic filter changes.

### Pendant services

Two ceiling pendants for pipeline services should be designed: one for the surgical team and one for the anesthesiologist. The anesthetic pendant should be retractable, have limited lateral movement, and provide a shelf for monitoring equipment. It should have oxygen, nitrous oxide, and 4 bar medical compressed air, medical vacuum, scavenging terminal outlets, and at least four electrical sockets. The surgeon pendent or cart should have the capacity to hold video camera electronics, a light source, and various recording devices such as a VCR, printer, or videodisc recorder. Moreover, some carts also have room to hold the laparoscopic insufflator and electrocautery units.

### Floor

OR flooring should be made of 2 mm-thick antistatic PVC roll/tile/epoxy coating. The floor should have a slight tilt from all the walls, converging at the water drain outlet. The floor surface must be slip resistant, strong, and impervious, with minimum joints; e.g. mosaic with copper plates for antistatic effect or jointless conductive tiles/terrazzo, linoleum etc. The recommended minimum conductivity is 1 mOhm with a maximum of 10 mOhm There should be a central drain outlet from the floor, centered underneath the OR table. A 0.05 × 50 mm copper grounding strip should be used for earthing and one lead should be brought out for every 45 $m^2$ area.

## Walls

The radiation protection of a general-purpose fluoroscopy suite necessitates a wall thickness in all directions equivalent to 2 mm of lead (15 cm of concrete or 25 cm of brick with plaster). While lead is always accepted as the standard material for radiation protection, ordinary building materials may be equally suitable provided they are thick enough. As for the floor, the surface of the walls must be slip-resistant, strong, and impervious, with minimum joints. Laminated polyester or smooth paint provides a seamless wall surface; tiles can break and epoxy paint can chip. Washable paint in a light color (off-white, light blue, or green) is ideal. There should be provision for an X-ray film illuminator, wall-mounted camera, plasma screen, and drawers for endoscopic disposables recessed into the wall.

## Main door

The main door to the OR must be of adequate width (1.2–1.5 m) to facilitate smooth patient trolley, laser, C-arm unit, and ultrasonography machine entry and exit. Sliding doors are preferred, as they do not generate air currents. Door opening can be both automatic, with laser control, and manual.

## Lighting

Different levels of lighting are necessary in the OR and a means of dimming light may be needed during endoscopic procedures. A flat TFT monitor display for endocamera vision requires the installation of dimmable lighting to create optimum light levels. However, TFT monitors are now being replaced by HD monitors, which may not need dimmable lights. Color-corrected fluorescent lamps are preferred to produce even illumination of at least 500 Lux at working height, with minimal glare. In the operating area, overhead light should be shadowless and give 25 000–125 000 Lux of light (50 000–100 000 Lux at the center and at least 15 000 Lux at the periphery), as in the general OR. Light-emitting diode (LED) light provides a unique multicolor temperature facility, which proves helpful during open surgery, and may be required in the event of an endoscopic complication. LED light has the advantage of lower heat generation, adjustable light characteristics, and unlimited lifespan. Lights should be freely movable in both the horizontal and vertical planes, and for this movement equipment booms are generally preferred.

## OR table

The OR should have a mobile, modular operating table with electronically controlled hydraulic drive, and battery and mains operation, and be of adequate width and weight-bearing capacity. It should have a stable base construction with a rotatable top and large twin-disk castors for easy maneuverability. The operating tabletop needs to be subdivided into multiple sections: head plate, upper back plate, lower back plate, seat plate, and leg plates for lithotomy position. To be compatible with fluoroscopy, the entire tabletop should be devoid of cross bars. Provision for kidney bridge elevation is helpful if open exploration is required. There should be multilayered radiolucent foam padding for patient comfort and safety.

## C-arm

A mobile C-arm unit is essential in an OR dedicated to urology. It should have balanced and graduated movements at any angle. It should provide a high-quality image to allow quick and precise diagnosis (brightness should be monitored so that image quality is not affected by changing lighting environments). Functions of the image intensifier should include DICOM imaging capabilities, last-image hold memory, image processing, and text/graphics. Image display should be on a high- resolution TFT monitor. The data output from the C-arm may also be connected to one of the hanging screen monitors for easy viewing by the operating surgeon. Traditionally C-arm units like the Surgico 60 DHF™ (PHILIPS, India), a digitalized mobile surgical C-arm image intensifier system, are used. It is an electronically controlled unit with a C-arm stand, X-ray generator and image intensifier, charge-coupled device (CCD) camera, monitor with trolley and image memory. The voltage can be adjusted with a range of 40–100 kV with automatic cutoff at 100 kV, when the machine shuts off. The current (milliampere) readings can also be varied, but the display will not show millamps until and unless the exposure switch is pressed. The fluoroscopy timer displays the exposure time with a preset reading of 300 seconds. Once this is reached, the machine will give an overload indication and no exposure will be obtained unless the timer is reset to 0.

Now a new range of C-arms with high-frequency, powerful generators operating with a variable pulse width between 7 and 30 ms are available. They are monoblock generators with a rotating anode. These machines deliver short, sharp pulses, which minimizes dose exposure and maximizes image quality. Newer machines have automatic pulse regulation that helps in continuous imaging. They have an active cooling system, which keeps the generator temperature low and prevents overheating of the unit. Radiation exposure is an important aspect to be considered. The principles of as low as reasonably achievable (ALARA) should be followed.

Collimation, adjustment of frame speed, should be available to reduce radiation. Manual adjustment of current and voltage reduces radiation exposure more than keeping the machine on auto mode.

## High-definition camera systems

Laparoscopic and endoscopic camera heads consist of a coupler and a CCD. Single-chip cameras have a single CCD. The coupler links the camera with the lens and can be used for focusing. The optical zoom feature adjusts the image size and magnification. Three-chip cameras have three CCDs; here, each chip is responsible for reproduction of a single color and it produces more natural colors.

There are two types of camera: standard definition (SD) and high definition HD. These are defined by horizontal and vertical resolution. The SD camera had an aspect ratio of 4:3 and a resolution of 640 × 480 horizontal and vertical lines. As compared to SD, HD cameras have an aspect ratio of 16:9 and 1280 × 720 horizontal and vertical lines. The 1080 HD systems offer an aspect ratio of 16:9 and 1920 × 1080 horizontal by vertical lines: this is almost seven times the resolution of an SD system.

The other two important features about camera systems are temporal resolution and scanning. Temporal resolution is the number of captured images per unit time expressed as frames per second. Scanning is of two types. In progressive scanning the whole frame is captured as you image. The other type of scanning is interlaced scanning in which two fields of half images are combined to produce a single image. Progressive scanning offers twice the temporal resolution compared to interlaced scanning. The scanning type can be identified by the suffix “p” or “i,” e.g. 720p or 1080i. Presently 1080p is one of the highest standards of HD cameras available for laparoscopic surgery. Using these new systems, vision is so good that the anatomical structures that were not seen with a flat SD image now become clearly visible.

Setting up a camera in the OR should include covering it with a camera cover; if the camera is sterilizable it can be used without a cover. A light source must be connected and the camera should be white-balanced. White balancing is a digital phenomenon in which the camera counters any impurities of color. This means that if any particular color has a higher level in the image, say the color blue, then the other two colors are increased in proportion, in this case red and green, to make the white areas of the image appear white. After white balancing the camera should be focused, at which point it is ready to be used.

## Sterilization

There should be a separate room for cleaning and disinfection of endoscopic instruments, which should have adequate ventilation to remove toxic vapors and airborne pathogens (see also Chapter 1). Automated disinfection machines for endoscopic instruments are desirable. However, there should also be provision for manual rinsing and cleaning. If endoscopes and other accessories cannot be autoclaved, there needs to be provision for chemical sterilization and ethylene oxide. Endoscopic procedures need delicate and expensive equipment, like telescopes, flexible ureteroscopes, and flexible nephroscopes. Rapid sterilization is required if many procedures are to be performed in a day, and for this we recommend a Sterrad sterilization system close to the OR, which provides a high level of sterilization with a processing time of half an hour.

## OR configuration for endourologic procedures

The configuration of an endourology OR is different from that of a general OR, as equipment has to be strategically located. This will minimize procedural time by allowing intuitive control and shorter changeover times, as equipment settings can be freely defined and activated. The OR should integrate cameras, lights, video conferencing units, endoscopic and anesthetic equipment, the C-arm, and the operating table, and all should be capable of being operated from the sterile area. The anesthetic trolley should be on a mobile cart supported by the anesthesiologist’s equipment boom, and located at the cephalad end of the patient on the same side as the procedure. There should be a minimum of three hanging display screen monitors, supported by a boom, moveable in all directions, and placed in front of the surgeon (Figures 9.1 and 9.2). The display monitors should be interconnected with changeable viewing between fluoroscopic image, endovision image, ultrasound image, and hospital information management system (HIMS) image.

Quite often both kidneys need to be operated on under the same anesthesia. This can be done in two ways. In the first, the C-arm unit remains fixed while the anesthesia boom and table rotate through 180°. In the second, the anesthesia trolley and table remain fixed while the surgeon’s position changes. Display screens accordingly also change the direction in which they face. The light cable source, lithotripsy device, endocamera cable, and irrigation tubing are attached to the equipment boom on the right side behind the surgeon.

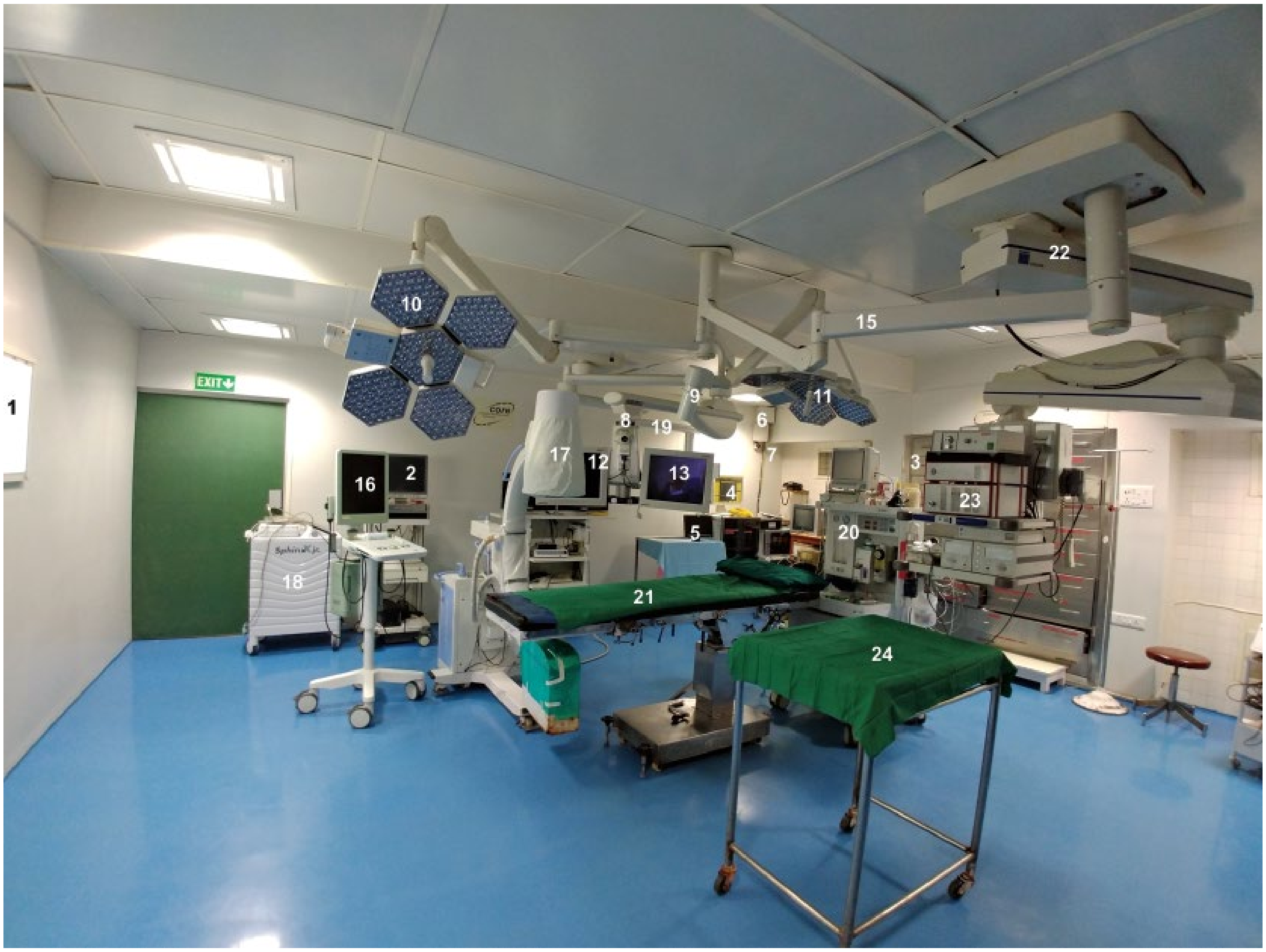


**Figure 9.1** Surface view of a dedicated fluoroscopy-compatable endourology OR. For explanation of numbers, please see the key to Figure 9.2. Reproduced with permission of Mary Ann Liebert, Inc. Publishers.

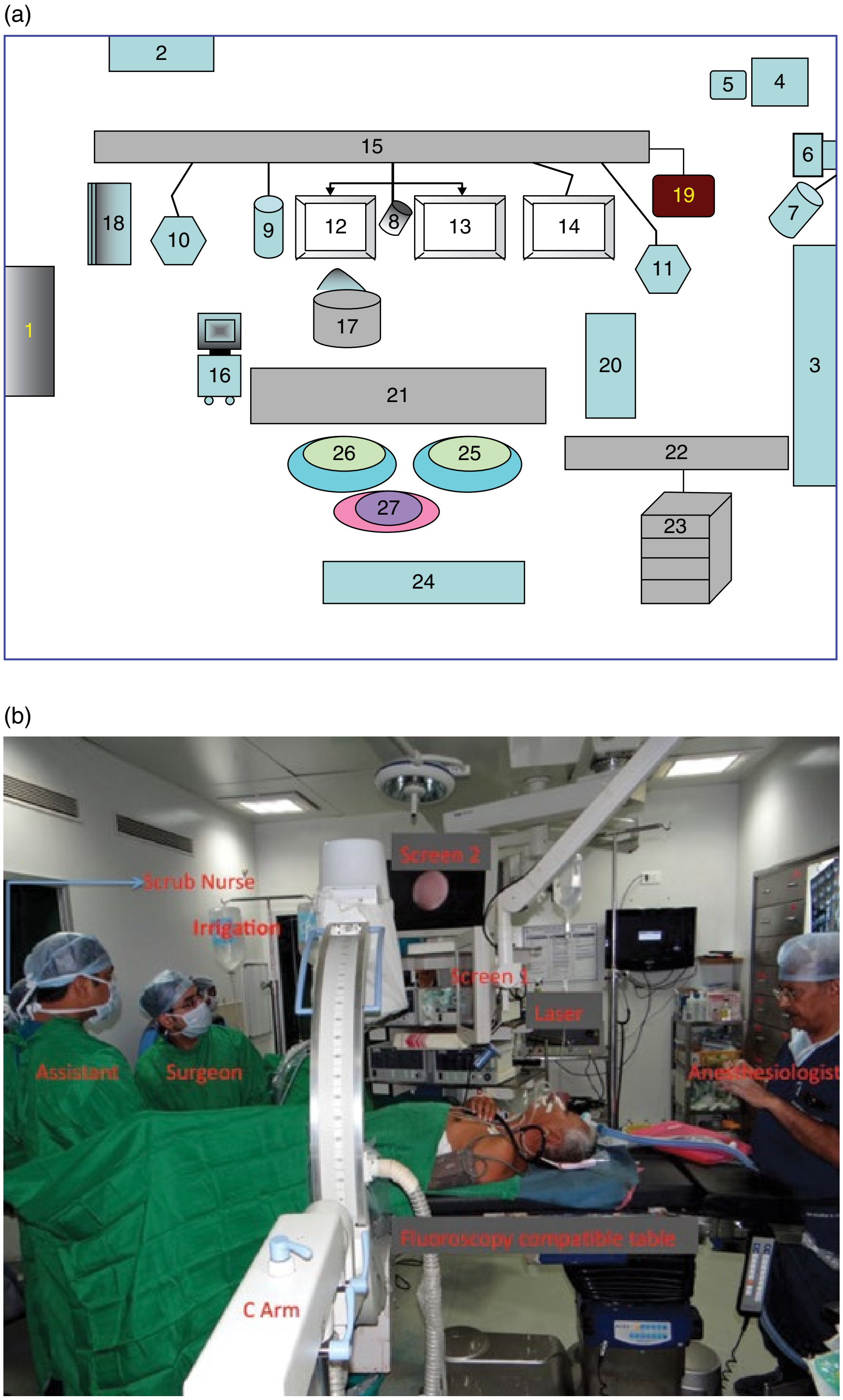
Figure 9.2a shows the essentials of a strategic equipment setup for left percutaneous nephrolithotomy (PCNL).

### Principles of OR room set up for ureteroscopy

The OR design should be as described earlier in chapter and the OR table should be fluoroscopy-compatible. The patient is positioned in the lithotomy position with both the limbs resting on lithotomy stirrups or Allen's stirrups (Figure 9.2b). Limbs should be well padded and all pressure points should be well secured. Special care should be taken to prevent pressure onto the lateral aspect of knee to prevent damage to the common peroneal nerve. The surgeon stands at the foot end; anesthesiologist and anesthesia cart are at the head end. The surgical assistant and the scrub nurse stand to the right of the surgeon. The C-arm fluoroscopy unit should be positioned across the abdomen and should be able to move from xiphisternum to pubic symphysis. For a right-sided procedure the C-arm should be placed on the right side of the patient. The endovision screen should be facing towards the surgeon. There should be another endovision screen for the assistant; this screen can be placed on the camera cart. The distance between the screen and surgeon should be equal to five times the diagonal dimension of the screen. The camera, light source, and energy source (except laser) can be mounted on a trolley or cart and should be positioned on to the side opposite to the C-arm. Whenever laser is used it should positioned opposite the side on which the C-arm is kept. The irrigation fluid can be mounted on a stand and kept at the foot end of the patient on either side.

### Principles of OR room set up for PCNL

Here we describe an OR arrangement during a PCNL procedure done in prone position (Figure 9.2c). The general design of an OR for PCNL remains the same as described elsewhere in this chapter. The OR table should be compatible with fluoroscopy and should have attachments for


(a)
2
5
4
15
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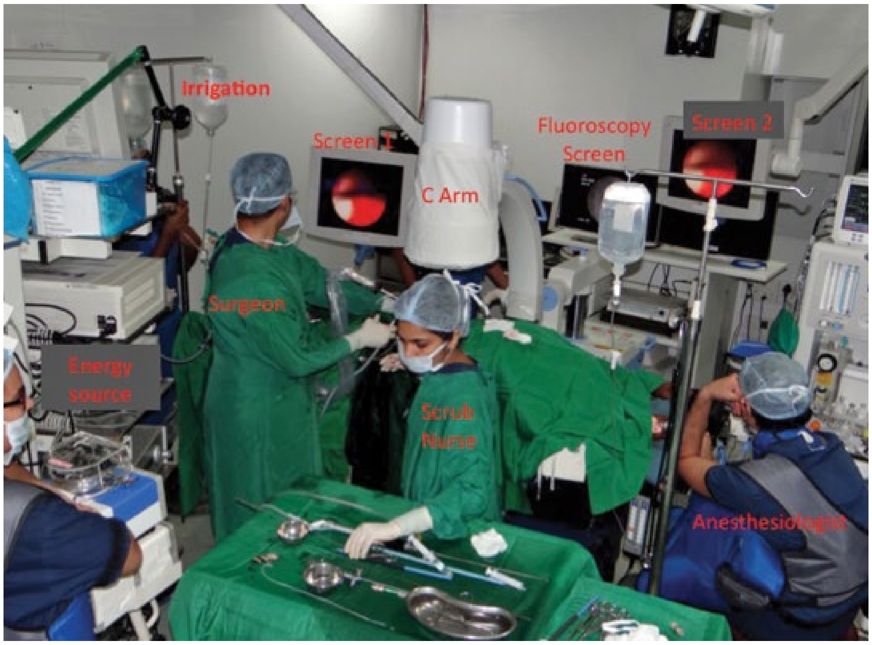
1
17
16
21
20
3
26
25
22
27
23
24
(b)
Scrub Nurse
Irrigation
Screen 2
Screen 1
Laser
Assistant
Surgeon
Anesthesiologist
Fluoroscopy compatible table
C Arm

**Figure 9.2** (a) Strategic equipment placement in a case of percutaneous nephrolithotomy. 1, X-ray screen in wall; 2, plasma screen; 3, drawers recessed in wall; 4, electronic work station; 5, HIMS computer; 6, speaker; 7–9, cameras 1–3; 10 and 11, OR LED lights 1 and 2; 12–14, hanging screens 1–3; 15, boom for hanging screens; 16, ultrasound machine; 17, C-arm; 18, laser machine; 19, anesthesia boom; 20, anesthesia trolley; 21, OR table; 22, equipment boom; 23, endoscopic instrument; 24, nurse trolley; 25, surgeon; 26, assistant; 27, nurse. Reproduced with permission of Mary Ann Liebert, Inc. Publishers. (b) OR setup for left-sided ureteroscopy. (c) OR setup for right-sided PCNL. (d) OR setup for left-sided upper urogenital tract laparoscopic surgery. (e) OR setup for pelvic robotic surgery.

(c)


Irrigation
Screen 1
C Arm
Fluoroscopy Screen
Screen 2
Surgeon
Energy source
Scrub Nurse
Anesthesiologist

(d)

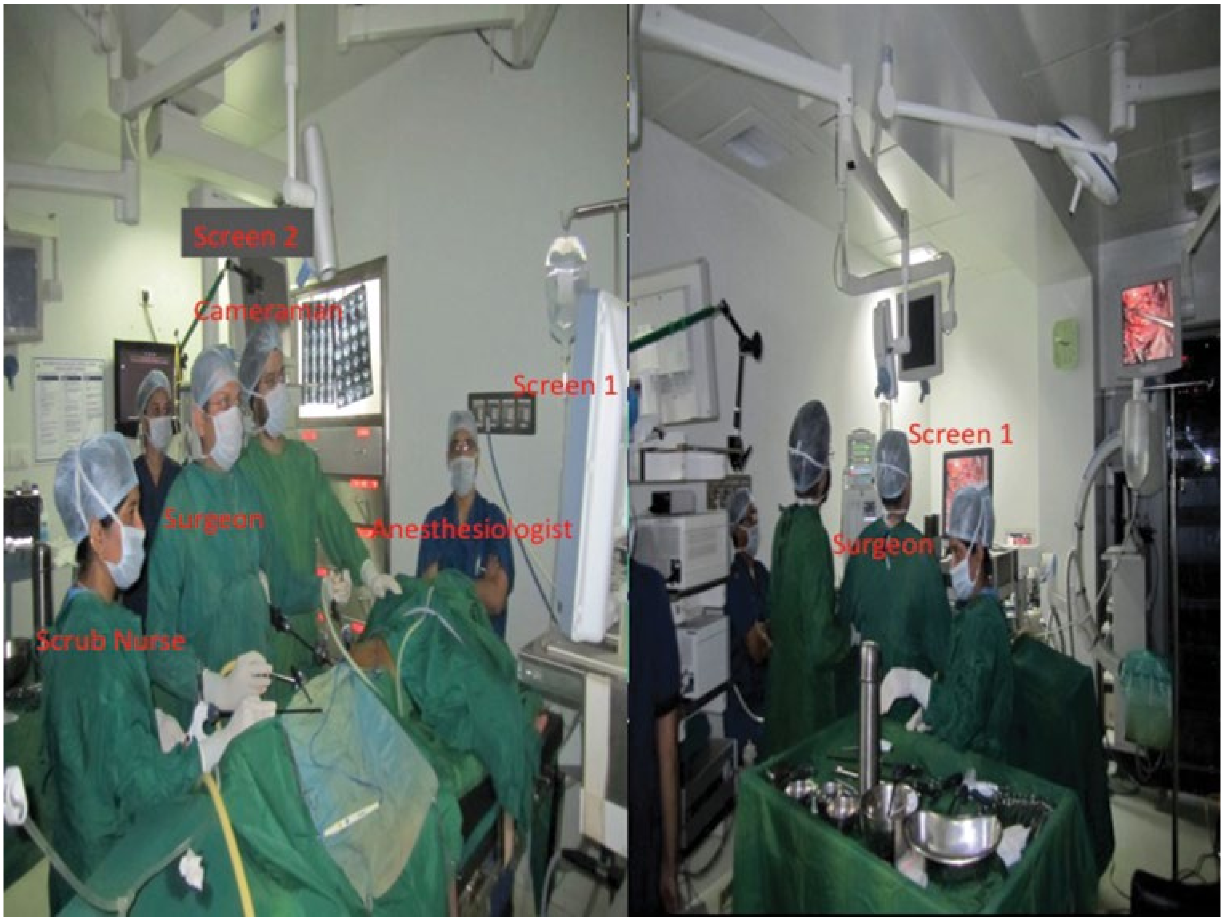

Screen 2
Cameraman
Screen 1
Surgeon
Anesthesiologist
Scrub Nurse
Screen 1
Surgeon

**Figure 9.2** (Continued)

(e)

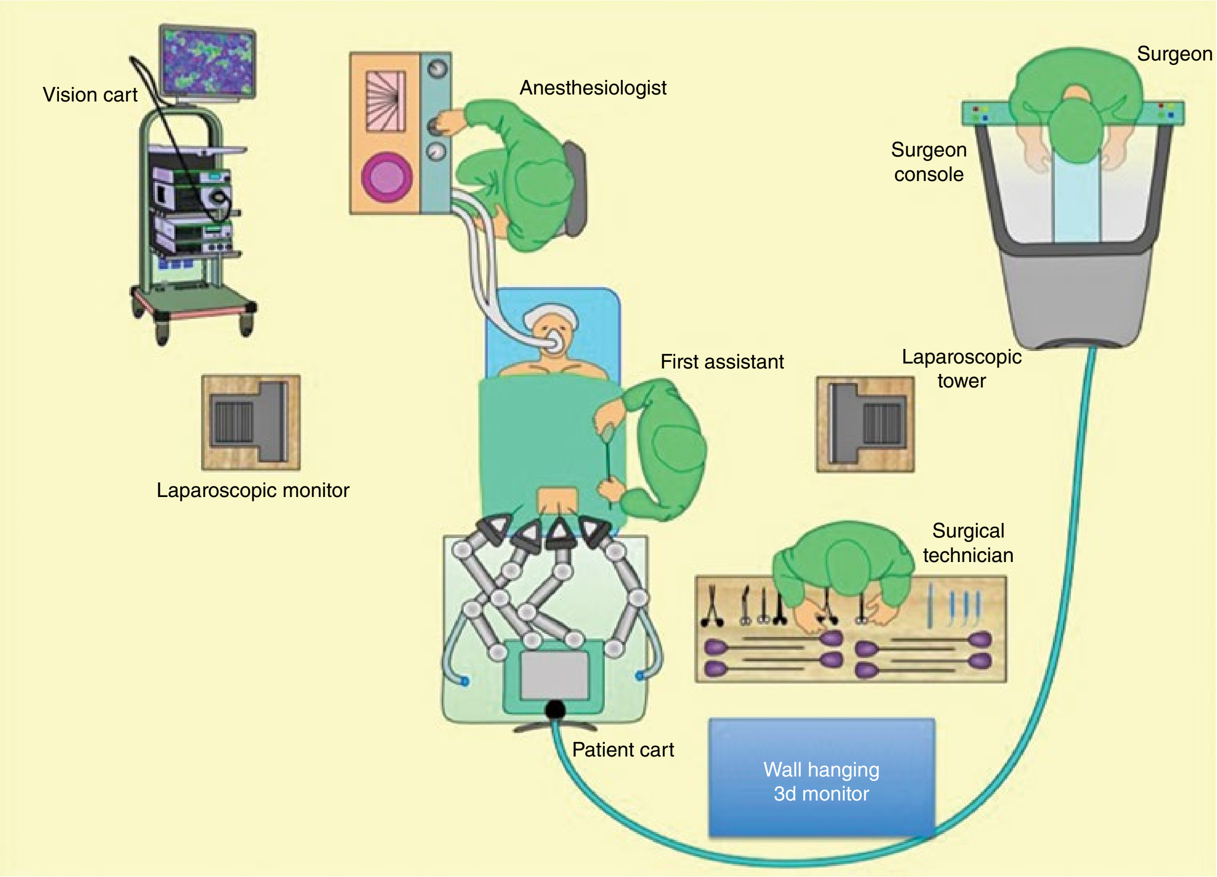


**Figure 9.2** (Continued)

lithotomy stirrups. For a right-sided PCNL, which is being done in prone position, the anesthesiologist and anesthesia trolley are positioned at the head end. The patient is positioned in prone position with two bolsters placed below the lower chest and hips. The operating surgeon stands on the side to be operated, i.e. on the right side for a right-sided PCNL. The surgical assistant stands to the left of the surgeon and the scrub nurse should stand to the right of the surgeon. The C-arm and the ultrasound machine are positioned opposite to the surgeon, with their respective screens facing the surgeon. Two endovision screens, one on either side of the C-arm, face the surgeon. The camera unit, light source, and energy source are placed on a boom/pendant/cart behind the surgeon. The laser machine is also placed behind the surgeon. All the lines should be tangle-free and the irrigation fluid is mounted on a stand and placed at the foot end of the patient.

## Principles of OR room set up for upper genitourinary tract laparoscopic surgery

While planning the OR room setup for laparoscopy one should keep in mind that the surgeon should always be optically correct, which means that their eyes, the organ of interest, and screen should be in the same line (Figure 9.2d). The distance between the monitor and the surgeon should be equal to five times the diagonal of the screen. The level of the screen should be 15° below the level of eyes so that there is no strain on the neck muscles. The OR table should be adjustable to 24 cm from the ground, which will be approximately the level of the waist of the operating surgeon. The height of the operating table should be equal to 0.49 times the height of the surgeon. For upper genitourinary tract surgery the patient should be in a lateral position with the ipsilateral side up and on the ipsilateral edge of the table. All pressure points should be secured. The anesthesiologist is at the head end and the surgeon stands on the ipsilateral side of the patient. The camera driver stands cranial to the operating surgeon; the scrub nurse stands at the foot end with the second assistant stand on the contralateral side. One screen is placed in front of the operating surgeon and the other screen is placed behind for the second assistant to see. The camera, light source, $CO_2$ insufflator, electrosurgical units, and various other light sources are kept in front of the surgeon on a vision cart/boom/pendant.

### Principles of OR set up for robotic surgery

The OR should be spacious, as stated earlier in the chapter (Figure 9.2e). Robotic systems have three components, each of which is at least 60 cm in width. In addition to this, the robotic OR is also the laparoscopic OR in most institutions. Considering the above, the size of the robotic OR should be 7.6 × 7.6 × 4 m. All the cable connections between the three robotic carts should be tension- and tangle-free. There should be enough space in the OR to facilitate robotic docking and for hassle-free movement of OR personnel.

The OR table, patient, and vision cart should be clearly visible to the operating surgeon from the console. The vision cart can be used to place $CO_2$ insufflators and electrosurgical units. Additionally, a laparoscopic tower can be used to place the $CO_2$ insufflator, electrosurgical units, and laparoscopic light source.

The type of surgery will determine the robotic OR setup. In case of a pelvic surgery, depending on unit policy the patient-side surgeon, second assistant, and scrub nurse will stand on either the left or right of the patient. We prefer that the patient-side surgeon and other surgical assistants stand on the left of the patient. This also means that the vision cart will be on the right of the patient. The patient-side surgeon has two monitors to view: the first is on the right of the patient and the other is towards the foot end of the patient, which is either wall- or ceiling-mounted. It is preferable to have a three-dimensional monitor as it will give a similar view to the bedside surgeon and the console surgeon. The patient-side surgeon should preferably use the screen at the foot end of the patient as to be coaxially aligned with this screen. The anesthesiologist and the anesthesia cart are at the head end of the patient and should be 60 m away from the patient's head end; this gives working space to the bedside surgeon. All the intravenous lines and tubing should have an extension. If the surgical assistants stand to the right of the patient the OR setup will be a mirror image of the one described above.

For the upper genitourinary tract surgery, the position of the anesthesiologist and console surgeon remain the same. For right-sided upper tract surgery, the patient-side surgeon stands on left of the patient and the vision cart with $CO_2$ insufflator and electrosurgical units are placed to the right of the patient. The patient-side surgeon views a screen placed to the right of patient and is coaxially aligned with the same. For left-sided upper tract surgery a mirror-image setup of the one described above should be used.

## Modular operating theatres

The prefabricated modular operating theatre offers the advantage of speedy construction combined with design of the highest quality and standards, while allowing for future expansion and development in surgical technique. The standard package includes an operating table, operating lights, endoscopy equipment, and a range of monitors that surround the patient [4].

Two dedicated endourology modular ORs are currently available, one from Karl Storz (Karl Storz OR1™; Karl Storz, Tuttilingen, Germany) and the other from Richard Wolf GmBH (Core™), which can be installed on demand by the respective technical teams. The Karl Storz OR1 provides the modular OR layout for performing minimally invasive endourologic and laparoscopic procedures. Key features include optimal picture quality from various camera systems and other signal sources, integration of Karl Storz endoscopic equipment, the full range of functions of devices and peripheral systems made by other manufacturers, such as the OR table and room lighting, and simple and secure documentation of intraoperative recordings and the OR environment at a central location. Core has a modular, networked structure to link various devices in the operating theatre. The system provides interactive monitoring and centralized control from a single operator panel, and has speaker-independent voice control that enables devices such as cameras, lights, video conferencing units, image archiving systems (PACS), high-frequency equipment, room functions, and the operating table to be operated from the sterile area. Medimage, a digital patient imaging and document management system, facilitates intraoperative visualization of preoperative image data on monitors located within the operating area.

### Integrated surgical data-acquisition systems

Documentation is a very important part of surgical management of patient. It is of a great medicolegal value as in a court of law anything that is not documented has not been done. Traditionally all the data acquisition was done by using multiple recorders: one for the endoscopic camera, one for ultrasound, one for the C-arm, and one for the surface camera. Then came the central workstations with inputs from different sources. Video was recorded in one unit but simultaneous recording was not possible and it was a device only used for recording.

We now have integrated documentation systems, which capture patient data, procedure data, images, and video. These systems are in turn connected to hospital information system so that this data can be accessed from anywhere in the hospital. These modern systems have a central control unit (Figure 9.3a), which has facilities patient data entry; surgical checklists can also be incorporated into them. The OR lights, electrosurgical units, and various screens in the OR can be controlled through one workstation (Figure 9.3b). In addition, the same system helps in video recording (Figure 9.3c), editing, and video relaying. There are a few data acquisition systems on the market:

1) Advanced Image and Data Acquisition (AIDA)™ (Karl Storz). AIDA can be integrated with the existing hospital information system. The patient information has to be put in manually or using a DICOM work list. The preoperative checklist (Figure 9.3c) can be incorporated into the system and can be followed up as per institutional protocol. Once this is done recording can be started; video recording as well as still image capture is possible. Recording can be done in full HD and three dimensions. There is also an option of multiple capture, i.e recording from different independent sources simultaneously, e.g video from the C-arm and endovision camera can be simultaneously recorded. Editing a video is also possible, and still images can also be used to generate reports. AIDA can be interlinked with STORZ communication bus (SCB), enabling communication with other devices like the $CO_2$ insufflator, light source, and electrosurgical units. All of these devices can be operated centrally using this system.
2) ENDOALPHA™ (Olympus Surgical, Orangeburg, NY, USA). The ENDOALPHA system by Olympus is a system that integrates surgical systems, allows central control of medical equipment like endoscopic equipment, surgical lamps, video management equipment, room lights, operation table, etc. All this equipment can be controlled via a touch screen or by voice commands. The settings as per requirement of the surgical team at different stages of the surgery can be stored and can be reproduced at a particular stage of surgery.

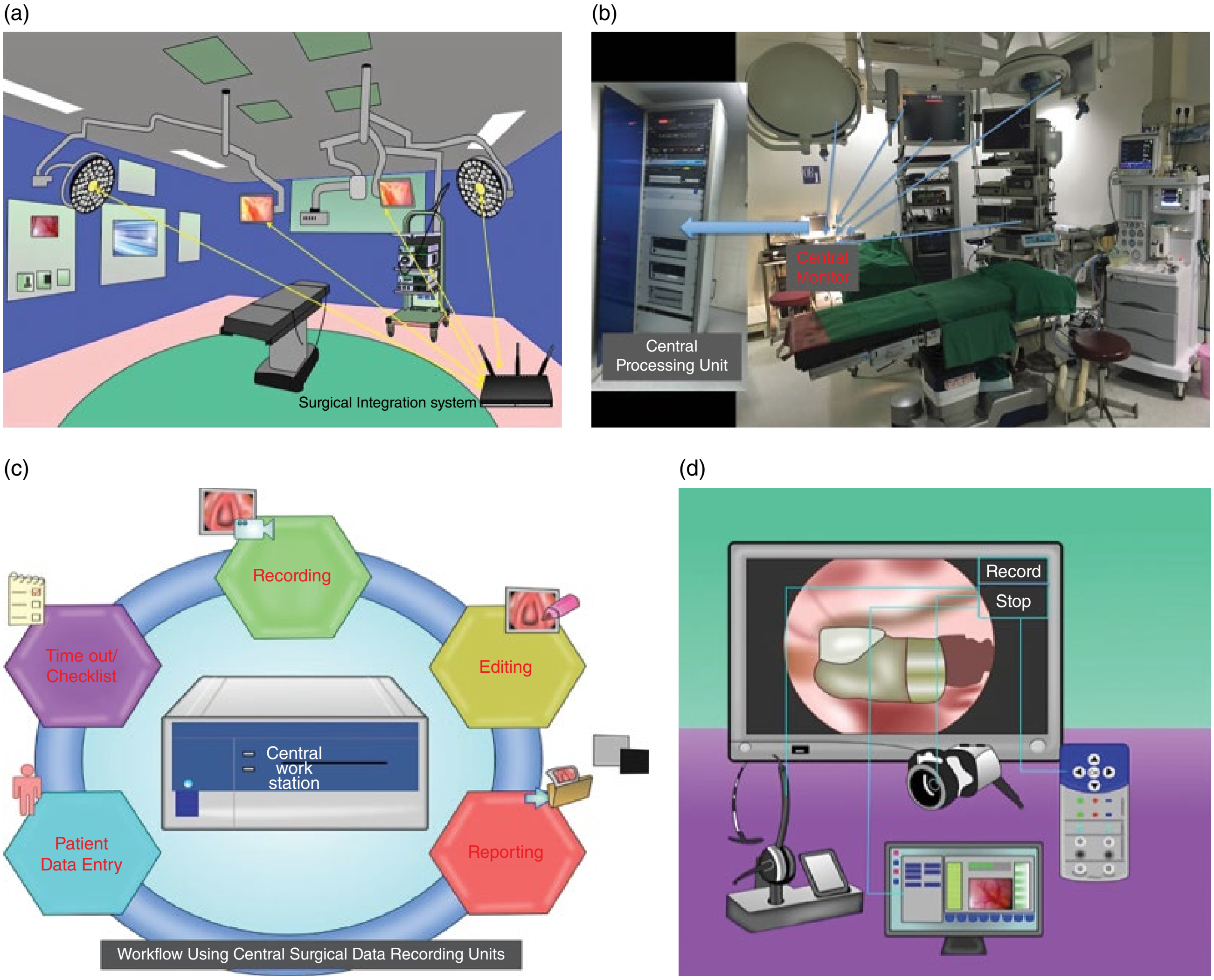

(a)
Surgical Integration system
(b)
Central Monitor
Central Processing Unit
(c)
Recording
Time out/ Checklist
Editing
Central work station
Patient Data Entry
Reporting
Workflow Using Central Surgical Data Recording Units
(d)
Record
Stop

**Figure 9.3** (a) Surgical central integration system. (b) Photographic representation of a surgical central integration system. (c) Workflow using central surgical data recording units. (d) The central integration units can be controlled by remote, wireless headsets, touch screen, and a laparoscopic camera head.

For example, while gaining access to the calyx one needs the OR lights on, so that surgeon can see the point of entry of needle on the skin. Once the surgeon starts doing nephroscopy the OR lights need to be dimmed. Normally all this has to be done manually but in ORs with central integration systems it can be done from a central control or using voice commands. These measures improve the autonomy of operative team and also reduce the time between requests and the resultant action. Thus such systems enhance workflow and ergonomics in the OR. These systems also have a provision for documentation and can be connected to the hospital information system. The patient details can be filled in or imported from the hospital information system. As the procedure is started it can be recorded and simultaneously broadcasted live. For recording a central monitor with touch screen can be used. There is also a foot pedal control available for taking snapshots, and starting and stopping recording, which can be controlled by the surgeon. Once the recording is over, a report can be created in the form of images with comments. Video can be created and can be immediately transferred to the hospital information system.

3) SCD Information Management System™ (Stryker). This device has a capability of digital data capture, multiple device control, and data connectivity. There is a provision for patient data entry and surgical time-out and it is capable of full HD recording. The central control unit can be controlled remotely by touch screen, wireless headset, or by buttons on the camera head (Figure 9.3d). These features make it possible for the surgeon to use the device while operating. This system has a WiFi connection, allowing videos to be streamed live. Other features include being able to create surgeon profiles and storing the desired settings for a particular surgery.

## Data management

In the current era of information technology, data capture, archival, and relay have become a frequently used teaching and training aid in operative surgery [5] (see Chapter 3). The ability to project computer and video information to a class or auditorium is now almost essential in many tertiary care hospitals, driven by the exponential increase in computer usage by both teaching staff and students. This need for versatile, large-screen electronic display systems is the dominant factor influencing the design of AV facilities, and is typically the most expensive single equipment element of any presentation system. Other technologies have grown up around the electronic display capability, and the expectations of users have become more sophisticated.

### Data capture

A surgical video system (SVS) is an integration of components used to perform minimally invasive surgery. In the OR, an SVS consists of an endoscope, attached video camera, light source, video processor, and one or more video displays.

#### Endoscope

Digital videocystoscopy and ureterorenoscopy use high-resolution monochrome CCD chip technology [5]. Three-chip systems provide better overall image quality than one-chip systems. The use of HD cameras and monitors during minimally invasive procedures can provide the surgeon and operating team with more than twice the resolution of SD systems. If an HD camera is selected it is imperative to invest in computer hardware and software capable of editing and outputting HD video.

#### Video camera

There are many options for avoiding poor-quality video capture in surgical procedures on the body surface. The simplest and most cost-effective method in this setting is to employ a video camera mounted on a tripod (surface camera) or installed on the wall with movable pulley (overhead camera). These are available from any number of consumer electronics outlets and in a variety of formats. Although it is possible to obtain reasonable quality video recordings by using the automatic exposure settings on most cameras, this often requires diversion of the operating light away from the operative field to avoid overexposure of the image. Almost all cameras, however, will have a predefined setting for bright environments, and this is an ideal alternative to use in this situation.

#### Video light source

Additional advances in imaging have resulted from the use of high-intensity light sources, generated by either halogen or xenon sources. The ability to adjust light intensity using several mechanisms has been a recent advance. Newer CCDs or image sensor-based endoscopic cameras feature electronic exposure. Recent innovations in illumination technology use single- or multipoint shadow-inducing systems.

#### Video and image capture

When performing endourologic surgery, video capture is not usually an issue. A signal can be taken directly from the lineout plug of the camera-processing unit and inputted directly into an analog or digital VCR using an S-video connection. Some endoscopic video processors come equipped with digital video (DV) outputs, which capture HD video. Of importance in a dedicated OR is an efficient to-and-fro data capture for HIMS. HIMS uses a network of computers to gather, process, and retrieve patient care and administrative information for all hospital activities to satisfy the functional requirements of all those involved in the care of patients. It is also helpful to the hospital authorities for developing comprehensive healthcare policies. HIMS incorporates an integrated computerized clinical information system for improved hospital administration and patient healthcare. It also provides an accurate, electronically stored medical record of the patient. There are innumerable software packages currently available for installing HIMS as per local preferences. The software has to be installed on all computers in the OR complex. Separate hardware for HIMS exists which has outputs for S-video and composite video. The output is connected to the OR panel and through it to the various data-capturing units working during the procedure. In this way, multiple images and videos can be captured and stored in the patient data file for future reference in HIMS. SVS integrate a digital image-capture system that allows the immediate capturing of still images from endoscopic procedures. A less-expensive alternative is a digital still image capture adapter, which can be connected to endoscopic camera systems. Digital still images usually can be recorded in jpeg, tiff, or bmp formats, depending on the necessary quality of the image to be edited (see Chapter 3).

## Data archiving

Customized OR software can be designed for individual needs. The following provides a general outline of the requirements of a data management system.

### Workstation

In the modern OR there should be an electronic workstation located in one corner. This workstation (Figure 9.4) has inputs via cables connected to the surface cameras, C-arm, ultrasound machine, and endovision camera. The cable input enters the OR panel where the composite AV signal is converted to S-video signal. The S-video output can be transmitted to any of the hanging display monitor (TFT screens) in front of the surgeon. Each screen has multiple cables; hence any image (fluoro/endovision/HIMS) can be viewed on any screen. The workstation also has a video processor with digital video (DV) output. HD video [6] is thus captured and recorded on a electronic storage device or on DVD for archiving and future editing. The OR panel is also connected via a two-way circuit to HIMS. The necessary information, including history, examination, X-ray, and computed tomography (CT) scan images, can be relayed to the hanging display monitor in front of the surgeon during the operation. At the same time, the OR details

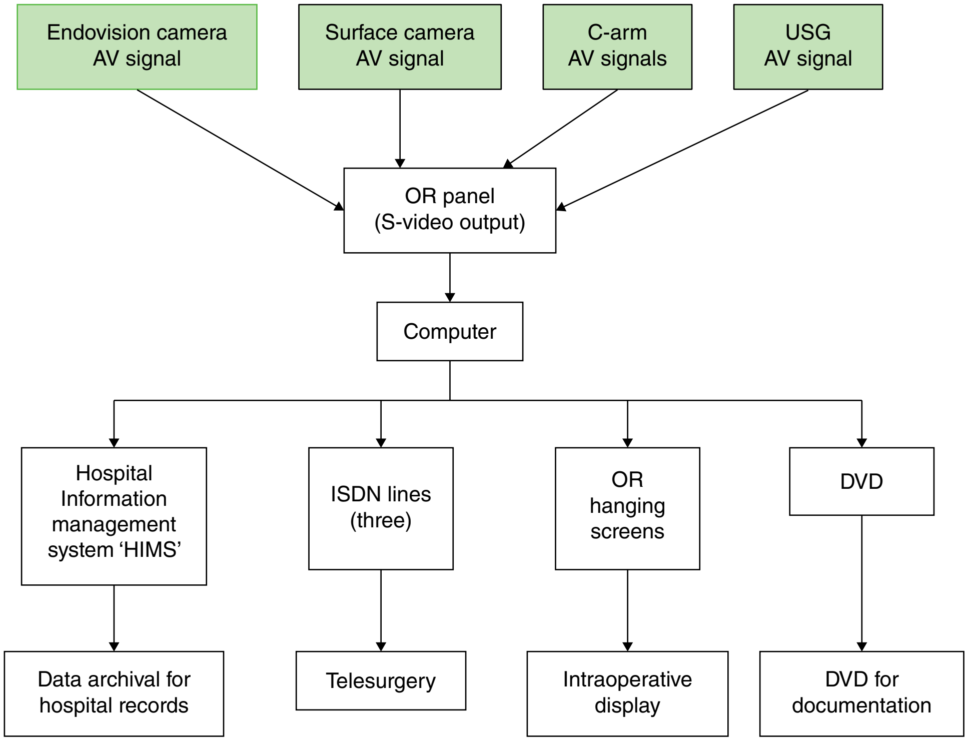


**Figure 9.4** Data management through the OR workstation. USG, ultrasound guided. Reproduced with permission of Mary Ann Liebert, Inc. Publishers.

can also be fed to HIMS for data archival. The workstation has three ISDN line connections.

#### Endovision camera

A signal can be taken directly from the lineout plug of the endocamera processing unit and inputted directly into an OR panel on the workstation.

#### Surface camera

At least three surface cameras should be present in the OR for video capture [7]. One camera is directed at the tabletop, and may be mounted on a light source or on a hanging boom. Another camera should be wall-mounted near the ceiling, and provides a view of the complete OR. This camera can be zoomed in or out as required by remote control. The third camera should be on one of the TFT screens. This position captures the face of the surgeon and is important during video conferencing when the surgeon is performing the procedure while watching the screen and simultaneously talking to the audience in the auditorium; these images will give the impression to the auditorium that the surgeon is facing and talking to them.

#### Fluoroscopic and ultrasound images

Most C-arm units [8] and ultrasound machines have a coaxial output jack on the back of the device. To arrange for data transfer, the coaxial jacks need to be connected with a coaxial cable and connected to the OR panel.

### Data relay

Various aspects need consideration for a state-of-the-art transmission relay system. Preliminary knowledge of the individual components of the relay system is essential for optimum utilization. These can be divided into components of local data relay and of the local and distant data relay system.

#### Local data relay components

The relay components are electrically interfaced to a control station within the OR. This control station has the capability to route voice, video, data, and physiologic information to and from the surgical suite. This capability is achieved through strategic equipment placement and an electrical infrastructure that allows the distribution of power and low-voltage wiring. Information is not only distributed within the OR but also to remote locations such as image archiving systems (PACS), classroom, and auditorium.

#### Modulator

The AV signal is converted into a UHF signal so that it can be received through a TV antenna input. Various electronic modulators are commercially available.

- A *combiner* has two inputs that respectively receive an NTSC combined visual and audio signal and a DTV signal wherein the NTSC signal and the DTV signal are in adjacent channels. The combiner has sharply tuned filtering interposed between the inputs and the output, tuned to pass the DTV signal while reflecting the NTSC signal such that these combine to form the combined output signal.
- An *RF amplifier* is used to convert a low-power radiofrequency (RF) signal into a larger signal of significant power.
- An *audio mixer* is an electronic device for combining, routing, and changing the level, tone, and/or dynamics of audio signals. The modified signals (voltages or digital samples) are summed to produce the combined output signals.
- A *video mixer* is an electronic device used to combine or “mix” two or more (PAL or NTSC) video signals, then output the sum as one new composite video signal. The picture-in-picture (PIP) and picture-on-picture (POP) support unit allows users to watch TV channels or DVD movies together with the computer screen, if a PC is connected to this unit. The PIP zoom function allows the PC image to occupy the main screen, with a video subwindow inserted. This video subwindow can take one of three sizes – one-quarter, one-ninth, or one-sixteenth of the screen – and can be relocated anywhere on the screen. POP is designed for cable TV channel preview. The channel preview can be set as 3 × 3 or 4 × 4 matrix with up to 16 channels at a time.

#### Optical fiber composite overhead ground wire

This type of cable (optical ground wire; OPGW) is used in the construction of electric power transmission and distribution lines. The optical fibers within the cable can be used for high-speed transmission of data. Because of the physical properties of image transference, optical fiber has a lower attenuation than coaxial cable and is not subject to electromagnetic interference.

#### Wireless local area network

Using electromagnetic waves, WiFi networks allow wireless devices to communicate with one another through access points or antennae. The advantages of a wireless network are the lack of having to install a wired network and the ability to communicate with mobile users.

#### Local OR data relay system

Most surgical meetings today devote a major session to the live operative workshop. Preliminary knowledge of the individual components of the relay system is essential for optimum utilization.

### Control room

A small control room in the vicinity of the OR is useful for the data relay system. The control room receives cable connections from all of the data-capturing components, and can route voice, video, and data to and from the surgical suite. Information is not only distributed within the OR but also to remote locations such as image archiving systems, classroom, and auditorium. One layout for electrical circuitry is shown in Figure 9.5.

To channel transmit OR proceedings to remote places, the composite AV signals from the OR is first relayed via cables to the control room. Here the signal is passed through the modulator, combiner, and video mixer (Figure 9.6). The emerging RF signal is thus transmitted to remote places, such as the plasma screen recessed in the wall of the OR. The operating surgeon through the microphone can interact with observers at remote places in a similar way. As described above, advanced video transmission features can be incorporated in the relay system via PIP and POP.

Similarly, signals can be relayed from remote places to the OR (Figure 9.6). For example, the AV signal from the auditorium is sent to the modulator in the auditorium and the emerging RF signals are then relayed to control room (Figure 9.7). The signal is then sent to the modulator, combiner, and audio mixer. The final amplified RF signal can be relocated to any remote place, including transmission to the plasma screen in the OR.

Four clinical scenarios for local data relay are shown in Figure 9.6. The first shows a teacher in a remote location accessing the live operative video display to monitor the progress of an operation. The AV signals from the OR are relayed to the video mixer and modulator. The signal from the modulator is mixed in the combiner and the emerging RF signal is transmitted to the teacher's room. The teacher can order specific commands about the procedure from this remote location to the operating resident in the OR through a wireless microphone. The audio signal is relayed to the audio mixer, and then to the speaker installed in the OR or through the modulator, which creates the RF signal that is relayed into the OR through the installed LCD screen.

The second scenario shows a teacher who is operating in the OR and relaying AV signals to the classroom or the auditorium for a two-way interactive operative workshop. Here, the AV signal is relayed to the video mixer for POP support or directed to the video modulator and combiner. The selected signal is amplified, switched into an RF signal, and transmitted to the plasma screens or projectors in the auditorium or classroom. The audio feedback from the audience is collected through the microphones and relayed to the audio mixer. After passing through the modulator and combiner, the RF signal is displayed on the LCD screen in the OR or, after passing through the audio switcher, an audio signal is relayed through the speaker installed in the OR.

The third scenario shows a teacher or observer who is remotely monitoring the progress in various ORs. The video signal from the various ORs is transmitted to the

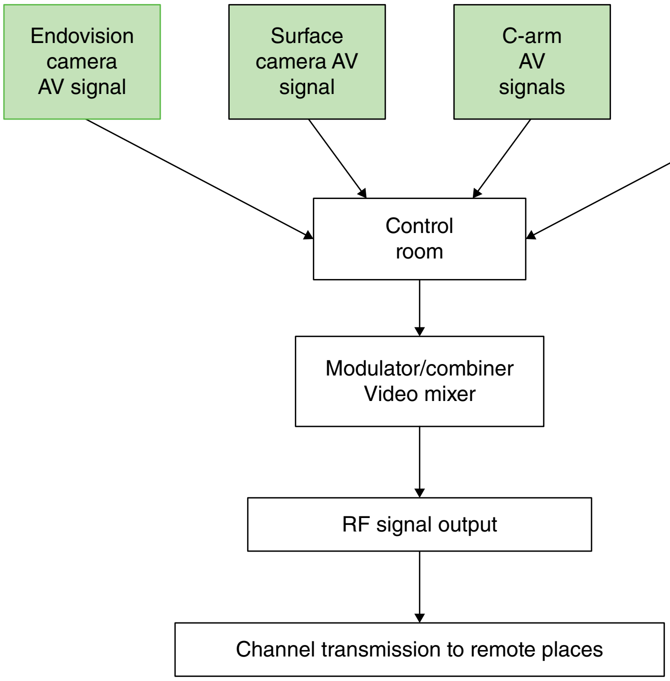

Endovision camera AV signal
Surface camera AV signal
C-arm AV signals
USG AV signal
Control room
Modulator/combiner Video mixer
RF signal output
Channel transmission to remote places

**Figure 9.5** Data management through the control room, USG, ultrasound guided. Reproduced with permission of Mary Ann Liebert, Inc. Publishers.

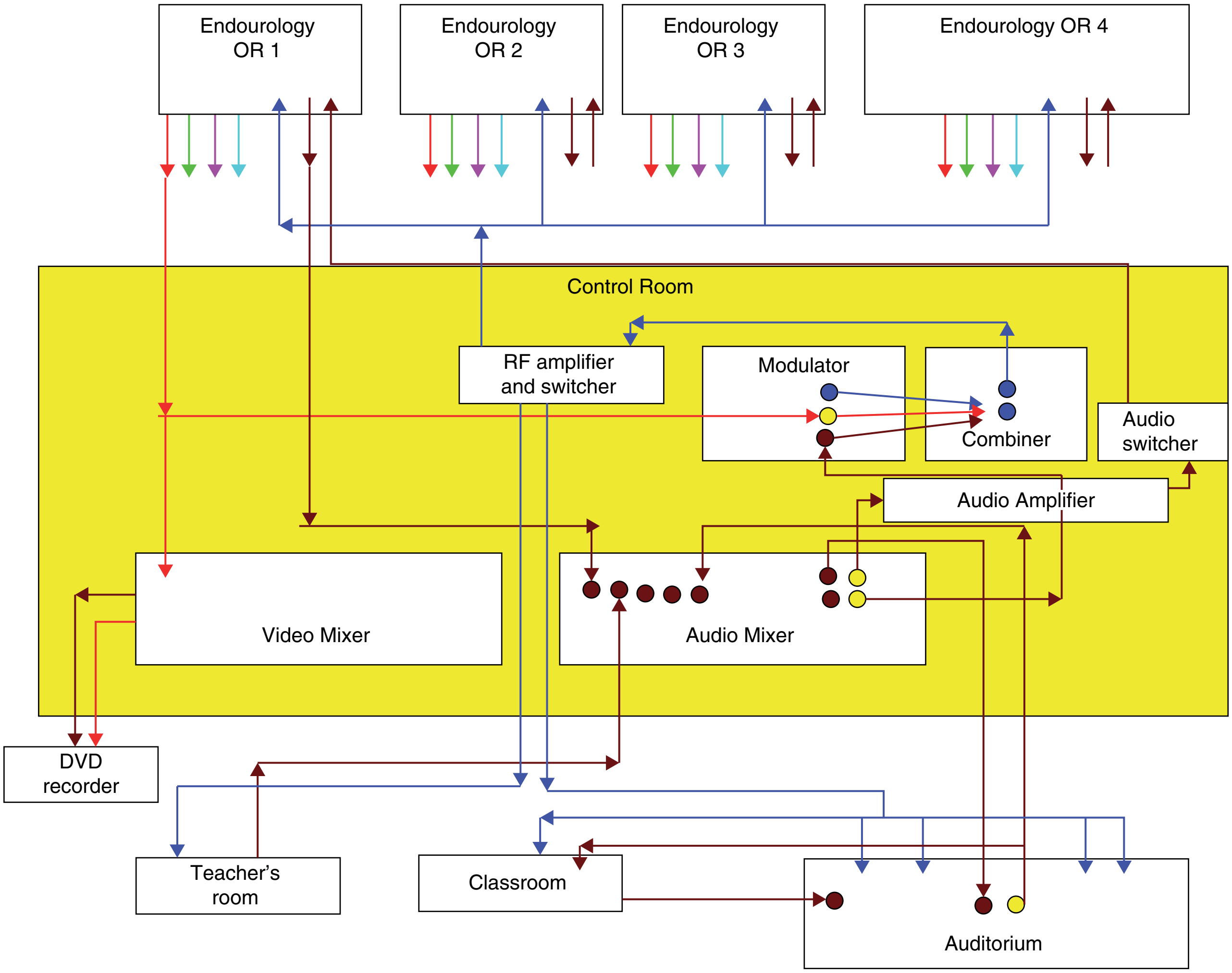

Endourology OR 1
Endourology OR 2
Endourology OR 3
Endourology OR 4
Control Room
RF amplifier and switcher
Modulator
Combiner
Audio switcher
Audio Amplifier
Video Mixer
Audio Mixer
DVD recorder
Teacher's room
Classroom
Auditorium

**Figure 9.6** Local data relay flowchart with to and fro local data management. There are four endourology theaters depicted in the OR complex. Each OR has four outgoing optical cables (colored red, green, purple, and light blue), two endovision screens, fluoroscopic imaging, and ultrasound imaging. There may be multiple outgoing cables depending on the needs of the hospital. There are two incoming cables (colored blue for RF signal and brown for audio). Reproduced with permission of Mary Ann Liebert, Inc. Publishers.

modulator and combiner, and as an RF signal is then sent to the teacher. The teacher can select the individual OR they wish to monitor using a channel selector.

The last scenario shows a surgeon who wishes to watch the OR proceedings on DVD. The video signal from the OR is fed into the video mixer. The DVD recorder then records the output signal, and a DVD can then be given to the surgeon to watch.

For teleconferencing to distant places and countries, an ISDN network facility needs to be connected to the computer in the workstation in the OR. Just like a regular telephone line, the ISDN enables the OR transmission to be dialed to any ISDN location anywhere in the world. Through the B channel, the ISDN line can support simultaneous two-way communication for two devices, such as a computer and a telephone, or a computer and a video camera for teleconferencing. Through the ISDN line, data can be sent to remote locations and at the same be received by the workstation, sent to the control room, and then transmitted anywhere else required.

## Conclusions

A dedicated OR design is essential for endourology and allows efficient state-of-the-art care in the modern information technology era. The older cart-based paradigm restricts the ergonomic configuration of the OR and creates potential mechanical, electrical, and biologic hazards to the patient and OR staff. In order to decrease clutter, ease personnel movement, improve ergonomics, maintain the sterile field, and facilitate the use of advanced imaging, an appropriately designed OR is essential. These design elements may prove to be critical to the next generation of dedicated fluoroscopy-compatible endourology suites, and will facilitate further advances in procedures.

The data archival, management, and relay system enables efficient and cost-effective transmission of data. This arrangement has been used extensively in our own hospital with resultant high-quality video recordings being presented at a number of national and international surgical meetings. In addition to being used for recording video, members of the OR staff can refer to the video display to monitor the progress of the operation, and it can be used as a teaching aid for residents present in the OR during the procedure.

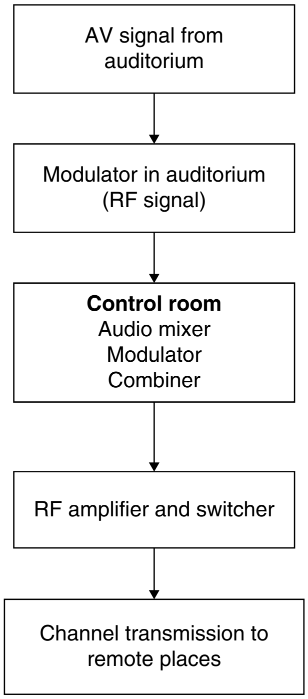

AV signal from auditorium
Modulator in auditorium (RF signal)
Control room
Audio mixer
Modulator
Combiner
RF amplifier and switcher
Channel transmission to remote places

**Figure 9.7** Data relay from the auditorium. RF, radiofrequency. Reproduced with permission of Mary Ann Liebert, Inc. Publishers.

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# 10

# Endoscopic Training/Simulation

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## Introduction/background

Urologists developed endoscopy in surgery with a focus on lower tract endoscopy in the late nineteeth and early twentieth centuries, with pioneers such as Grunfeld, Nitze, Ringleb, Goldschmidt, Desormeaux, Kelly, Brenner, and Casper. Luminaries such as Beer, Luys, Young, Davis, Buerger, Albarran, Heitz-Boyer, Goldschmidt, Stern, McArthy, Nesbit, Alcock, and Flocks continued to evolve the techniques and equipment. Retrograde and antegrade endourologic approaches to the upper tract were introduced by Cromwell and Kelly and subsequently developed by Marshall, Rupel and Brown, Fernstrom and Johansson, Goodwin, Bagley, Clayman, Smith, Lange, Segura, and Amplatz [1, 2].

The term "endourology" was coined by Drs. Elwin Fraley, Arthur Smith, Paul Lange, and Ralph Clayman and their team at the University of Minnesota. The principles and techniques associated with endourology has become a cornerstone for what we teach trainees in order to practice modern-day urology [3]. Medical educators for endourology continually search for the optimum modalities and methods for both skills training and competency assessment.

Taxonomies for the acquisition of technical skills outside of surgery have been developed by Dreyfus and Dreyfus, Dave, and several others [4, 5]. Figure 10.1 shows a combination of these two taxonomies and provides a matrix for classifying and understanding the progression of technical skill for urology [6].

As a trainee moves from what Dave's taxonomy describes as imitation to manipulation, what is happening according to Dreyfus and Dreyfus is a maturation of recollection of knowledge from non-situational to situational. This probably represents the "low bar" for the end of a training program prior to practice as it stands today. As someone evolves from manipulation to precision, their recognition of cues and knowledge moves from decomposed to a more holistic view. This translates to moving from "competent" to "proficient" and represents what happens early in one's independent practice. Note that there are still errors being performed as one's brain wants to begin multitasking and shifting to "automaticity" mode that represents less cognitive load. The evolution from precision to articulation is when we can start to multitask and represents a parallel transformation to "expertise." Here, our decision-making abilities become less analytical and more intuitive, freeing up the cognitive load to be able to multitask. This is probably where most practicing endourologists are functioning for most skills that are performed on a regular basis. Becoming a true "master" represents high-functioning on autopilot. At this level, an individual's awareness has evolved from monitoring the situation to completely being absorbed (virtuoso). Invention and skillful troubleshooting happen naturally during this phase.

The Halstedian apprenticeship model heavily relies upon the accumulation of considerable operative experience gathered during several years of demanding training [7]. Such "on the job training," with the combination of attestations, case volumes, skills evaluations, and index cases, has been accepted as effective, although correlation to "objective" performance educational outcomes has been poorly studied for endourology.

In parallel, the evolution of endourology has been accelerated and represents a core skillset for the practicing urologist. There are unique learning objectives for endourology related to image-guided surgery, rigid and flexible scope manipulation, advanced Seldinger techniques, endoluminal manipulations, laparoscopy, and robotics. The learning curves associated with these skillsets represent [3] possible barriers to optimal practice and endourology fellowships are often required to obtain proficiency and expertise in these skills. The increasing awareness of patient safety, along with the growing

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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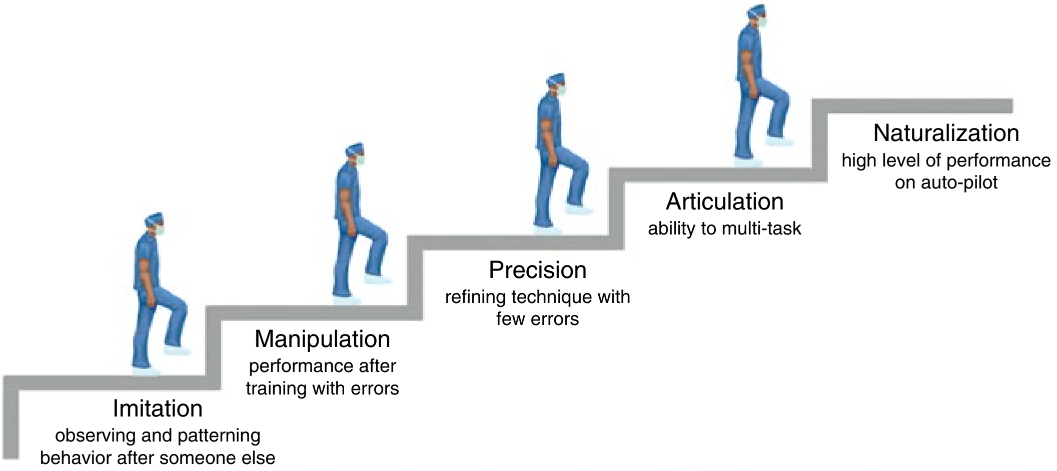
Companion website: www.wiley.com/go/smith/textbookofendourology


Naturalization
high level of performance on auto-pilot
Articulation
ability to multi-task
Precision
refining technique with few errors
Manipulation
performance after training with errors
Imitation
observing and patterning behavior after someone else

| Mental Function | Novice | Competent | Proficient | Expert | Master |
|---|---|---|---|---|---|
| **Recollection** | non-situational | situational | situational | situational | situational |
| **Recognition** | decomposed | decomposed | holistic | holistic | holistic |
| **Decision** | analytical | analytical | analytical | intuitive | intuitive |
| **Awareness** | monitoring | monitoring | monitoring | monitoring | absorbed |

**Figure 10.1** Understanding technical skills acquisition: a matrix of the models and Dave and Dreyfus [6].

debate on the ethicality of completing initial learning curves on patients, and the necessity of assessing the competency in a more reasonable fashion, also urge the clinical providers to seek an adjunct modality to enhance the traditional education and training pattern.

Surgical performance in endourology is based on a combination of both technical and nontechnical skills. Medical simulation provides a no-risk platform for learners not only to acquaint and develop new skills, but also to refine and perfect their abilities to achieve expertise and mastery [3]. When integrated into medical education, simulation not only enables the trainees to bypass the early error-prone period and reduce the steepness of the technical skills learning curve [7], but also develop nontechnical skills during training, which all contribute to secure the patient's safety and well-being [8].

## Current state of simulation in endoscopic urological training

> *Engineering is the art of modeling materials we do not wholly understand, into shapes we cannot precisely analyze so as to withstand forces we cannot properly assess, in such a way that the public has no reason to suspect the extent of our ignorance.*
>
> (Dr. AR Dykes)

Simulation development for training in endourology, as was the case for all of healthcare, was more of an art than a science. The fledgling healthcare simulation industry, in an effort to protect intellectual property, would often keep their early prototypes a close secret and would subsequently waste precious time and money in re-engineering major design flaws with advanced prototypes or, worse yet, compromise on learning objectives. The excitement associated with the promise of simulators as a solution for both training and assessment turned into disillusionment for many healthcare educators.

Today, a boom of information technology, wireless technologies, material science, manufacturing, and, most important, the conceptual evolution of simulation-based education are influencing simulation in endourology. Simulation, as a valid and safe supplement modality in healthcare education, is slowly becoming embraced by academic medical centers around the world, and is being used to train and assess all of the domains that are linked to performance in healthcare including technical and nontechnical skills for both individuals and healthcare teams.

Tables 10.1–10.6 summarize the available simulators for urological skills training. They are classified by procedural application and simulator type.

## Validity evidence

The validity evidence of these simulators are posted in these tables (Tables 10.1–10.6). Validation studies are indispensable to ascertain the appropriateness of simulation-embedded curriculum for a given purpose; for instance, whether a curriculum actually transfers knowledge and whether that transfer actually translates into improved performance.

When interpreting the data in these tables, one must keep in mind that much of the literature to date in endourology has presented validity evidence, according to Gallagher et al. [9] and McDougall et al. [12], which is based on the 1974 American Psychological Association (APA) Standards for Educational and Psychological Tests [10]. The 2014 [11] version of the APA Standards represented a significant shift in philosophy. Current literature validity evidence in healthcare is slowly shifting with our APA colleagues towards this modern approach to validity [2, 11] and is now being presented with a more holistic approach, whereby construct validity represents the whole of validity and is defined around a purpose. For the purposes of interpreting the past literature and integrating it into the current approach to interpreting validity evidence, we can think of construct validity as being made up of several aspects that don't "stand alone," but contribute evidence towards that central "construct," Classically, face validity "aspects" is completely subjective and does it seem to accomplish what it is trying to at "face value." Some aspects of realism of the simulator are captured here, but are not to be confused with "acceptability." Content "aspects" of validity addresses whether the detailed content of the curriculum/trainer address the learning objectives. It, too contributes evidence around the "construct" towards a judgment of the appropriateness of the simulator as a teaching tool. Concurrent validity "aspects" contribute to the "construct" through examining the extent to which the results of the test correlate with the gold standard known to measure the same domain. Predictive validity aspects examine the extent to which an assessment predicts future performance. Discriminant validity "aspects" examine the ability of a simulator to differentiate ability levels within a group with similar experience; it tests whether measurements that are supposed to be unrelated are unrelated [12]. Much of the literature to date examines discriminant aspects of validity evidence and misclassifies this as distinct "construct" validity in the modern-day interpretation.

## Emerging technologies and future directions

Fidelity, or the degree of similarity compared to reality, is an important factor to consider during the development of simulation devices. The degree of fidelity should align with the learning objectives and desired outcomes. Depending upon the application and purpose, anatomic, physiologic, emotive, and tissue fidelity may all be important and distinct elements [2].

Emerging technologies such as virtual reality (VR), augmented reality (AR), mixed reality (MR), three-dimensional (3D) printing, and conformable sensors all offer possible opportunities to bridge the gaps between the curricular needs and simulator development. By utilizing and combining these modalities, simulation systems are being created with more lifelike, precise, and patient-specific features, could closely mimic the interactive clinical environment in real time. An effort towards an open-source standardized platform that connects systems from different manufacturers and modalities is being created through a US Department of Defense contract that promises to accelerate the capabilities for simulation across healthcare, but especially in surgery. This is known as the Advanced Modular Manikin program (https://www.advancedmodularmanikin.com/). It is a combination of these technologies and projects that will lead to true patient-specific rehearsal opportunities.

The benefits and application of simulation are not limited to the proficiency-based disciplines; they are also valid in the vast majority of disciplines and domains of healthcare. Given the massive investment, ongoing consumption, and the time needed for validation, simulation-based curricula have had difficulty in *directly* demonstrating a return and benefit of investment in the short term. Hence, further studies investigating the effectiveness of simulation in improving patient safety and outcomes should be encouraged. In summary, the training and assessment of endourologic skills is and will continue to be improved with the use of ever-evolving simulation technologies; moving our discipline towards a "competency" model of education and privileging.

Video 10.1 outlines endoscopic training and simulation.

**Table 10.1** Available simulators for urethrocystoscopic skills simulation training.

| Type | Trainer/ simulator | Manufacturer | Built-in assessment | Cognitive component | Haptic feedback | Face validity | Content validity | Construct validity | Concurrent validity | Predictive validity | Discriminant validity | Cost (USD) | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Bench** | ETXY-Uro Adam | ProDelphus, Brazil | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈5200 | [13] |
| **Bench (lo-fi)** | Glass Globe | CHE, Netherlands | N/A | N/A | Yes | Yes[a] | No | Yes[a] | No | No | No | N/A | [14] |
| **Bench** | Urinary tract model | UW CREST, USA | N/A | N/A | Yes | No | No | Yes | No | No | No | ≈1500–1800 | [14, 16] |
| **Bench** | Uro-Scopic Trainer | Limbs and Things, UK | N/A | N/A | Yes | Yes[a] | No | Yes[a] | No | No | No | ≈2900 | [17] |
| ***Ex vivo*** | Boar urinary tract | Mayo Clinic, USA | N/A | N/A | Yes | No | No | Yes | No | No | No | N/A | [18] |
| **Human cadaver** | Fresh frozen human cadavers | UA, USA & BAUS, UK | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | N/A | [19, 20] |
| **Live animal** | Live porcine | CCMIJU, Spain | N/A | N/A | Yes | Yes | Yes | No | No | No | No | N/A | [13] |
| **VR** | Urinary tract simulator | GWU, USA | No | No | Yes | Yes | Yes | No | No | No | No | N/A | [21] |
| **VR** | Uro-Mentor | Simbionix, USA | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No | ≈105 000 | [22–32] |
| **VR** | Uro-Trainer | Karl Storz, Germany | Yes | Yes | Yes | No | Yes | Yes | No | No | No | N/A[b] | [33] |

[a] Validated with Uro-Mentor.

[b] Not commercially available.

BAUS, British Association of Urological Surgeons; CCMIJU, Minimally Invasive Surgery Centre Jesús Usón; CHE, Catharina Hospital Eindhoven; CREST, Center for Research in Education and Simulation Technologies; GWU, George Washington University; lo-fi, low fidelity; UW, University of Washington; VR, virtual reality.

**Table 10.2** Available simulators for ureterorenoscopic skills simulation training.

| Type | Trainer/ simulator | Manufacturer | Built-in assessment | Cognitive component | Haptic feedback | Face validity | Content validity | Construct validity | Concurrent validity | Predictive validity | Discriminant validity | Cost (USD) | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Bench** | Adult Ureteroscopy Trainer | Ideal Anatomic Modelling, USA | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | N/A | [34] |
| **Bench** | Cook URS Model | Cook Medical, USA | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | N/A[c] | [35] |
| **Bench** | Endo-Urologie-Modell | Karl Storz, Germany | N/A | N/A | Yes | Yes | No | Yes | No | No | No | N/A[c] | [36] |
| **Bench** | EndoUro-Trainer | Samed, Germany | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈3800 | [37] |
| **Bench** | Scope Trainer | Mediskills, UK | N/A | N/A | Yes | Yes | Yes | Yes | No | Yes | No | ≈3000 | [38, 39] |
| **Bench** | Urinary Tract Model | UW CREST, USA | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈420–1800 | [15, 16] |
| **Bench** | Uro-Scopic Trainer | Limbs and Things, UK | N/A | N/A | Yes | Yes | No | Yes | Yes | No | No | ≈3000 | [36, 40–44] |
| **Bench (lo-fi)** | Penrose Drain | UT, Canada | N/A | N/A | Yes | No | No | No | Yes | No | No | ≈16 | [44] |
| **Bench + *ex vivo* + live animal** | ETXY-Uro Adam | Neoderma, Brazil | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈5200 (bench only) | [13] |
| ***Ex vivo*** | Porcine *ex vivo* model | UCI, USA & CCMIJU, Spain | N/A | N/A | Yes | Yes | Yes | Yes | Yes[a] | No | No | N/A | [13, 43, 45] |
| **Human cadaver** | Human cadavers | BAUS, UK | N/A | N/A | Yes | Yes | Yes | Yes[b] | No | Yes[b] | No | N/A | [19, 46, 47] |
| **Live animal** | Live porcine | CCMIJU, Spain | N/A | N/A |  | Yes | Yes | Yes | No | No | No | N/A | [13] |
| **VR** | Uro-Mentor | Simbionix, USA | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | ≈105 000 | [22, 25, 26, 28, 29, 31, 36, 40, 42, 46, 48–50] |

[a] Validated with Uro-Scopic Trainer and Uro-Mentor.

[b] Validated with Uro-Mentor.

[c] Not commercially available.

BAUS, British Association of Urological Surgeons; CCMIJU, Minimally Invasive Surgery Centre Jesús Usón; CREST, Center for Research in Education and Simulation Technologies; lo-fi, low fidelity; UCI, University of California, Irvine; URS, ureterorenoscopic; UT, University of Toronto; UW, University of Washington; VR, virtual reality.

**Table 10.3** Available simulators for transurethral resection skills simulation training.

| Procedural application | Type | Trainer/ simulator | Manufacturer | Built-in assessment | Cognitive component | Haptic feedback | Face validity | Content validity | Construct validity | Concurrent validity | Predictive validity | Discriminant validity | Cost (USD) | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **HoLEP** | bench | Holmium Surgical Simulator | KMU, Japan | No | No | Yes | Yes | Yes | No | No | No | No | N/A | [51] |
| **HoLEP** | VR | UroSim | VirtalMed, Switzerland | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | ≈78 000 | [52] |
| **PVP** | VR | GreenLight Sim | Boston Scientific/UW CREST, USA | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | 0[a] | [53–55] |
| **PVP (Diode)** | VR | Myo Sim | VirtalMed, Switzerland | Yes | Yes | Yes | No | No | Yes | No | No | Yes | ≈78 000 | [56] |
| **TURBT** | bench | Bristol TURBT Trainer | Limbs and Things, UK | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | N/A | [31] |
| **TURBT** | VR | Uro-Trainer | Karl Storz, Germany | Yes | Yes | Yes | No | Yes | Yes | No | No | No | N/A[b] | [57, 58] |
| **TURBT & TURP** | bench | Resection trainer (Simbla Simulator) | Samed Dresden, Germany | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈4200 | [59] |
| **TURP** | bench | Bristol TURP Trainer | Limbs and Things, UK | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈1200 | [31, 60, 61] |
| **TURP** | VR | PelvicVision TURP simulator | Melerit Medical, Sweden | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | N/A[b] | [62–64] |
| **TURP** | VR | Uro-Trainer | Karl Storz, Germany | Yes | Yes | Yes | Yes | Yes | No | No | No | No | N/A[b] | [65] |
| **TURP** | VR | UroSim/ TURP Mentor | VirtalMed, Switzerland & Simbionix, USA | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | ≈78 000 | [66–68] |
| **TURP** | VR | UW TURP Trainer | CAE Healthcare, Canada | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | N/A | [69–71] |
| **TURP** | human cadaver | Fresh Frozen Cadavers | BAUS, UK | N/A | N/A | Yes | Yes | Yes | No | No | No | No | N/A | [19] |

[a] Available for use by the company for temporary loan.

[b] Not commercially available.

BAUS, British Association of Urological Surgeons; CREST, Center for Research in Education and Simulation Technologies; HoLEP, Holmium Laser Enucleation of the Prostate; PVP, photoselective vaporization of the prostate; TURBT, transurethral resection of bladder tumor; TURP, transurethral resection of prostate; UW, University of Washington; VR, virtual reality.

**Table 10.4** Available simulators for percutaneous nephrolithotomy skills simulation training.

| Type | Trainer/ simulator | Manufacturer | Built-in assessment | Cognitive component | Haptic feedback | Face validity | Content validity | Construct validity | Concurrent validity | Predictive validity | Discriminant validity | Cost (USD) | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Bench** | FluoroLess C-arm Trainer (CAT) | UW CREST, USA | N/A | N/A | Yes | Yes | Yes | No | No | No | No | ≈10 000 | [72] |
| **Bench** | PCNL-Trainer[b] | Samed Dresden, Germany | N/A | N/A | Yes | No | No | No | No | No | No | ≈4400 | N/A |
| ***Ex vivo*** | *Ex vivo* perfused porcine kidney[b] | RKUH, Germany | N/A | N/A | Yes | Yes | No | No | No | No | No | N/A | [73] |
| **Live animal** | Live porcine[b] | MPUH, India & XHCMU, China & SIU, USA | N/A | N/A | Yes | Yes | Yes | Yes[a] | No | Yes[a] | No | N/A | [74–77] |
| **VR** | PERC Mentor | Simbionix, USA | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | ≈105 000 | [31, 77–79] |

[a] Validated with PERC Mentor.

[b] The simulator cannot function independently and requires a C-arm or ultrasound for guiding purposes.

CREST, Center for Research in Education and Simulation Technologies; MPUH, Muljibhai Patel Urological Hospital; PCNL, percutaneous nephrolithotomy; RKUH, Ruprecht-Karls University of Heidelberg; SIU, Southern Illinois University; UW, University of Washington; VR, virtual reality; XHCMU, Xuanwu Hospital of Capital Medical University.

**Table 10.5** Available simulators for urological laparoscopic skills simulation training.

| Procedural application | Type | Trainer/ simulator | Manufacturer | Built-in assessment | Cognitive component | Haptic feedback | Face validity | Content validity | Construct validity | Concurrent validity | Predictive validity | Discriminant validity | Cost (USD) | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Partial/radical nephrectomy** | Bench | Partial nephrectomy renal model | UCI, USA | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | N/A | [80–82] |
| **Partial/radical nephrectomy** | *Ex vivo* | Porcine kidney | KUL, Belgium | N/A | N/A | Yes | Yes | Yes | Yes | No | Yes | No | N/A | [83, 84] |
| **Partial/radical nephrectomy** | Live animal | Rabbit model | KUL, Belgium | N/A | N/A | Yes | No | No | Yes | No | No | No | N/A | [85] |
| **Partial/radical nephrectomy** | VR | LAP Mentor | Simbionix, USA | Yes | Yes | Yes | Yes[a] | Yes | Yes[a] | Yes[a] | Yes[a] | No | ≈90 000–130 000 | [86–90] |
| **Partial/radical nephrectomy** | VR | LapSim | Surgical Science, Sweden | Yes | Yes | Yes | No | Yes[a] | Yes[a] | No | No | No | ≈50 000 | [91, 92] |
| **Partial/radical nephrectomy** | VR | Procedicus MIST | Mentice, Sweden | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | ≈35 000–50 000 | [31, 93] |
| **Pyeloplasty** | Bench | 3D Silicon Model | HSC, Canada | N/A | N/A | Yes | Yes | Yes | No | No | No | No | ≈100 | [94] |
| **Pyeloplasty** | Bench | Pyeloplasty Simulator Model | UW CREST, USA | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈90–220 | [95] |
| **Pyeloplasty** | *Ex vivo* | Chicken crop modeL | SYU, China | N/A | N/A | Yes | No | No | Yes | No | No | No | N/A | [96] |
| **Pyeloplasty** | *Ex vivo* | Porcine bladder | SLKKH, Germany | N/A | N/A | Yes | No | No | Yes | No | No | No | N/A | [97] |
| **Ureteral reimplantation** | Bench | Hydrogel model | Cleveland Clinic, USA | N/A | N/A | Yes | Yes | Yes | Yes | No | No | No | ≈150 | [98] |
| **UVA** | Bench | Latex UV model | MMU, Canada | N/A | N/A | Yes | Yes | Yes | No | No | Yes | No | ≈20–50 | [99] |
| **UVA** | *Ex vivo* | Chicken chest model | AMCUH, Netherlands | N/A | N/A | Yes | No | No | Yes | No | No | No | N/A | [100] |
| **UVA** | *Ex vivo* | Chicken skin model | KPMC, USA | N/A | N/A | Yes | No | Yes | Yes | No | No | No | N/A | [101] |
| **UVA** | *Ex vivo* | Porcine intestine | BCM, USA | N/A | N/A | Yes | No | No | Yes | No | No | No | N/A | [102] |
| **UVA** | Live animal | Live porcine | MMU, Canada | N/A | N/A | Yes | Yes | No | No | No | No | No | N/A | [99] |

[a] Validated in basic laparoscopic skills, not in nephrectomy procedures.

AMCUH, AMC University Hospital; BCM, Baylor College of Medicine; CREST, Center for Research in Education and Simulation Technologies; HSC, The Hospital for Sick Children; KPMC, Kaiser Permanente Medical Center; KUL, Katholieke Universitert Leuven; MMU, McMaster University; SLKKH, SLK Klinikum Heilbronn; SYU, Sun Yat-sen University; UCI, University of California, Irvine; UVA, Ureterovesical Anastomosis; UW, University of Washington; VR, virtual reality.

Table 10.6 Available simulators for urological robotic skills simulation training.

| Procedural application | Type | Trainer/ simulator | Manufacturer | Built-in assessment | Cognitive component | Haptic feedback | Face validity | Content validity | Construct validity | Concurrent validity | Predictive validity | Discriminant validity | Cost (USD) | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Partial/radical nephrectomy** | VR | Surgical Education Platform (SEP) | SimSurgery, Norway | Yes | Yes | No | Yes | Yes | Yes | No | No | No | ≈45 000 | [31, 103–105] |
| **Partial/radical nephrectomy & RA**RP **(with Tube 3 Module)** | Hybrid | dV-Trainer (dVT) | Mimic Technologies Inc, USA | Yes | Yes | No | Yes | Yes | Yes | Yes | No | No | ≈100 000 | [106–119] |
| **RARP** | VR | da Vinci Skill Simulator (dVSS) | Intuitive Surgical, USA | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | ≈85 000[a] | [112, 115, 120–130] |
| **RARP** | VR | Robotic Surgical System (RoSS) | Simulated Surgical Systems, USA | Yes | Yes | Yes (with HoST) | Yes | Yes | Yes | Yes | No | No | ≈126 000 | [118, 131–134] |
| **RARP** | VR | RobotiX Mentor | Simbionix, USA | Yes | Yes | No | Yes | Yes | Yes | No | No | No | ≈75 000 | [135] |
| **N/A** | Hybrid | ProMIS | CAE Healthcare, Canada | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | ≈35 000–50 000 | [136, 137] |

[a] The simulator cannot function independently and requires a da Vinci Surgical System console.

RARP, robot-assisted radical prostatectomy; VR, virtual reality.

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# Part 2 Patient Positioning for Percutaneous Access

## 11

## Patient Positioning, the Supine Position, and the Rationale of ECIRS

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### Introduction

Prone patient positioning for percutaneous nephrolithotomy (PCNL) as a practice has been inherited from radiologists who employed it for the technique of percutaneous nephrostomy for the drainage of hydronephrotic kidneys. In fact, they used to put the patient in a prone position because in this position they could directly puncture the renal pelvis without passing through the renal parenchyma [1]. At a later time the pioneering urologists who developed the PCNL technique took the renal puncture out of the radiologists' hands [2]. This change required some time to be adopted, and in many centers the habit of using renal access by radiologists was maintained until recently [3–6]. Urologists started establishing for themselves more effective and safer methods of percutaneous access to the kidney via the calyceal system [2, 7], but changing the patient's position was not considered a relevant issue.

Over the years percutaneous access to the collecting system was occasionally achieved via supine or oblique positions when required by particular clinical conditions or challenging cases, but the prone position remained the norm. Therefore prone PCNL became the traditional approach following its introduction in the 1970s, and has remained so until nowadays [8]. It is only recently that urologists have started to increase their familiarity with the supine approach to PCNL, and this method is now used in about 20% of centers worldwide but with a very limited practice in North America and Australia [6, 9–13].

### The supine and supine-modified positions for PCNL

Dr. Josè Gabriel Valdivia Urìa from Zaragoza (Spain) started performing percutaneous renal surgery in the supine position with an air bag under the flank in the late 1980s. He first reported his positive experience with supine PCNL in a national journal in 1987 [14], and few years later [15, 16] in international journals, but his proposal did not become popular among urologists at that time.

It was only later that other urologists from all over the world started to adopt and appreciate the pure supine position, especially for high-risk and obese patients [17–21]. Additionally a variety of supine-modified positions for PCNL, including the modified supine [22], Galdakao-modified supine Valdivia [23, 24], semisupine [25], and supine-oblique [26] positions were described.

### The anesthesiologic advantages of the supine positions

Anesthetists started highlighting their problems with the prone PCNL position and sharing them with urologists only in the last few years [27–31], in spite of their extensive previous experience with this position for much longer neurosurgical or orthopedic procedures [32–43].

The variety of original devices proposed over the years (like the Montreal mattress, various paddings, the Pronew protective helmet, the ETView tracheoscopic ventilation tube, and reinforced endotracheal tubes) prove the anesthetists' concerns about some of the major hazards of the prone position [44], including accidental extubation and kinking of the endotracheal tube during positioning of the patient, hampered ventilation and altered circulation, torsion of the neck, pressure and transient ischemia of the eyeballs, overstretching, and pressure injuries of the peripheral plexuses [45]. Subsequently urologists became more sensitive to this kind of problem too [12, 46–51].

In the supine and supine-modified positions the anesthetist enjoys optimal cardiovascular and airway control,

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has an easy access to the neck if central venous cannulation or any other invasive monitoring such as intraarterial catheters becomes necessary (although seldom required), easily maintains proper monitoring throughout, may effortlessly perform resuscitation maneuvers in case of emergency, and does not deal with all the cardiovascular, ventilatory, hemodynamic, pharmacokinetic, or metabolic effects typical of the prone position [48, 52, 53].

## The urological and management advantages of the supine positions

1) Positioning the patient in the supine position is easy and comfortable, with no intraoperative changes as there are for prone PCNL, instead requiring to turn the patient twice (at the beginning of the procedure from supine to prone, before starting standard PCNL and after having applied the ureteral catheter for retrograde pyelography, and then at the end from prone to supine, before awakening the anesthetized patient). Therefore there is less of a need for nurses, less occupational risk for all the involved operators due to the shifting of heavy loads, less risk of pressure damage to the peripheral nerves of the patient, and the possibility of preparing a single definitive sterile draping of the patient [12, 24, 54].
2) The antegrade surgeon can work sitting down, with the hands outside of the fluoroscopic field, as the X-rays are roughly perpendicular to the axis of the needle and of the percutaneous tract afterwards [12, 24, 54]. Overall X-ray exposure during the percutaneous procedure may also be reduced, thanks to the combined retrograde ureteroscopic contribution to PCNL (see later).
3) The risk of colon injury seems reduced, because in the supine positions the colon moves away from the puncture area by an average of 2.5 cm, decreasing the risk of its perforation compared to prone positioning [55–59].
4) The horizontal or slightly downward inclination of the Amplatz sheath maximizes irrigation outflow, consequently lowering intrarenal pressures. Low intrarenal pressures imply less risk of pyelovenous, pyelolymphatic, and pyelointerstitial backflow of bacteria and endotoxins, and thus less uroseptic risk [60], less fluid resorption, thus less risk of fluid imbalance [48], and better spontaneous drainage of stone fragments [12, 24, 54].
5) The supine positions are optimal and unique for the treatment of upper tract urolithiasis in urinary diversions (conduits and orthotopic reservoirs), as well as very useful in cases of combined opening of ureteral strictures or ureteroileal stenoses [24, 54].

## Disadvantages of the supine positions

1) In the supine positions the kidney is more mobile than in the prone position, especially in very slim and obese/morbidly obese patients, because it is not kept fixed by gravity combined with the rigidity of the posterior abdominal wall, and by the scarce or soft perirenal/pararenal fat tissue of such patients. Because of this hypermobility and respiratory movements the renal puncture may become more difficult. Solutions: a coordinated abdominal counterpressure on the mobile kidney may be exerted by the surgeon with the hand free from the puncturing needle or other devices. If the patient is under general anesthesia a brief apnea in maximal inspiration may help. The introduction through the access needle of the "through and through" guidewire (obtaining the so-called kebab or skewered patient) may additionally contribute to the reduction of the kidney hypermobility, at least during tract dilation and Amplatz sheath application [54].
2) The optimal irrigation outflow decreases the filling of the collecting system; thus nephroscopy might be difficult because of the limited distension of the renal cavities, sometimes further worsened by the active aspiration of the ultrasonic lithotripter. Solutions: filling of the collecting system may be transiently and delicately increased by the additional irrigation from a syringe or by a manual pump from the retrograde ureteroscope; temporary elevation of the saline bags may also help to improve endoscopic vision and working space if needed.
3) A superior calyceal puncture may be more challenging. Solutions: the anesthetist may help with apnea in maximal inspiration, if the patient is under general anesthesia. A renal displacement technique has also been described [61], although it might be at risk of parenchymal kidney damage. In any case, in supine positions superior calyces are usually entered in a retrograde manner by ureteroscopy rather than through the usual lower pole puncture, avoiding the risk of upper pole access implying a high risk of pleuric and hepatosplenic injury. In fact, in this position the angle between the upper and lower calyces is wider [12, 54].
4) The tract length might be longer, especially in obese patients, with decreased nephroscope mobility, and more torque on renal parenchyma, meaning a greater risk of bleeding [62]. Solution: use extra-long equipment in the case of obese patients.
5) The working space is very restricted, if compared to the large working field of the prone position. Manipulation of some rigid nephroscopes may also

be awkward [24, 54]. Solutions: elevation with jelly pillows opens the angle of the flank to be operated. Putting the patient very near to the border of the operating table prevents the collision of the nephroscope (especially those with the light cable directed downwards) with the edge of the operating table. Nowadays most rigid nephroscopes have all the cables and irrigation/working channels on their upper part, so collision is not a relevant problem anymore.

## The Galdakao-modified supine Valdivia position

In the 1990s Dr. Gaspar Ibarluzea from Bilbao (Spain), facing a difficult post-extracorporeal shock-wave lithotripsy (ESWL) Steinstrasse, tried the combination of the supine Valdivia position with a modified lithotomic arrangement of the lower limbs. After having appreciated the urological, anesthesiologic, and practical advantages of this new position he started using it regularly for left PCNL (because of the fixed features of the radiological table he used) and named it the Galdakao-modified supine Valdivia (GMSV) position [23, 63].

The GMSV position, combining the supine Valdivia position with a modified arrangement of the lower limbs, presents all the anesthesiologic, urologic, and management advantages of the supine positions, additionally supporting an easy simultaneous combined antegrade and retrograde approach to the upper urinary tract for stone treatment with both rigid and flexible endoscopes, i.e. endoscopic combined intrarenal surgery (ECIRS) [23, 24, 54].

## Patient positioning in the GMSV position

- The operating table should be radiolucent, mobile in order to leave the abdomen free of radiopaque interposed bars, able to easily host a C-arm for fluoroscopy, and arranged with padded leg stirrups for the modified lithotomic position of the lower limbs. The floor underneath is covered by absorbent paddings in order to prevent fluid spilling.
- The operating room, being very crowded, requires thorough, standardized, and coordinated preparation, achieved through well-organized team work which includes the urologists, the aneasthetist, and all the nurses. Ultrasound and fluoroscopy are placed on the side to be operated (Figure 11.1a), the anesthetist and the required equipment are behind the head of the patient (Figure 11.1b), and lithotripsy devices (laser and ballistic/ultrasonic lithotripters) are behind the antegrade surgeon, sitting in front of the flank to be operated (Figure 11.1d). The C-arm with the radiology technician (Figure 11.1c) and the video tower (Figure 11.1d) should be in front of the antegrade surgeon and on the other side of the patient. The antegrade irrigation should be near the C-arm and the head of the patient (Figure 11.1c), retrograde irrigation near the video tower and the legs of the patient (Figure 11.1d), the scrub nurse between the antegrade and the retrograde surgeons, with the retrograde surgeon between the lower limbs of the patient (Figure 11.1d), and the antegrade table is behind the antegrade surgeon. The retrograde scrub nurse table is placed between the antegrade and the retrograde surgeon. The organization differs in the case of right and left surgery [64]. The operation modes of all the devices must have been previously checked; all required materials like lead aprons, jelly pillows, and paddings must be ready in the operating room. All the operators must work without obstacles, having everything they need within arm's reach and positioned comfortably.
- The patient lies supine, with the flank to be operated very near to the border of the operating table to allow free mobility of the nephroscope once the patient has been definitely arranged (Figure 11.1a).
- The flank to operate on is elevated 20–30° with plumcake-shaped jelly pillows (Figure 11.1a) (or towels, a 5 l saline bag, or an inflatable cushion). This inclination may be adapted to the patients' requirements: in very thin patients, or in those with mild forms of retrorenal colon, or in case an upper calyceal access is needed, the elevation of the flank should be increased >30°, sometimes obtaining an almost perpendicular position, with the patient largely lying on the opposite flank.
- The first reference line, i.e. the posterior axillary line, is marked. This is the anterior limit of the puncture (Figure 11.1a).
- The leg of the side to be operated is arranged, extended, and only slightly abducted; the contralateral one is lifted, flexed, and well abducted, with both lying on padded stirrups and fixed (Figures 11.1a–c). Children may avoid the classical lithotomic position with padded stirrups for the lower limbs, and a simple stable opening of the legs on the operating table may be sufficient.
- The arm on the side to be operated is bent at the thorax on an adequate support (we use soft towels or a cushion), and the contralateral one lies abducted less than 90° on a padded support for anesthesiological management (Figures 11.1a,b).
- Then the other two reference lines, i.e. the twelfth rib cranially and the iliac crest caudally, are marked (Figure 11.1a), representing the posterior natural limit,

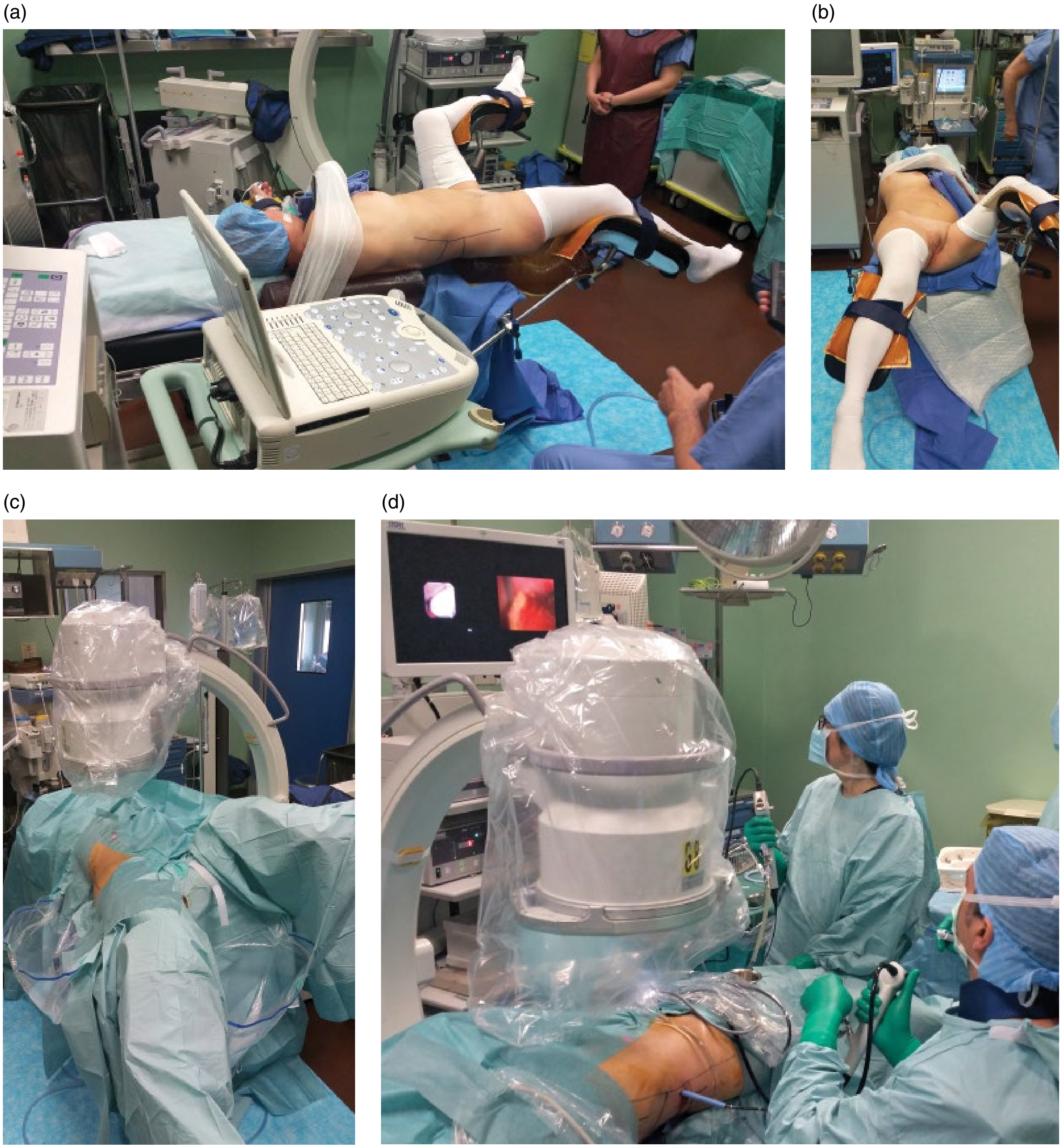

**Figure 11.1** Patient in the Galdakao-modified supine Valdivia (GMSV) position: (a) view of the elevated flank with the reference lines and (b) of the modified lithotomic position of the lower limbs. (c) After thorough positioning sterile drapings are applied, with irrigation bags to avoid fluid spillage; (d) the flank and the perineum are left free for antegrade and retrograde access respectively.

the lateral margin of the paravertebral muscles representing the posterior natural limit.

- In obese patients the fat falls on the side opposite to the one to be treated and might be fixed and flattened by applying strips of sticking plaster.
- Particular care should be taken when positioning a patient with skeletal deformities, adapting it in different ways from time to time, and paying particular attention to avoid pressure damage during the procedure.

- The unique sterile draping is an assembly of adhesive drapings including those from the cystoscopy set, all fixed with adhesive strips, provided with two bags, one under the flank and the other under the perineum, to avoid fluid spilling (Figure 11.1c) [64].

## Additional advantages of the GMSV position

A combined retrograde approach is comfortably performed and combined with antegrade surgery, thanks to the easy access to the urethra. Of course, retrograde access is also possible in prone-modified positions [65–67], although is evidently less comfortable and ergonomic.

The possibility to gain a suitable retrograde working access during PCNL enables endoscopically guided percutaneous access for a safe renal puncture, integrated with fluoroscopy and ultrasound, the standard imaging modalities, and provides an effective tool able to improve stone clearance, decrease the number of percutaneous accesses, and reduce overall radiation exposure. This is ECIRS, i.e. endoscopic combined intrarenal surgery [12, 24, 54].

## ECIRS, the rationale

The conceptual value of ECIRS extends beyond a safe endoscopically guided renal puncture, or the possibility to improve stone clearance through a single percutaneous tract thanks to the simultaneous contribution of the flexible retrograde ureteroscopy. ECIRS is a comprehensive approach to PCNL, allowing for versatile personalized stone management, and a perfect tailoring of all the intraoperative choices to the real-time situation of the patient and on the dynamic anatomy of the collecting system containing the urolithiasis on the whole [54].

In ECIRS retrograde flexible ureteroscopy replaces the step of the cystoscopic ureteral catheter application for retrograde pyelography, allowing preliminary direct visualization of the urethra, ureteral orifice, ureter, ureteropelvic junction, pelvis, and calyces with their infundibula, and the instructive evaluation of their dynamic features for an optimal planning of the following strategy. Of course, if the upper tract is not compliant, the retrograde approach must not be forced, and the traditional ureteral catheter is applied, but when possible it is advantageous and safe, as with applying a urethral catheter using vision instead of inserting it blindly. The diagnostic role of retrograde flexible ureteroscopy goes on intraoperatively, assisting all the steps of the percutaneous renal access, stone treatment, and exit strategy.

The active role of retrograde flexible ureteroscopy is optional (ECIRS may be used when there is no other retrograde contribution other than a diagnostic one), however it may be essential for safe antegrade or retrograde guidewire application to facilitate renal access and to improve stone clearance, managing or treating stones which are difficult to reach through a single percutaneous tract.

Of course, the idea of using flexible ureteroscopy as an adjunct to PCNL is not new at all [7, 68–72], but for various reasons (probably economic, because a second surgeon is required, and the use of flexible ureteroscopes with all their devices and the risk of rupture may constitute an additional relevant cost) [73] was never fully accepted and considered an essential step of PCNL, but rather an occasional and complementary contribution in difficult cases. Nowadays flexible ureteroscopes are ubiquitous in clinical practice, more advanced, miniaturized, and durable, with the additional option of single-use digital flexible ureteroscopes. So only the experience of the operators and their openness to try innovative solutions are needed for its widespread use during PCNL.

## The diagnostic role of retrograde flexible ureteroscopy during PCNL

1) The lower urinary tract is preliminarily evaluated. Simultaneous problems like false urethral passages, large obstructing and easily bleeding prostatic adenomas, calcified intravesical stents, or tight ureteral orifices may be identified and dealt with.
2) The dynamic anatomy of the ureter and upper urinary tract is preliminarily appreciated. Ureteral spasms or strictures, ureteral stones, a tight ureteropelvic junction, inelastic infundibula, and staghorn stones strongly adhering to the mucosa of the calyx may be recognized in advance, adapting the surgical strategy and the kind and size of the instruments to the patient, without forcing the anatomy and causing damage.
3) Preliminary evaluation of the stone features (not only those already known from preoperative computed tomography scanning such as their number, hardness, location, shape and size, but also dynamic characteristics like mobility and possibility of displacing them) is carried out. This may also help in the planning of the PCNL strategy.
4) Each step of the renal access (puncture, guidewire application, dilation of the access tract, Amplatz sheath application) (Figures 11.2–11.6) may be checked endoscopically (Figures 11.2d, 11.3c, 11.4b, 11.5b, 11.6b), integrating ultrasound (Figure 11.2a)

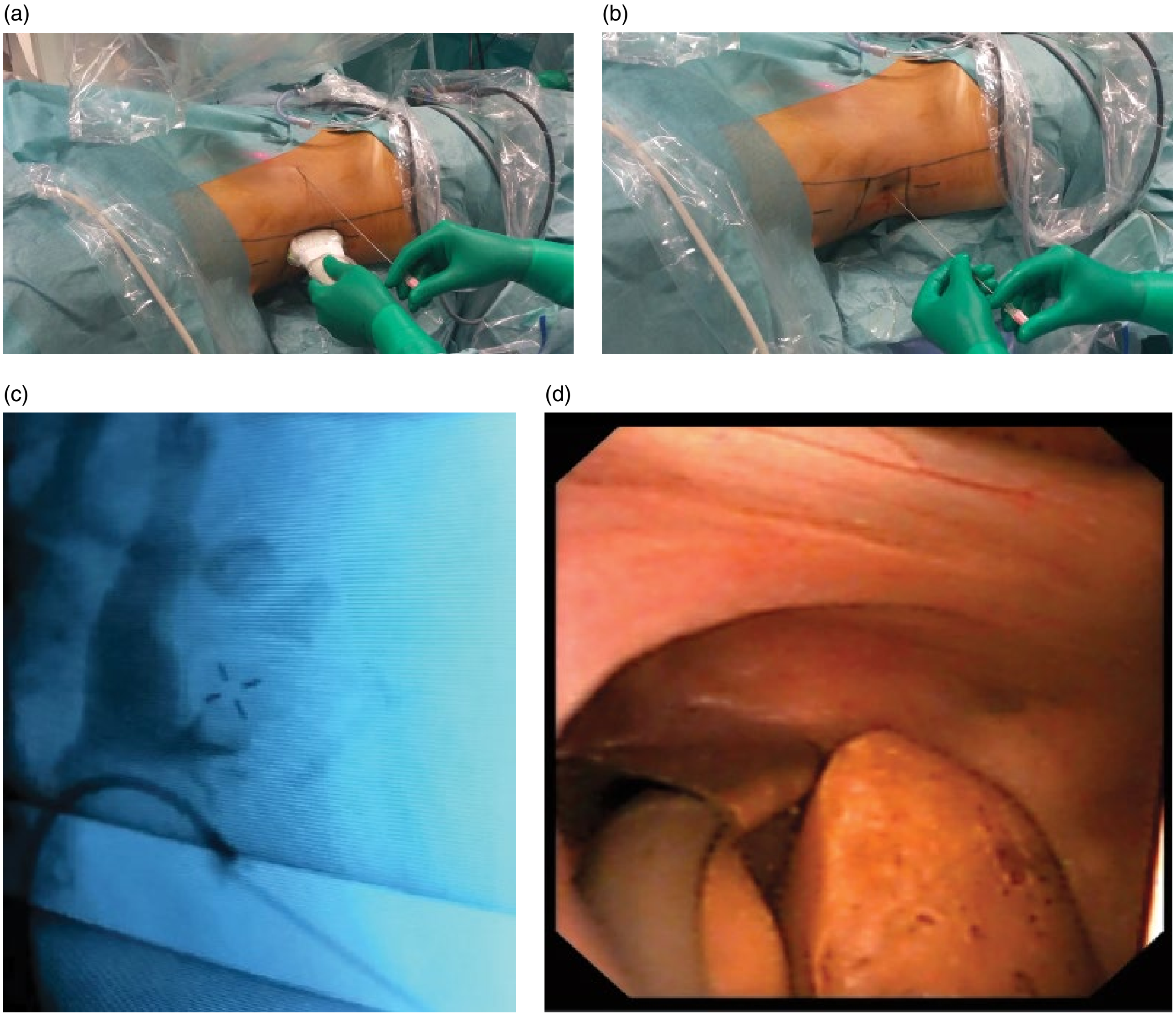

**Figure 11.2** (a) Ultrasound-checked (b) fluoroscopy-guided renal puncture may be followed endoscopically with retrograde flexible ureteroscopy (c, fluoroscopy; d, digital view).

and fluoroscopy (Figures 11.2b,c, 11.3a,b, 11.4a, 11.5a, 11.6a). In this way overall radiation exposure may be significantly reduced, thanks to the direct endoscopic control [74].

5) Antegrade lithotripsy through the rigid (Figure 11.7a) and the flexible nephroscope (Figure 11.1d) can be followed retrogradely, in order to avoid descent of fragments below the ureteropelvic junction.
6) Final endoscopic exploration of all calyces in search of residual fragments, in combination with the flexible nephroscope (Figure 11.8a), may be performed, aiming at an optimal stone-free rate.
7) A final evaluation of all renal cavities supports the decision for a stentless or a stented procedure, along with the assessment of the descent of the contrast medium from the pyelocalyceal system below the ureteropelvic junction and within the ureter.

## The active role of retrograde flexible ureteroscopy during PCNL

1) Guidewire application from the percutaneous renal access down the ureter may be endoscopically assisted (Figures 11.3a,b), but if the wire initially coils within the pelvis or a renal calyx, antegrade retrieval of a retrogradely inserted guidewire is also possible, after the

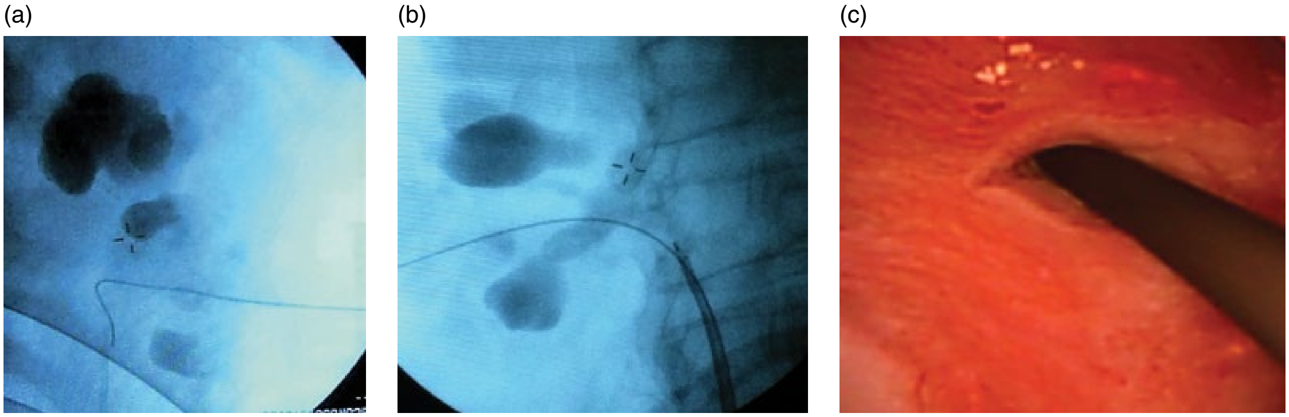

**Figure 11.3** The hydrophilic guidewire may be applied antegradely and descend into the ureter (a, fluoroscopy), sometimes guided by the flexible ureteroscope (b, fluoroscopy), also checking the guidewire exiting from the renal papilla (c).

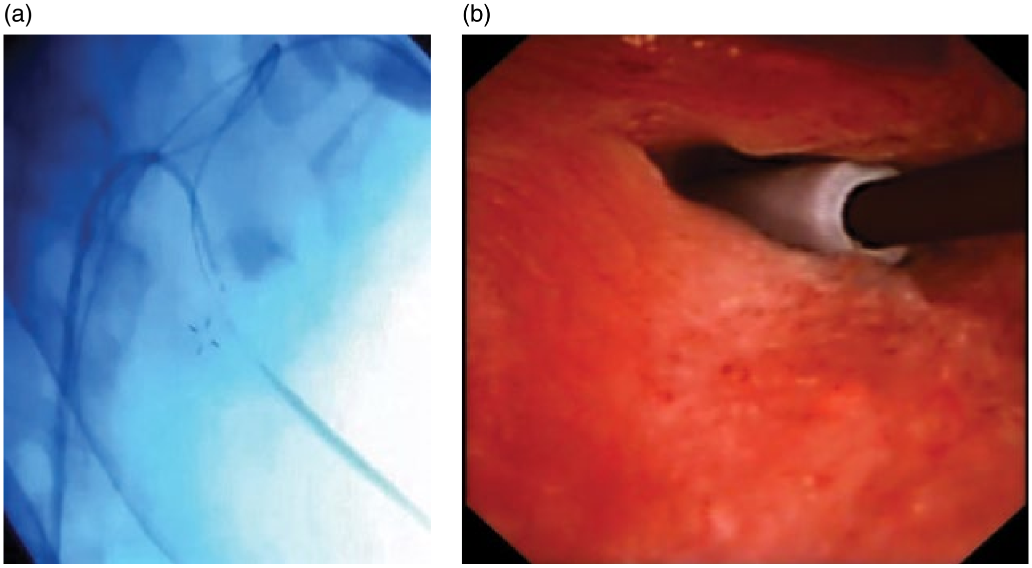

**Figure 11.4** Insertion of a fascial dilator: (a) fluoroscopic and (b) endoscopic control.

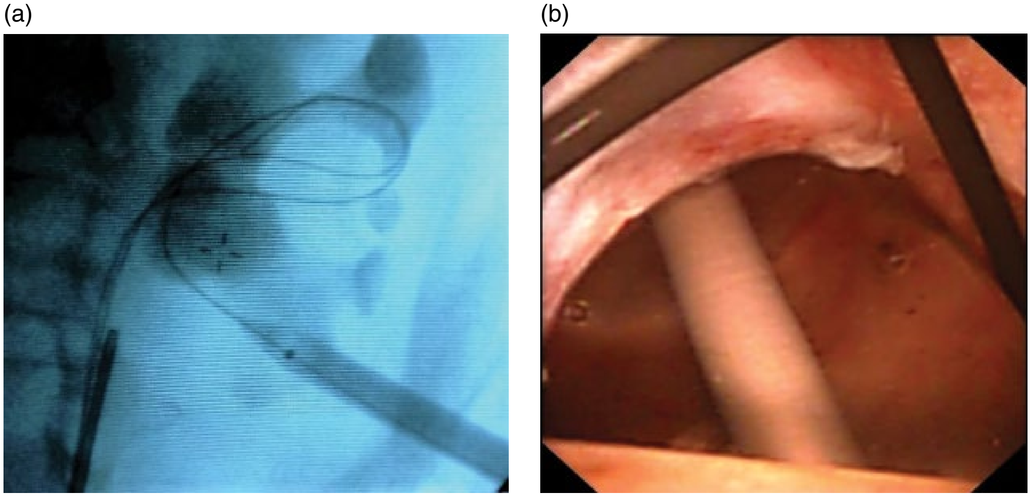

**Figure 11.5** Insertion of a balloon dilator: (a) fluoroscopic and (b) endoscopic control.

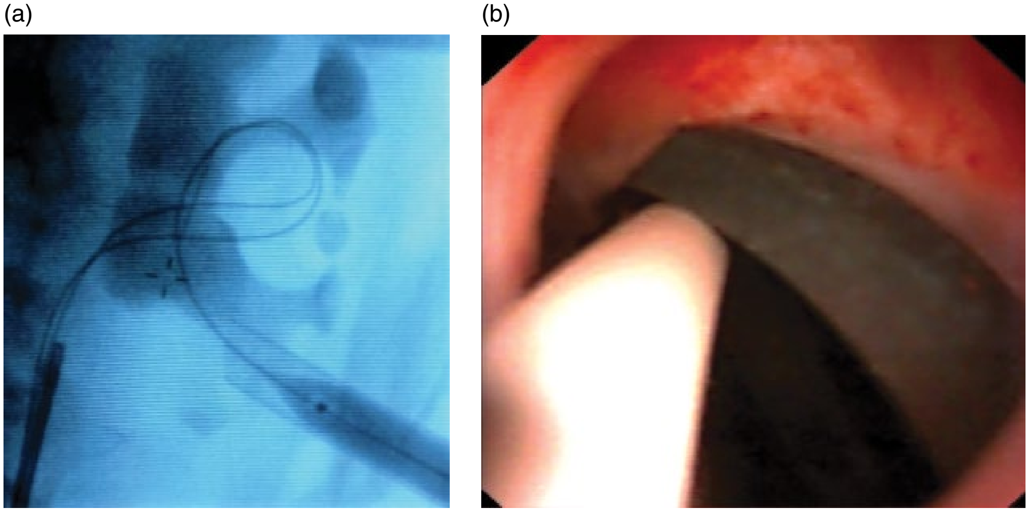

Figure 11.6 Insertion of the Amplatz sheath: (a) fluoroscopic and (b) endoscopic control.

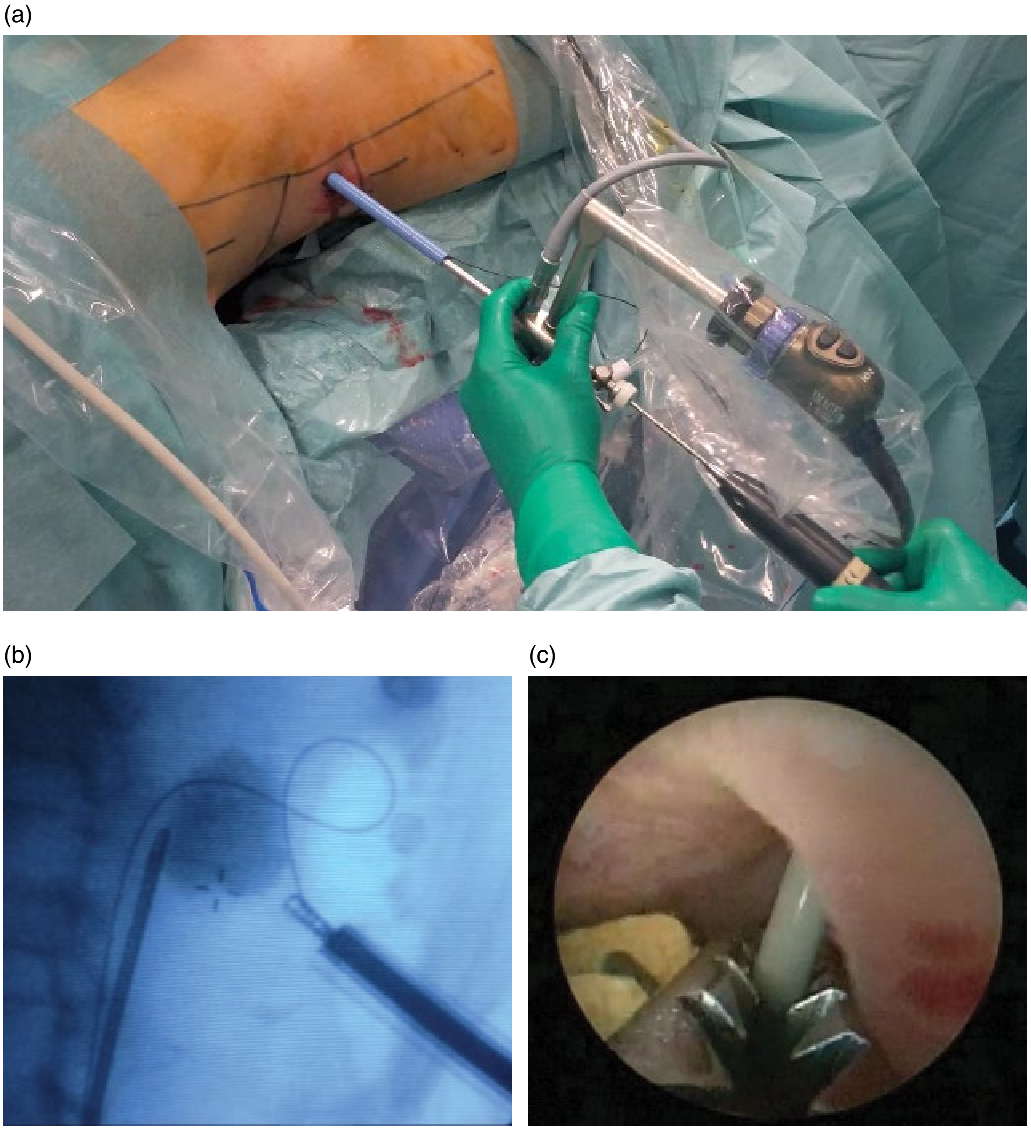

Figure 11.7 Rigid nephroscope and ballistic/ultrasonic lithotripsy (a), after extraction of a retrograde guidewire from the Amplatz sheath (b, fluoroscopy; c, endoscopy).

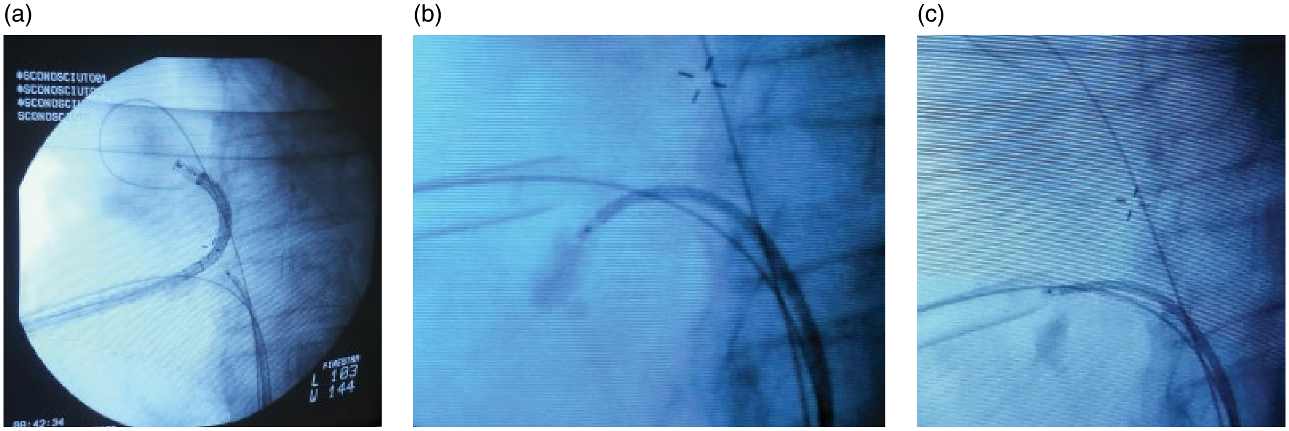

**Figure 11.8** Cooperation between flexible nephroscope and flexible ureteroscope, exploring all the calyces in search of residual fragments (a, fluoroscopy). Sometimes stones are located in calyces parallel to the Amplatz sheath (b, fluoroscopy), so the contribution of the retrograde flexible ureteroscope becomes essential and fragments may be snared within a basket and delivered outside through the Amplatz sheath (c, fluoroscopy).

percutaneous access has been gained (Figures 11.7b,c), obtaining the maximally safe "kebab" patient.

2) All the steps of the renal access (puncture, guidewire application, dilation of the access tract, Amplatz sheath application) (Figures 11.2–11.6) may be corrected if needed, avoiding related complications due to wrong or insufficient insertion or overadvancement of the various devices; this would otherwise possibly cause hemorrhagic complications.
3) The creation of the water path around staghorn stones impacted within a calyx by means of the retrograde irrigation facilitates the insertion of the hydrophilic guidewire, and supports the choice of the technique of tract dilation and of the size of the access tract. In absence of space between stone and mucosa no tapered dilators like balloon or silicon dilators (requiring a space of at least 1 cm within the calyx to host their tip) may be smoothly applied, but Alken dilators (requiring no other space than that sufficient to host the ball-shaped tip of the first stylet) should be employed instead. If the infundibulum of the access calyx is thin and inelastic adapt your instruments to the patient, and not vice versa. Choose a miniaturized access and avoid breaking the infundibulum, which would cause unnecessary bleeding.
4) Stones in calyces which are difficult difficult to reach with either the rigid or the flexible nephroscope through the access tract can be treated (Figure 11.8b,c). The active contribution of the retrograde flexible ureteroscope in the stone management and treatment avoids the need for multiple percutaneous tracts [75–77], thus reducing the risk of bleeding and related complications [78].
5) Final retrieval of residual fragments in combination with the flexible nephroscope is feasible, either extracting them retrogradely or passing the ball through the Amplatz sheath (Figure 11.8c).

## Conclusion

Modern-day PCNL is very different from the initial 30 Fr rigid-only PCNL of the 1970s, having undergone considerable evolution, mainly driven by a variety of improvements in access techniques, endoscopic instrumentation technology, lithotripsy devices, and drainage management.

The introduction of the supine and supine-modified positions is also part of this evolution, enabling safer procedures from an anesthesiologic point of view, and an easily combined antegrade and retrograde surgery (ECIRS), allowing a thorough tailoring of the procedure to the patient and the urolithiasis. ECIRS has no obvious clinical superiority if compared to standard prone PCNL [79], but it is certainly a new, safe, and effective way of interpreting PCNL and is here to stay, having started to gain acceptance and popularity within the urological community [9, 11, 12].

Video 11.1 gives an overview of ECIRS.

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# 12

# Prone, Lateral, and Flexed: Patient Positioning for Percutaneous Nephrolithotomy

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## Introduction

Positioning for percutaneous nephrolithotomy (PCNL) is an important, yet often neglected, aspect of the procedure. Operators invariably become wedded to one position, yet with knowledge and experience of other positions there is the freedom to choose the most appropriate technique for the case at hand. Since the introduction of percutaneous renal surgery for stone disease by Fernstrom and Johansson in 1976 [1] there has been a proliferation of case series addressing various modifications to patient positioning, including the lateral decubitus [2–4], modified lateral [5], reverse lithotomy [6], split-leg [7–9], and supine [10] positions. However, most of these have not gained widespread acceptance other than prone and, to a lesser extent, the supine positions. Today, PCNL is usually performed with the patient in the prone position. A recent survey of Endourological Society members found that 86% of respondents used the prone position, 10% supine, and 4% lateral decubitus [11]. We have previously described a prone-flexed modification that confers several advantages over the conventional prone technique [12].

In this chapter, we review in detail both the conventional prone technique as well as our prone-flexed modification. Additionally, we describe the lateral technique and our lateral-flexed modification technique, which we find particularly useful in morbidly obese patients and those with severe kyphoscoliosis. We have also attempted to provide an anatomic explanation for the known complications associated with PCNL, including the rare complications related to patient positioning, and how attention to patient positioning can mitigate these issues. Finally, we also provide an overview of the literature comparing prone to supine PCNL.

## Prone and prone-flexed positions

Due to the retroperitoneal location of the kidneys and their proximity to the flank, PCNL is most commonly performed in the prone position with straightforward access to the collecting system [11]. However, when the procedure was being developed in the early 1980s, direct calyceal puncture was not thought to be important, provided that puncture was along the avascular line of Brödel. It has since been recognized that puncture directly into a calyx provides the safest access for stone removal [13, 14]. At present, the majority of PCNLs are performed with the patient prone and access is obtained through a posterior or posterolateral calyx. This position confers numerous advantages, with the main disadvantages being the time required for patient repositioning and anesthetic concerns in the morbidly obese (Table 12.1). We have previously shown that the prone-flexed position, a simple modification to conventional prone positioning, has several additional advantages [12] and can be implemented on most operating room (OR) tables that permit fluoroscopy. Some OR tables may have to be reversed in order to produce adequate space for the C-arm image intensifier. This space is increased significantly by flexion of the table during prone-flexed PCNL.

### Percutaneous lithotomy in the prone and prone-flexed positions (see Video 12.1)

#### Retrograde pyelogram and choice of calyx

To perform fluoroscopically guided access, a high-quality retrograde pyelogram is essential. Consequently, we begin all procedures with the patient positioned supine. Once the patient has been intubated under general anesthesia, and the genitalia prepped with providone-iodine,

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 12.1** Patient repositioning to and from prone adds to OR time.

| | Technique | Advantages | Disadvantages |
|---|---|---|---|
| Prone | Patient is prone with a padded bolster under the upper thorax to facilitate ventilation | Large field with wide choice of calyces for access<br>Easy end-on access to the posterior calyces<br>Easiest access to upper pole<br>Wide space for instrument manipulation<br>Renal pelvis is dependent with easier access to mobile stones<br>Optimal position for fluoroscopically guided access (bullseye or triangulation)<br>Minimal interference from the OR table | Patient repositioning from prone adds to OR time<br>May have difficulty with ventilation in obese patients<br>Risk of respiratory or cardiovascular compromise<br>Theoretical risk of ocular complications |
| Prone-flexed | Patient is prone, with a padded bolster under the upper thorax to facilitate ventilation<br>Flexed at the waist 30–40°<br>Knees are flexed 15–20° | Similar advantages to prone position<br>Further increased working space<br>Flattening the lumbar lordosis decreases instrument conflicts with buttock<br>May convert supra-11th to supra-12th or supra-12th to infracostal access by displacing the kidneys caudally<br>Reduces skin to stone distance<br>Reduces chance of spleen or liver injury | Similar disadvantages to prone position<br>Extra padding needed due to head-down position<br>May increase airway pressures |
| Prone split-leg | Patient prone, with the genitalia at the bottom of the OR table<br>Legs on padded adaptors and abducted up to 45° | Similar advantages to prone position<br>May perform ureteroscopy without patient repositioning or fear of contaminating instruments<br>Allows endoscopic-guided access | Similar disadvantages to prone position<br>Patient is further down the OR table, away from the anesthesiologist<br>May be difficult to demonstrate posterior calyces especially with dilated calyces<br>May require endoscopic-guided access |

flexible cystoscopy is performed. In men, this is performed with the patient supine, while the frog-leg position is useful in women. A 5 Fr Flextip (Cook Medical) ureteral catheter with a terminal side hole, which facilitates aspiration, is passed into the collecting system. Urine is completely aspirated and replaced with radiographic contrast to identify all calyces. Urine is less dense than contrast and, as a result, any urine left within the collecting system will tend to collect at the highest point within the kidney and float on top of the contrast. This property can be helpful to the surgeon when distinguishing anterior and posterior calyces. In the supine position, posterior calyces are identified by the presence of denser contrast within them, while anterior calyces appear paler due to the mixture of contrast with urine. Conversely, when the patient is repositioned prone, posterior calyces often appear paler. If too much pure urine without contrast is present, these calyces may be poorly visualized or even invisible.

A C-arm image intensifier is used to examine the anatomy of the collecting system and the position of all stones. Four fluoroscopic images are captured: a scout image to identify all calculi, an anteroposterior (AP), and two obliques. These images help create a mental three-dimensional (3D) picture of the calyceal anatomy, and can be referred to during the procedure. In the anterolateral view, the posterior calyces are viewed from the side and appear longer, whereas in the anteromedial view, they are seen through the central axis of the kidney and are viewed end-on, appearing shorter (Figure 12.1).

A ureteral occlusion balloon (Cook Medical) is then inserted over a guidewire, positioned at the ureteropelvic junction. A three-way valve is attached and connected to a 10 ml syringe and intravenous tubing leading to a bottle of contrast. This allows aspiration and infusion of additional contrast as needed during the case. Using an occlusion balloon has several benefits. First, the balloon prevents stone fragments from falling into the ureter. Second, the constant pressure of contrast in the renal collecting system ensures a persistent pyelogram, facilitating calyx identification when the patient is repositioned prone. Third, flow of contrast under gravity distends the collecting system, providing a larger target for access. Fourth, free return of contrast out through the needle allows the surgeon to rapidly confirm successful puncture of the chosen calyx. Finally, the occlusion balloon is secured externally to a Foley catheter using a Tegaderm™ (3 M) to allow for easy

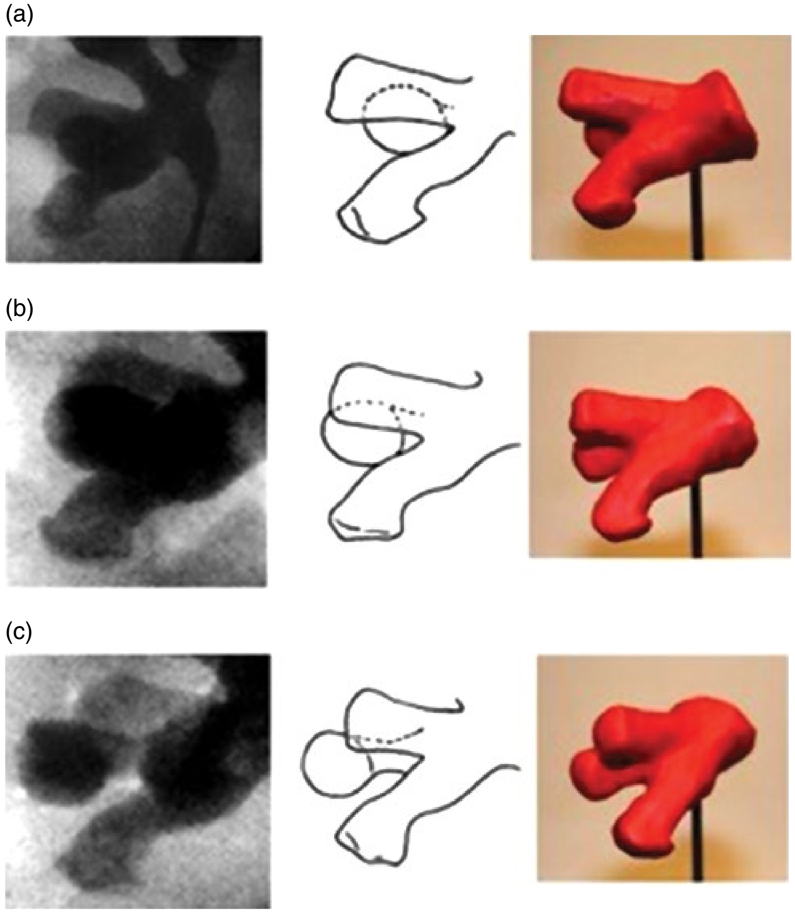


**Figure 12.1** 3D model of the lower pole renal collecting system of the right kidney with the patient in supine position. The posterior calyx is dependent, filling with dense contrast. Anterior calyces are paler due to the mixture of contrast with less dense urine. (a) With the C-arm rotated 30° toward the left side of the patient, the posterior calyx is viewed end-on and appears shorter. (b) Anteroposterior (AP) view. (c) With the C-arm rotated 30° toward the right side of the patient, the posterior calyx is viewed from the side and appears longer. Reproduced with permission of Mary Ann Liebert, Inc. Publishers.

separation, and wrapped in sterile towels where is exits from the urethra, allowing for sterile insertion of a double J stent on a tether in a retrograde fashion at the end of the procedure.

## Renal puncture and dilation of the tract

With a Foley catheter *in situ* and the ureteral occlusion balloon secured externally, we reposition the patient prone with the assistance of additional staff members. Generous padding is placed under the knees, feet, and chest to prevent pressure injury and to facilitate ventilation (Figure 12.2). The eyes are taped to prevent corneal abrasions and the head is placed in a prone position foam headrest with cut-out holes for the eyes, nose, and endotracheal tube. We have found that there is no one support that is universally appropriate for all patients, so several options are available at all times. In the prone position there tends to be hyperextension of the cervical spine but with flexion in the prone-flexed position the head drops forward and reverses this hyperextension. To prevent brachial plexus injury, the arms should be kept below the level of the chest, and are both externally rotated at the shoulder, and flexed at the elbow. Again, generous padding is utilized. Finally, a safety strap is placed across the buttocks.

In the prone position, the natural, anterior lordosis of the spine is exaggerated. This complicates access by compressing the working space and leads to instrument conflicts with the buttocks. To avoid this, the table can be flexed 30–40° at the level of the lower abdomen (Figure 12.2) to open the space between the 12th rib and the posterior iliac crest (Figure 12.3). Flexion of the hips not only increases the working space on the patient's flank [15], but also may rotate the ribs cephalad, further increasing the working space and, along with caudal displacement of the kidneys in this position, often converting a supracostal to an infracostal access or a supra-11th rib to a supra-12th rib access [12]. Wide skin preparation is performed from above the 10th rib to the buttocks and medially from the spinous process to the mid-axillary line, laterally. We use chlorhexidine-alcohol as it was shown to be superior to povidone-iodine at preventing surgical site infections in the perioperative period in a multicenter randomized controlled trial (RCT) [16]. Due to the copious amount of irrigation necessary for PCNL, we use an adhesive neurosurgical drape with a drainage pouch connected to suction to direct fluid away from the

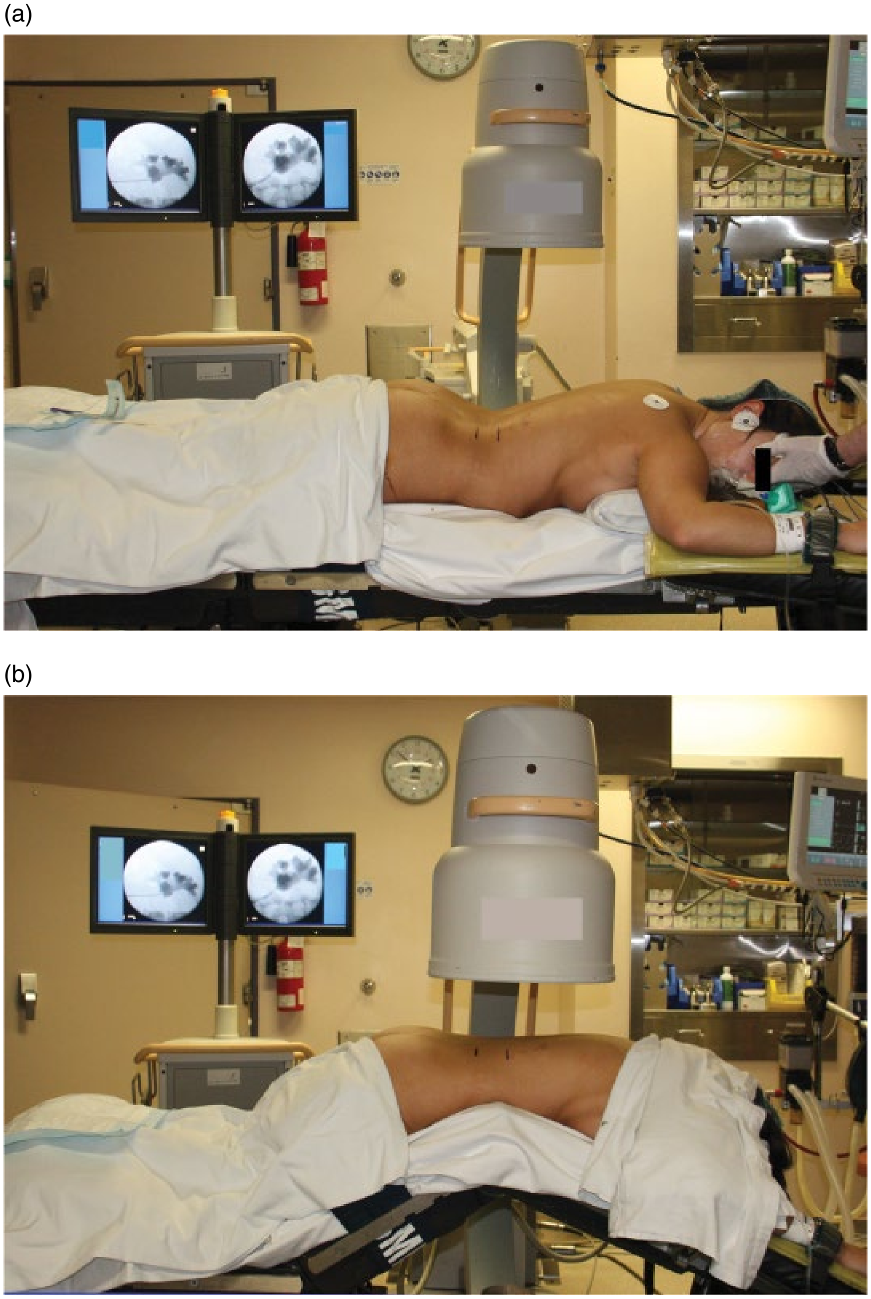


**Figure 12.2** Configuration of OR table with padding and C-arm [96]. Reproduced with permission of John Wiley and Sons.

patient. Only normal saline irrigation is used unless electrocautery is required, when it is changed to a nonelectrolyte solution. To prevent hypothermia, all irrigation fluid is heated to 42 °C in a warming cabinet.

### Bullseye technique

The C-arm is draped and used to identify the previously chosen posterior or posterior-lateral calyx. Due to the change to the prone position, the posterior calyces are now less dense as the heavier contrast flows anteriorly (Figure 12.4). We favor a conventional bullseye technique for performing renal puncture in the prone position; however, a triangulation technique can also be used. Both methods are described in this chapter. Prone and prone-flexed positioning allows maximal excursion of the C-arm around the OR table, giving the widest possible unobstructed imaging windows. Flexing the table in the prone-flexed position significantly increases the space below the table to allow movement of the C-arm. In the prone position, the posterior calyces move in the

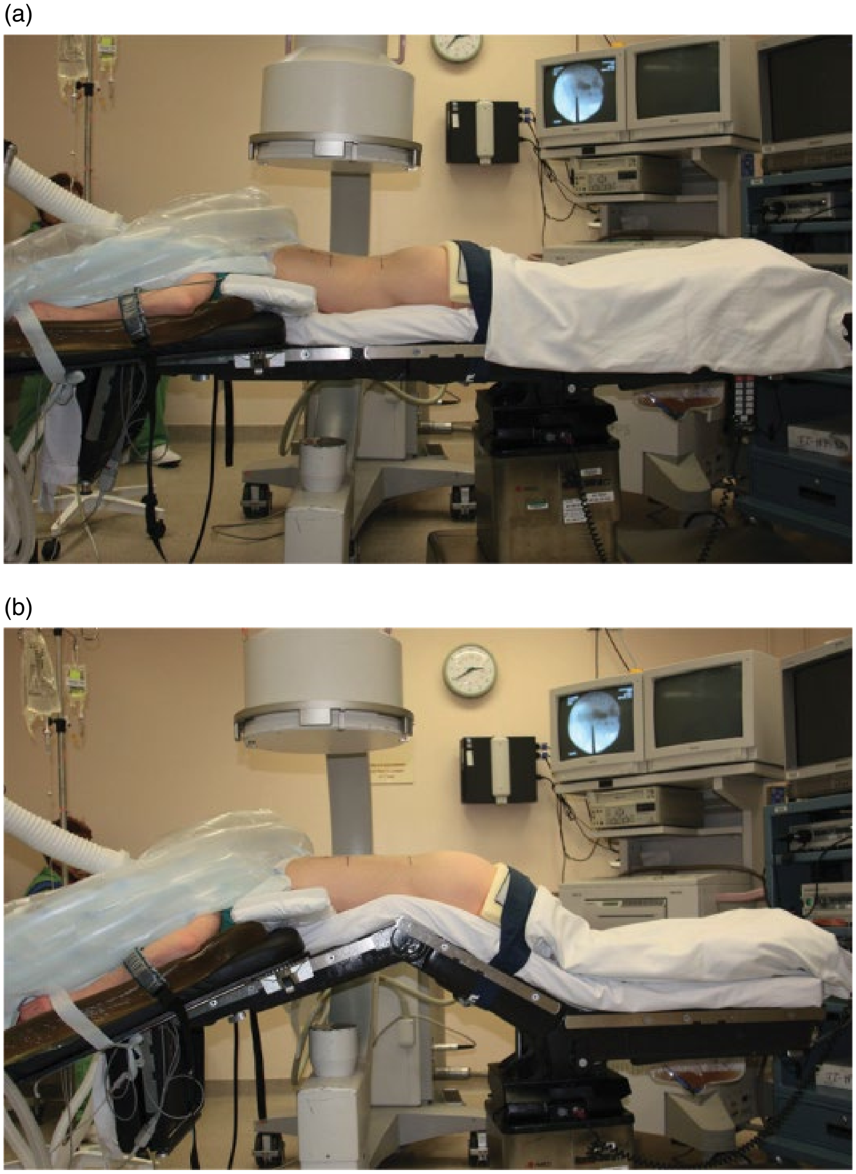


**Figure 12.3** (a) Prone and (b) prone-flexed patient positions. A padded support is placed under the patient's chest to improve respiration. With the OR table flexed 30–40°, the patient's flank is flattened and there is increased area available for puncture. Note also that prone-flexed positioning decreases obstruction from the buttocks with lower pole access.

opposite direction to the image intensifier of the C-arm (Figure 12.4). With the C-arm rotated 30° from the vertical, towards the operator, the posterior calyces move away, and shorten as one looks down the axis of the infundibulum. Using the bullseye technique, in this position, the calyx of choice is viewed end-on. We use an 18G Trocar needle to puncture the calyx in the center of the papilla. This needle lacks a beveled edge and, as such, resists deflection away from the axis of puncture. The needle is inserted and advanced along the line of the X-ray beam. To assess the depth of the needle, the C-arm is periodically rotated away from the operator (Figure 12.4). To minimize radiation exposure to the surgeon's hands, the needle can be held in a long Kelly forceps, aligned with the calyx under fluoroscopy, and advanced during expiration without fluoroscopy. Once the calyx is entered, and a free flow of contrast obtained, an Amplatz extra-stiff or super-stiff guidewire is passed down the needle into the collecting system.

Due to the presence of the occlusion balloon, we do not attempt to pass the guidewire down the ureter, although this may occur. A small depth-gauge ring on the needle is adjusted to skin level to mark the depth between the skin and the collecting system. Knowledge

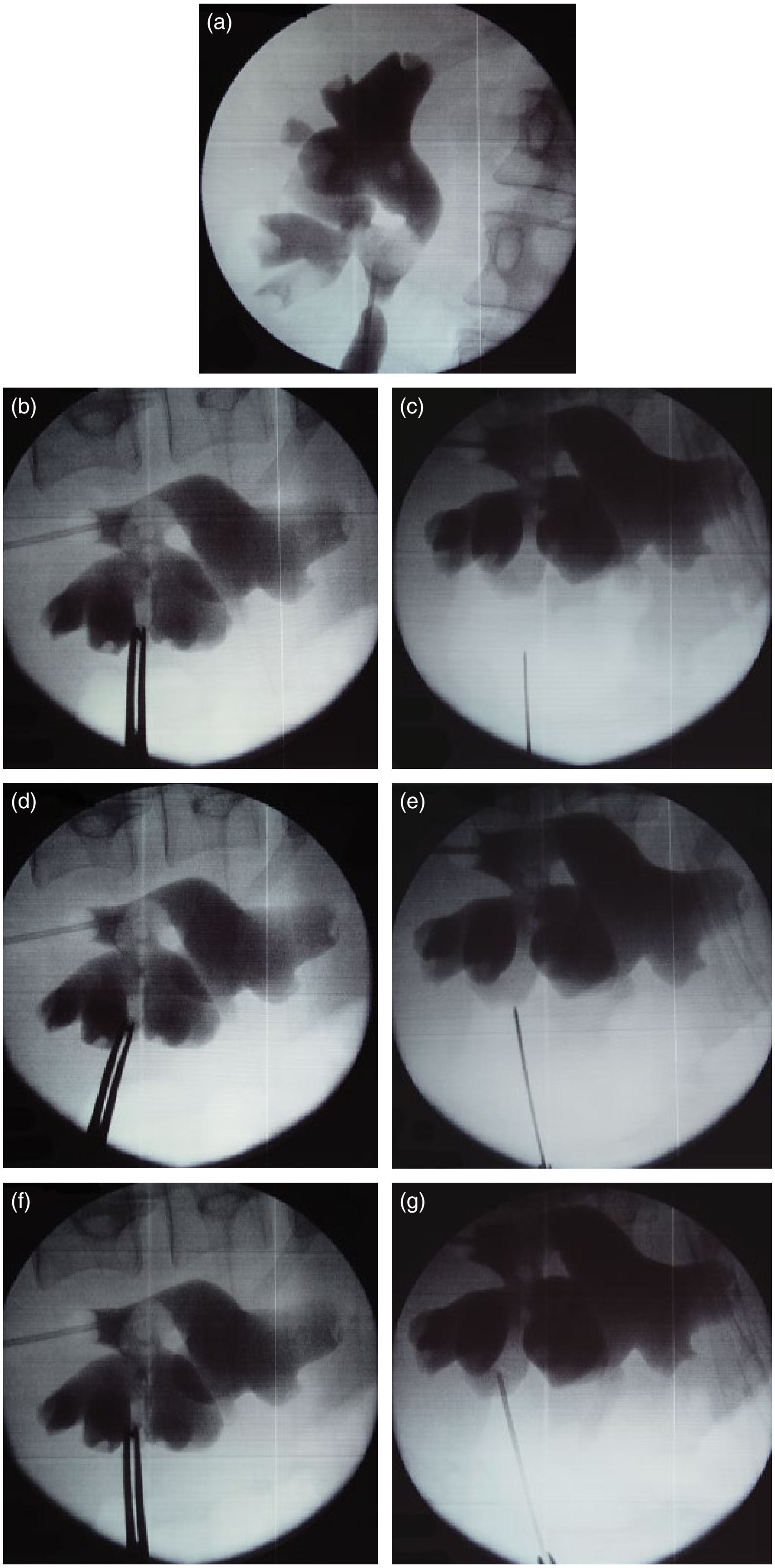


**Figure 12.4** Bullseye technique. (a) AP view with the patient in the supine position. All subsequent images are with the patient in the prone-flexed position. (b) AP view with the forceps holding the needle and aimed at the chosen posterior calyx. (c) 30° oblique view demonstrating the depth required for puncture. (d) AP bullseye view. (e) 30° oblique view. (f) AP view. (g) Oblique view with the chosen calyx successfully puncture by the needle.

of this measurement reduces radiation exposure during insertion of the fascial dilators and nephrostomy tract dilating balloon. Fascial dilators (6, 8, and 10 F) are used to dilate the tract and then a safety guidewire can be inserted using a 10 Fr dual-lumen catheter (Cook Medical). The tract is then further dilated to 30 Fr with a nephrostomy tract dilating balloon (Cook Medical) over which a 34 Fr Amplatz sheath with a 30 Fr inner diameter is passed. Although different methods of tract dilation exist, including balloons, Amplatz serial dilators, and the Alken telescopic dilator among others, we favor balloon dilation. We have found this to be both quick and atraumatic, although this comes at increased cost.

## Adjuncts to assist with patient positioning

The prone-flexed modification can add several advantages to the operating surgeon without any impediment to C-arm movement. Adopting this position on an OR table without a flex option is still possible through the use of bolsters. The "Montreal mattress" is a preshaped surgical bolster that can be used as an adjunct for the support of prone patients [17]. The advantage of this device is the central cavity which allows for free movement of the abdomen. Theoretically, this should lessen respiratory compromise and minimize cardiovascular effects such as inferior vena cava obstruction. Another option is the radiolucent Wilson frame, an adjunct used by spinal surgeons to mimic the prone-flexed position on a standard OR table. Its advantages include the ability to control the degree of flexion required as well as to use adjustable contour pads that allow for free excursion of the abdomen, preventing respiratory compromise. The main limitation to its use is the reduction in depth, preventing C-arm movement, instrument manipulation, the working space within the C-arm, and a reduction in magnification.

## Advantages and disadvantages of the prone and prone-flexed positions

As mentioned, the majority of PCNLs are still carried out with the patient in the prone position, with prior retrograde placement of a ureteral catheter or occlusion balloon under fluoroscopic control. This initial procedure can be performed with the patient either supine or prone. If performed while the patient is supine, it is necessary to position and drape the patient twice, prolonging OR time [18, 19]. By commencing the procedure with the patient in the prone position immediately following induction of general anesthesia, the patient will still require repositioning, but is draped only once [17]. A split-leg modification can facilitate access to the external genitalia, for simultaneous antegrade and retrograde approaches [7, 8, 20]. In the prone position it may be difficult to access the anteriorly displaced ureteric orifices for the retrograde study, but with practice this can become routine. Additionally, if the procedure is started in the prone position, identification of the posterior calyces, especially in obstructed systems, may be difficult, or impossible. The presence of pure urine within the collecting system, especially if dilated, may result in urine floating on top of the denser contrast and render them invisible. For this reason, it is our preference to begin the procedure with the patient supine where the dense contrast sinks down into the posterior calyces.

Prone positioning for PCNL allows access to the entire flank, with a wide choice of access sites, especially when multiple accesses are required. Although still possible in the supine position, upper pole access is significantly easier when the patient is prone. An upper pole puncture has many advantages, including the ability to work down the renal axis, with minimal torque, as the more mobile lower pole rotates to align with the nephroscope. This reduces the chance of renal parenchymal shear and bleeding. Selection of an upper pole calyx is indicated in obese patients, as the upper pole is closer to the posterior abdominal wall than the lower pole. It is also indicated in patients with staghorn calculi, or stones in a horseshoe kidney, and facilitates access to multiple lower pole calyces with a single tract. In contrast, from the lower pole, visualization of the upper calyces with a rigid nephroscope is rarely possible. Finally, dilation into the upper pole is easier due to more adherent attachments to Gerota's fascia limiting renal mobility, whereas the more mobile lower pole may move away from the operator during dilation and kink the guidewire. Despite these advantages, many authors still prefer a lower pole puncture with the reassurance that this approach will avoid thoracic complications. In our series, with a supracostal puncture, pleural complications occurred in 2.6% of patients [15].

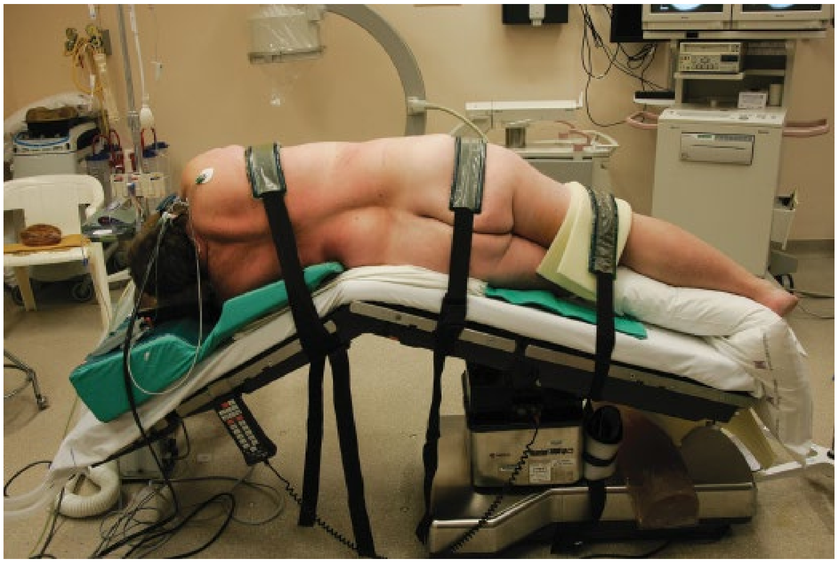
The prone-flexed modification that we describe provides several additional advantages over the traditional technique. First, and most obviously, the working space is further increased as the flank is significantly flattened, eliminating interference from the buttock during rigid nephroscopy through a lower pole tract (Figure 12.2) [12]. In addition, we have also shown that when in this position, the spleen is displaced medially and the kidneys are displaced inferiorly in the retroperitoneum [12]. This effect is most pronounced with the left kidney, which is lower than the right kidney in greater than 90% of cases. Also, due to this modification, with this displacement, a supra-11th rib access may be converted to a supra-12th rib, or a supra-12th to an infracostal access. Finally, the flank is significantly flattened, eliminating interference from the buttock during rigid nephroscopy through a lower pole tract [10].

## Lateral and lateral-flexed positions

Although the prone-flexed position for PCNL can be used for the obese patient, the lateral position has multiple advantages in these patients, and is sometimes the only feasible position for the morbidly obese patient with a body mass index (BMI) in excess of 50 kg/m$^2$ who cannot be ventilated prone or those with skeletal deformities, especially severe kyphoscoliosis. This position allows the protuberant abdomen and pannus to fall medially, taking the weight off the anterior abdominal wall as occurs when the patient is supine (Figure 12.5). This maximizes diaphragmatic excursion and facilitates general anesthesia. The pannus can also be supported separately if required.

The lateral-flexed position is familiar to any urologist who performs open and laparoscopic renal surgery. This position significantly widens the space between the 12th rib and the iliac crest, flattening the folds of adipose tissue and facilitating percutaneous access (Figure 12.6). The increased distance between the 12th rib and iliac crest, produced by this flexion, is even more pronounced than

(a)



(b)

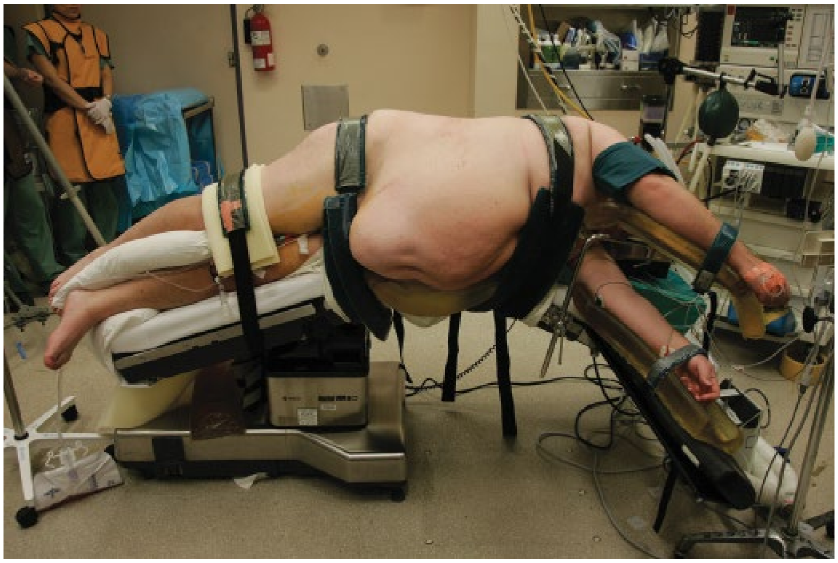


**Figure 12.5** Lateral-flexed patient position. (a) Posterior view. A wedge with a groove for the dependent arm is placed under the patient's torso. (b) Anterior view. Both arms are supported and flexed slightly at the elbow. Generous padding is used to prevent injury. Note that the pannus falls away from the patient, preventing respiratory compromise.

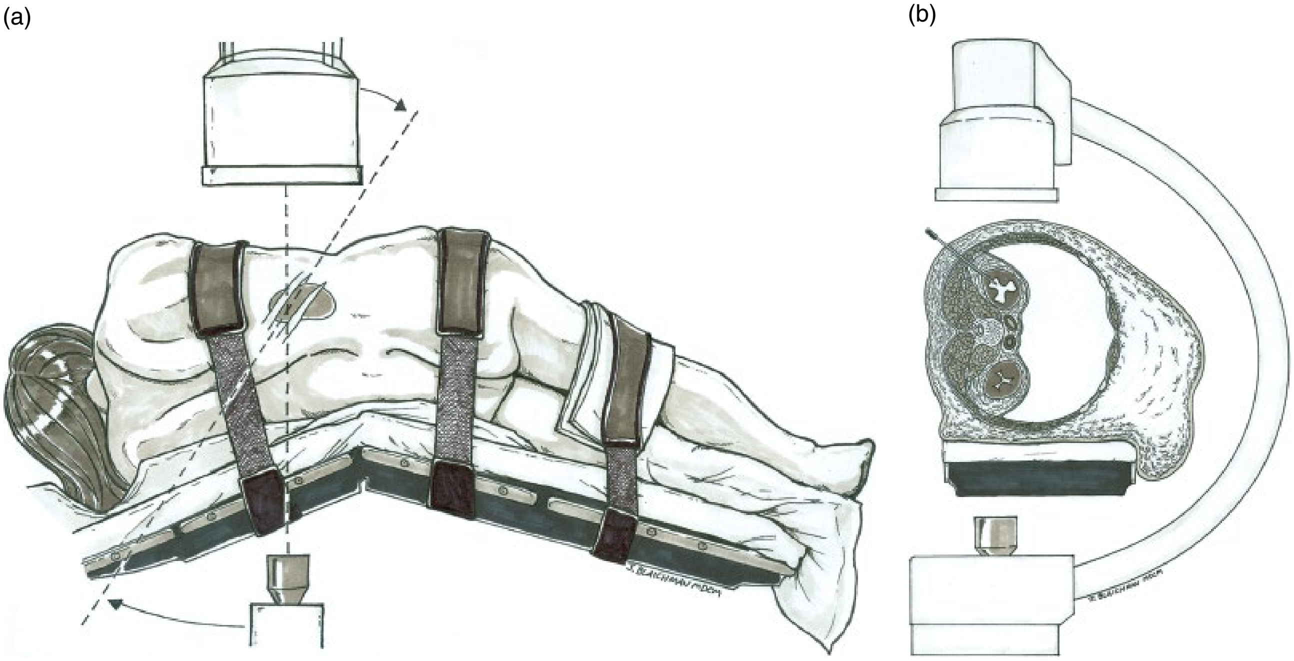


**Figure 12.6** (a) The C-arm is seen both vertical and in the oblique plane (angulated towards the feet), used for the triangulation technique, as described in the text. (b) A cross-sectional illustration, with the C-arm image intensifier positioned for the vertical anterioposterior view [96]. Reproduced with permission of John Wiley and Sons.

the increase produced by flexion with the patient prone. This also elevates the thoracic cage in relation to the kidney on that side and reduces the need for supracostal access. Also, in this position, the relative lack of adipose tissue over the costovertebral angle is frequently surprising in these morbidly obese patients and, provided the upper pole calyx is chosen for access, it is frequently possible to use a standard-length Amplatz sheath and nephroscope.

One disadvantage to flank positioning is that percutaneous access usually requires either ultrasound guidance or use of triangulation when using the C-arm image intensifier, as opposed to the standard bullseye technique. This is partly because of the restricted arc of rotation of most C-arms, but also because the metal side rails of most radiolucent tables prevent adequate visualization of the collecting system when the C-arm is rotated to an exaggerated position. A randomized study comparing access using ultrasound in the lateral-flexed position to fluoroscopy in the prone position achieved successful access in all cases ($n = 60$) with no difference in intraoperative bleeding but took longer (14.5 vs. 9.4 minutes for prone with fluoroscopy) [4]. Advantages of the lateral and lateral-flexed positions are outlined in Table 12.2.

## PCNL in the lateral and lateral-flexed positions (see Video 12.2)

As with prone or prone-flexed PCNL, the procedure begins with a retrograde pyelogram and insertion of a ureteral occlusion balloon. This is performed with the patient supine in order to choose the most appropriate calyx, as described earlier (Figure 12.7). In the lateral-flexed position the arms and legs are positioned as for open or laparoscopic renal surgery, and the patient is secured to the table with padded straps or tape over the upper chest and pelvis (Figure 12.5). An axillary roll or padded wedge with a groove to accommodate the dependent arm must be positioned to adequately support the chest and prevent positioning-related injury. Extra padding must also be placed under the dependent knee and ankle to prevent pressure-related complications.

The concept of triangulation is illustrated in Figures 12.8 and 12.9. With the C-arm in the AP configuration, it is possible to determine the cephalad–caudal axis direction for puncture. Oblique views are then similarly used to determine the AP direction of puncture. In this view, dropping the hand holding the needle to direct the needle laterally toward the anteroaxillary line will target the more anterior part of the kidney. Elevating the hand holding the needle will direct the needle toward the spine and will aim it toward the more posterior part of the kidney.

With the patient in the lateral position and the C-arm image intensifier placed on the abdominal side of the patient, the pelvicalyceal system is initially viewed in the AP position from above. The previously chosen calyx can be identified facing posteriorly towards the operator

**Table 12.2** Options for lateral patient positioning.

| | Technique | Advantages | Disadvantages |
|---|---|---|---|
| Lateral | Patient in lateral decubitus with no break in the OR table | Familiar to urologists who perform open renal surgery<br>Compared with prone, easier patient repositioning from supine<br>Easiest identification of the posterior calyces<br>Useful in morbid obesity or severe kyphoscoliosis<br>Least effect on cardiac and respiratory function<br>May be performed under epidural or local anesthesia alone<br>Renal pelvis is dependent with easier access to mobile stones<br>More ergonomic for the surgeon than prone position<br>May perform nephroscopy and ureteroscopy simultaneously | Patient repositioning is required<br>Fluoroscopy is technically limited necessitating triangulation or ultrasound-guided access |
| Lateral-flexed | Patient in lateral decubitus with 30–40° break in the OR table | Similar advantages to lateral position<br>Significantly increased working space<br>Reduces flank fat in morbidly obese patients<br>May elevate the lower ribs, reducing the need for supracostal access | Similar disadvantages to lateral position |
| Modified lateral "Barts technique" | Patient in lithotomy with ipsilateral pelvis elevated 45°<br>Shoulders rotated to be perpendicular to the OR table<br>Ipsilateral leg is flexed and adducted, contralateral leg is fully abducted | May perform nephroscopy and ureteroscopy without patient repositioning<br>Fewer cardiovascular and respiratory effects than prone<br>Improved access to flank compared to supine | Requires significant patient mobility<br>Not suitable for patients with musculoskeletal deformities<br>Fluoroscopy is technically limited, as with lateral |

(Figure 12.10). The line of access can then be chosen. This can be the shortest distance, at right angles to the back, or can be slightly oblique in order to work more along the axis of the kidney, angling up into a lower pole calyx or angling down into an upper calyx. The site of actual puncture is made two finger breadths lateral to the edge of the paraspinal muscles. If necessary, the site that was initially chosen may be adjusted either cephalad or caudad if a rib is in the line of the needle tract. The needle is held in a Kelly clamp and then advanced with fluoroscopic monitoring. With the C-arm vertical or rotated 10–20° towards the X-ray machine, to lengthen the calyx, the needle is angled in a caudal or cranial direction to point directly at the calyx (Figure 12.10). Holding this angle steady, the C-arm is swung with the intensifier towards the foot of the table looking up towards the lower pole of the kidney. This gives more of a lateral rather than AP view of the needle. The AP direction of the needle is then adjusted to again point directly at the chosen calyx. The needle is then advanced along this line, checking both angles at regular intervals until the calyx is punctured. The stylette is removed and contrast should flow freely from the needle.

## Special situations

### Morbid obesity

PCNL in the morbidly obese patient with a BMI greater than 40 kg/m$^2$ poses a challenge for both the operating surgeon and the anesthesiologist. From a surgical perspective, there are several aspects that must be considered. First, achieving satisfactory X-ray penetration can be problematic with older fluoroscopic units, making targeting difficult. Second, anatomic landmarks are also obscured and can make tract placement difficult. This can be especially problematic for upper pole punctures.

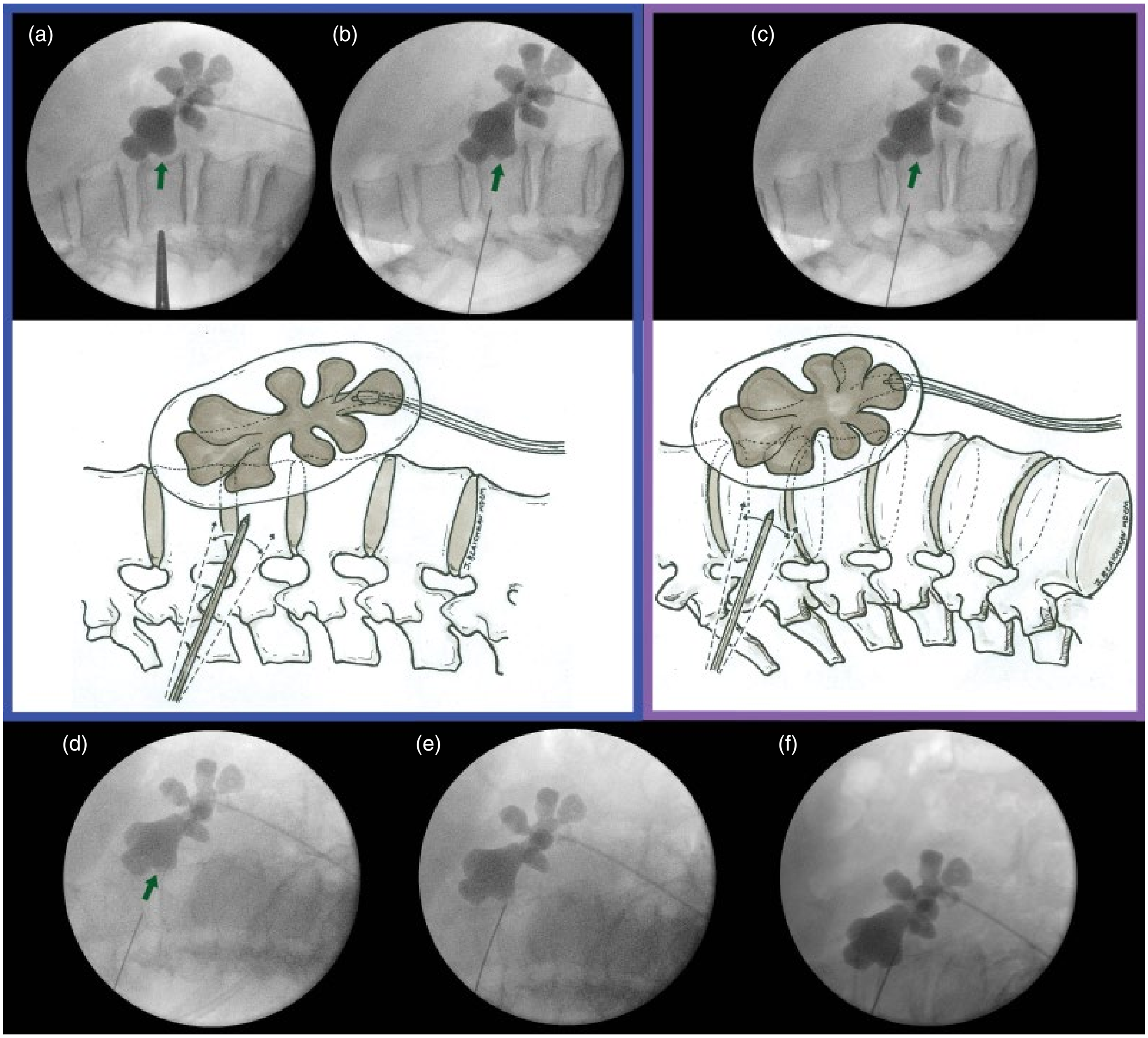


**Figure 12.7** Triangulation fluoroscopic technique in the lateral-flexed position for access into a posterior calyx. (a) The C-arm is initially positioned vertically, perpendicular to the floor. With the calyces distended with contrast, the posterior calyx previously chosen for puncture is identified and the calyx is directed towards the surgeon. A point on the skin, one to two finger breadths lateral to the paraspinal muscles and in line with the calyx in the cephalad–caudal plane, is chosen. In this fluoroscopic image, the targeted calyx is indicated with an arrow. (b) This site can be moved more cephalad or caudal if a rib is in the way, or to angle the tract superiorly into a lower pole calyx. In this case, the skin puncture site was moved more cephalad since the chosen point was over the rib. The needle is inserted and aimed directly at the chosen calyx under fluoroscopy with the C-arm vertical, as shown in (a) and (b). Movement of the hand in the cranial–caudal plane will move the needle in the left-right plane as shown in the illustration. (c) Once the needle has been inserted 2–3 cm, the C-arm is rotated obliquely towards the feet so the X-ray beam penetrates at a 45° angle to the initial view. This gives a side view of the needle, rather than an AP view from above. When the needle is viewed from the side (illustration), elevation (towards the ceiling) or lowering (towards the floor) of the hand holding the needle will adjust its tip in the AP plane, relative to the kidney. With the needle angle adjusted to aim directly at the calyx, the needle is advanced. (d) The C-arm is then rotated to the original vertical position to ensure the needle is still directed towards the calyx in this plane. (e) The needle is advanced in a stepwise fashion during expiration, checking the direction in the two planes until the calyx is entered. Here, seen in the oblique plane, the needle is about to enter the calyx. (f) Oblique view with the needle in the chosen calyx [96]. Reproduced with permission of John Wiley and Sons.

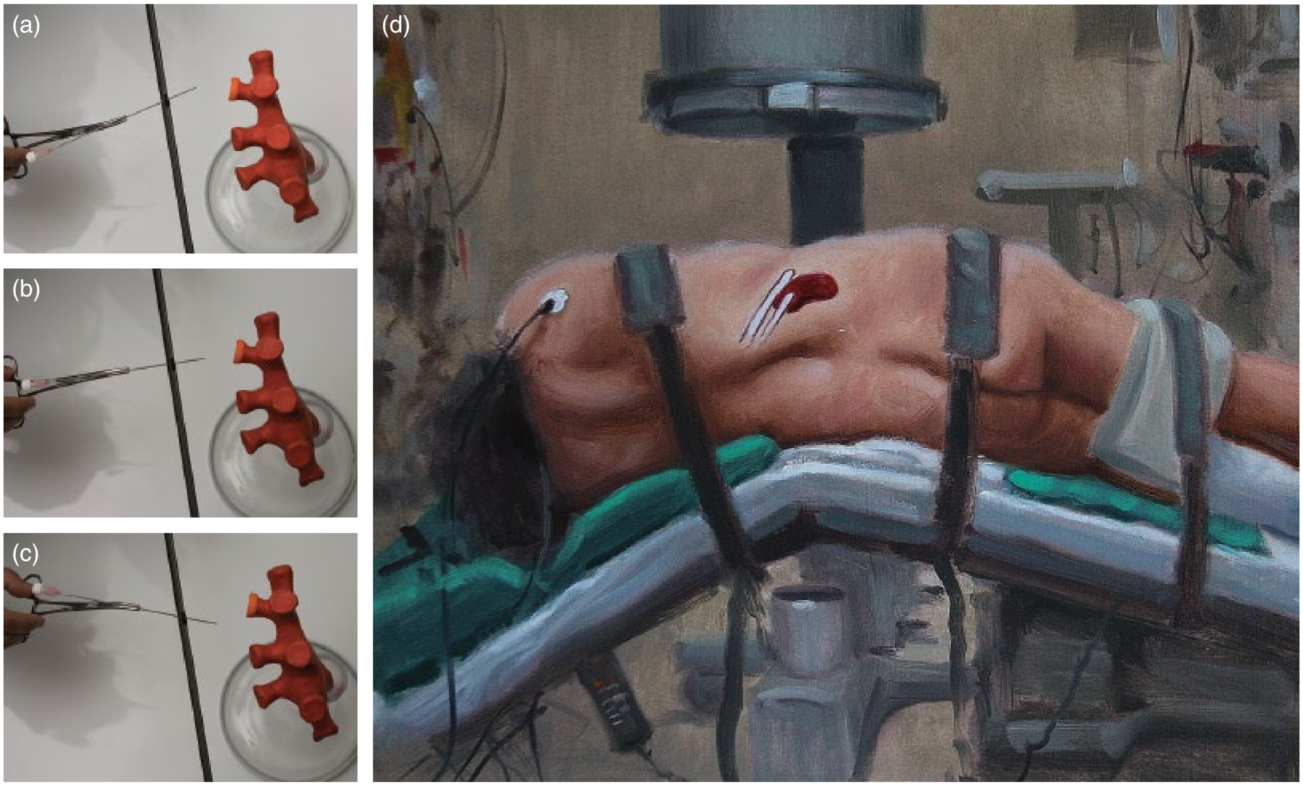


**Figure 12.8** AP views with the patient in the lateral-flexed position. In this demonstration, the target is an upper pole, posterior calyx, viewed from directly above. The chosen calyx is seen from the side, facing posteriorly. (a) Needle is aiming too cephalad to the target calyx. (b) Needle will have direct entry into the papilla of the desired calyx. (c) Needle is aiming too caudal to the target. (d) Illustration depicting the position of the C-arm necessary to obtain this view.

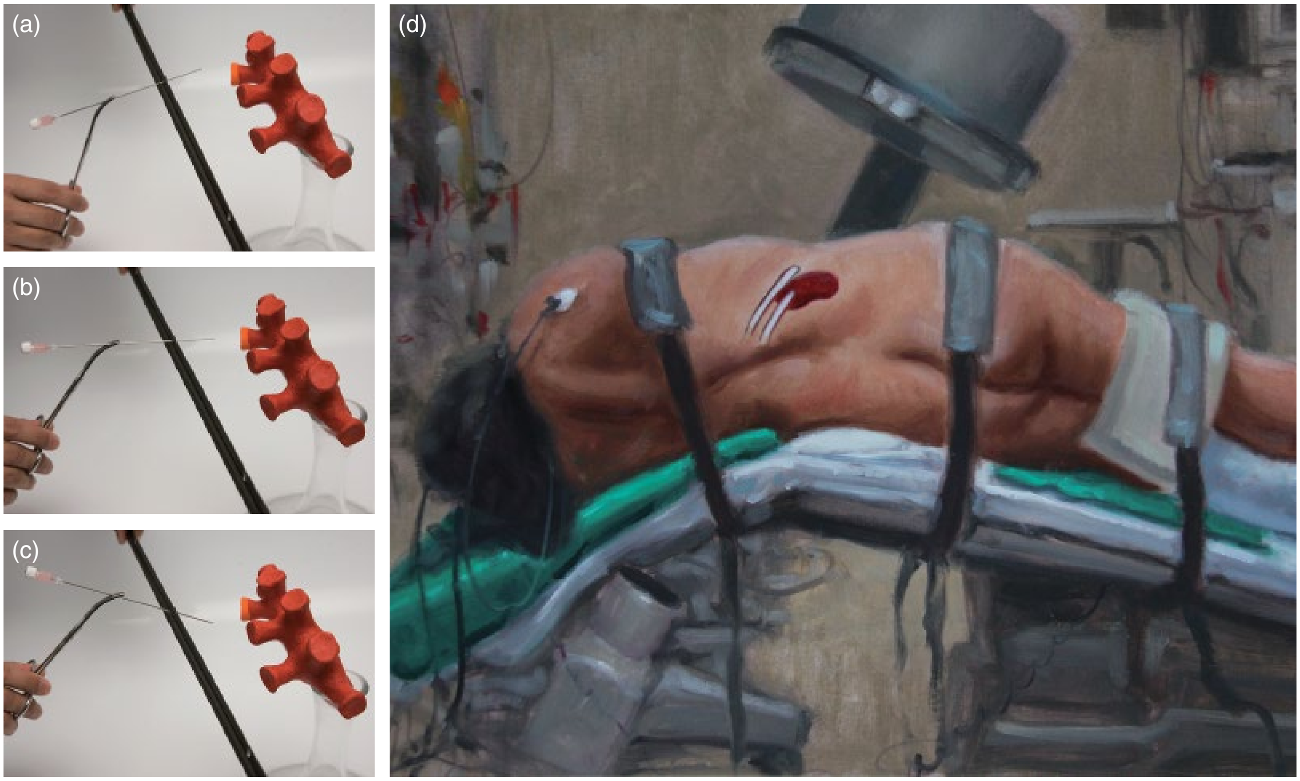


**Figure 12.9** Oblique views with the patient in the lateral-flexed position. With the C-arm offset approximately 30° towards the feet, the targeted posterior, upper pole calyx is identified. (a) Needle is aiming too far anterior to the target calyx. (b) Needle will have direct entry into the papilla of the desired calyx. (c) Needle is aiming too far posterior to the target. (d) Illustration depicting the position of the C-arm necessary to obtain this view.

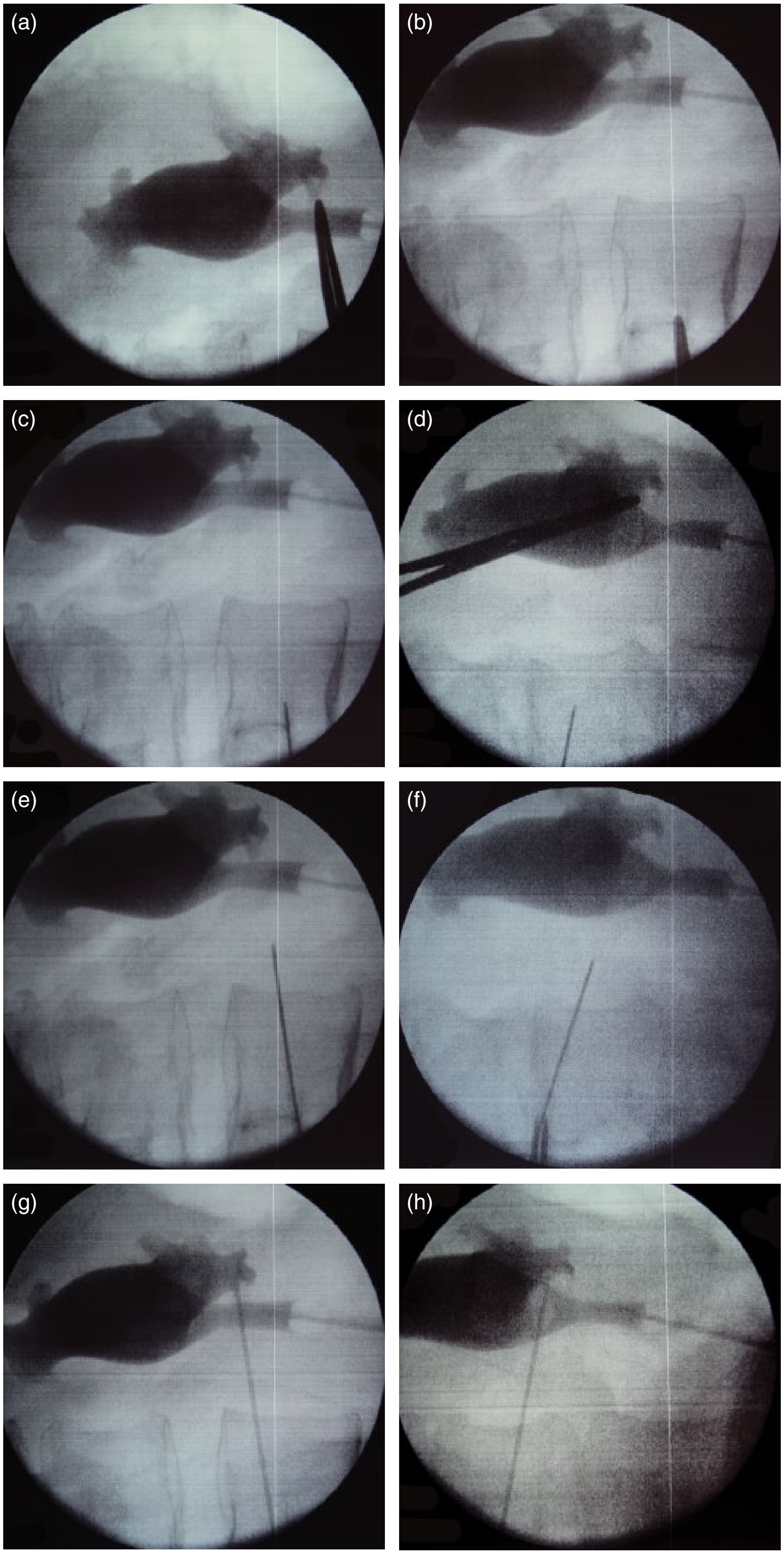


**Figure 12.10** Triangulation technique with an obese patient in the lateral-flexed position. (a) Forceps pointing to chosen posterior calyx viewed in AP direction. (b) Point of entry chosen with forceps marking point lateral to the paraspinal muscles in line with the targeted calyx. (c) AP view with the needle along the chosen path. (d) Oblique view with the needle pointing to the chosen calyx. (e) AP view with the needle approaching the calyx. (f) Oblique view with the needle on target, approaching the calyx. (g) AP view with the needle in the chosen calyx. (h) Oblique view with the needle in the chosen calyx.

Third, the depth of the tract is significantly increased and often requires extra-long instruments, including a sheath and rigid endoscopes. A subset analysis of the Clinical Research Office of the Endourology Society (CROES) PCNL Global study demonstrated that overall stone-free rates are decreased with obesity, with no difference in transfusion or overall complication rate [21]. Surprisingly, despite the increased complexity of these cases and the poor fluoroscopic image quality obtained when using the C-arm to search for small residual fragments, several authors have independently demonstrated that stone-free rates appear to be unaffected when PCNL outcomes are stratified by BMI [22–26].

In terms of patient positioning, the lateral-flexed position seems ideally suited for this clinical situation, with the benefits explained in detail above (Table 12.2). Other authors have similarly used lateral positioning to overcome these difficulties. Kerbl et al. described in detail the use of lateral positioning to successfully treat two patients with a BMI greater than 50 kg/m$^2$. In these patients, it was noted that the supine position could not be tolerated due to respiratory difficulties [2]. Gofrit et al. echoed these concerns and similarly adopted the lateral decubitus position in patients with a BMI greater than 40 kg/m$^2$ [3]. In contrast, conventional prone positioning may still be well tolerated even at extremes of BMI and has been used by several authors for the morbidly obese, including patients with a BMI well over 50 kg/m$^2$ [24, 25, 27, 28]. In a series of 21 patients with BMI >50 kg/m$^2$, reported by Keheila et al., PCNL was performed in prone position without respiratory compromise [28]. The authors recommend several special considerations for PCNL in the super obese including using extra-long instruments, custom long sheaths with suture “tails,” choosing the shortest tract possible, and leaving in place a nephroureterostomy tube rather than a nephrostomy tube. The prone position may still be well tolerated even at extremes of BMI and may be useful when the weight of the patient is greater than the tolerance of the OR table, requiring the use of two tables in close proximity. Wu et al. described a technique of awake endotracheal intubation and prone self-positioning in a patient with a BMI of 51 kg/m$^2$ [27]. In a large series, El-Assmy et al. favored supine positioning for morbidly obese patients, but conceded that prone positioning was necessary in some cases [23]. Finally, Curtis et al. described using a larger skin incision to expose the fascia prior to performing puncture using in the prone position in a patient with a BMI of 55.5 kg/m$^2$ [29]. Their technique was to use a larger skin incision to expose the fascia prior to performing puncture. This technique has the potential of avoiding the need for an extra-long working sheath but can only be used with the patient in the prone or lateral decubitus positions.

## Kyphoscoliosis/musculoskeletal abnormalities

The treatment of patients with severe musculoskeletal abnormalities poses a particular challenge to the surgeon, and PCNL is no exception. In these patients, the loss of bony landmarks, distorted position of abdominal organs in relation to the target kidney, and difficulties with imaging secondary to X-ray penetration and interference from orthopedic hardware make PCNL difficult. To date, there is limited published data describing PCNL in the patient with severe kyphoscoliosis. Gofrit et al. described a single case of severe kyphosis preventing prone positioning. In this case, the lateral decubitus position provided good access to the flank. However, an upper pole nephrostomy had been placed in the radiology suite in advance of the procedure and was used to access the renal pelvic and lower pole calculi [3]. In the largest series of PCNL in patients with spinal deformities, Izol et al. described 16 patients who underwent PCNL with access gained by the treating urologist in the prone position including patients with kyphoscoliosis (five), post-polio syndrome (four), osteogenesis imperfecta (three), myotonic dystrophy (three), and ankylosing spondylitis (one) [30]. A high success rate (93.7%) and complication rate (31.2%) was reported, including transfusion (two), prolonged urine leak (one), infection (one), and nephrectomy (one). Matlaga et al. described a technique for computed tomography (CT)-guided access and included six patients with scoliosis in their dataset [31]. Anecdotally, we have used both prone and lateral positions for this population. No position is universally appropriate and adaptability is of paramount importance. Preoperative CT images must be examined carefully to identify when the fluoroscopic window, which is frequently limited, and access may require assistance of an interventional radiologist or a urologist trained in ultrasound-guided PCNL. Additionally, such patients will require additional padding as they can be prone to both pressure ulcers and nerve injuries.

## Renal anomalies

Renal anomalies create an increased level of complexity in the management of patients with stone disease. The CROES PCNL Global study had 202 patients with renal malformation including ectopic (26), horseshoe (102), and malrotation (74) [32]. Although treatment failure rates were higher in patients with renal anomalies (5% compared to 1.7% with normal renal anatomy), stone-free and complication rates were otherwise equal. In these patients, the prone position and upper pole punctures are preferred.

Urolithiasis in horseshoe kidneys is common, occurring with a reported incidence of 20–60% [33]. The accompanying rotational anomaly results in calyces that are oriented more posteriorly and a renal pelvis that is more anterior than in "normal" kidneys [34]. The lower pole is also oriented more medially and is fixed in the midline by the isthmus that connects it to the contralateral kidney. As a result, upper pole access is preferred as this provides the least angulation looking down the axis of the kidney, and minimizes torque when manipulating stones located in the renal pelvis and lower pole calyces. In the subset analysis of the CROES PCNL Global study, 87% of patients with a horseshoe kidney were treated in the prone position with 13% in supine [32]. When puncture is performed through the lower pole calyces, the tract is significantly longer and at a right angle to the renal axis. Consequently, with this access, viewing the upper pole may be difficult or even impossible with a rigid endoscope. Finally, the puncture site through the skin is often located more medially, when accessing the mid or lower calyces, and this can result in injuries to the segmental arteries. Together, all these factors favor PCNL for horseshoe kidneys in either the prone or lateral positions [35].

## Surgical tables for select positions

There are numerous surgical tables available for both general urology and endourologic procedures, and, as such, a review of each is beyond the scope of this chapter. However, the ideal table will be adaptable to the needs of both the patient and surgeon. For PCNL, an OR table should have a radiolucent, carbon-fiber top with narrow side rails for straps or arm rests. To allow the maximum number of positioning options, the table should also have the ability to flex and raise the legs, and have attachments for leg stirrups for the lithotomy and split-leg positions. It should also be possible to slide the table top towards the head or feet. From a technical perspective, the table should also be offset with a narrow base, allowing wide movement of the C-arm and a large imaging window. Finally, it should be possible to accommodate patients up to 270 kg.

The carbon-fiber table developed by Skytron incorporates many of these features. This table has been modified to confer multiple advantages to the endourologist performing renal access for PCNL [36]. Included among these are a large, unobstructed imaging window that can be used with a C-arm rotated in even the most extreme positions, as well as the ability to position the patient in lithotomy, allowing access to the perineum. One disadvantage of this table is the inability to flex the patient for the prone-flexed position.

## Anatomic considerations: renal axis and mobility

Knowledge of renal and retroperitoneal anatomy is essential to performing PCNL with minimal patient morbidity and a low risk of iatrogenic organ injury. The kidneys lie in the retroperitoneum with the psoas muscle lying posteromedially, which results in the long axis of the kidneys being deviated so that the upper pole is more medial in the coronal lane. The upper pole is also closer to the posterior abdominal wall and more densely attached to Gerota's fascia [37]. The lower pole is more anterior and freely mobile. These findings can easily be appreciated during open and laparoscopic renal surgery.

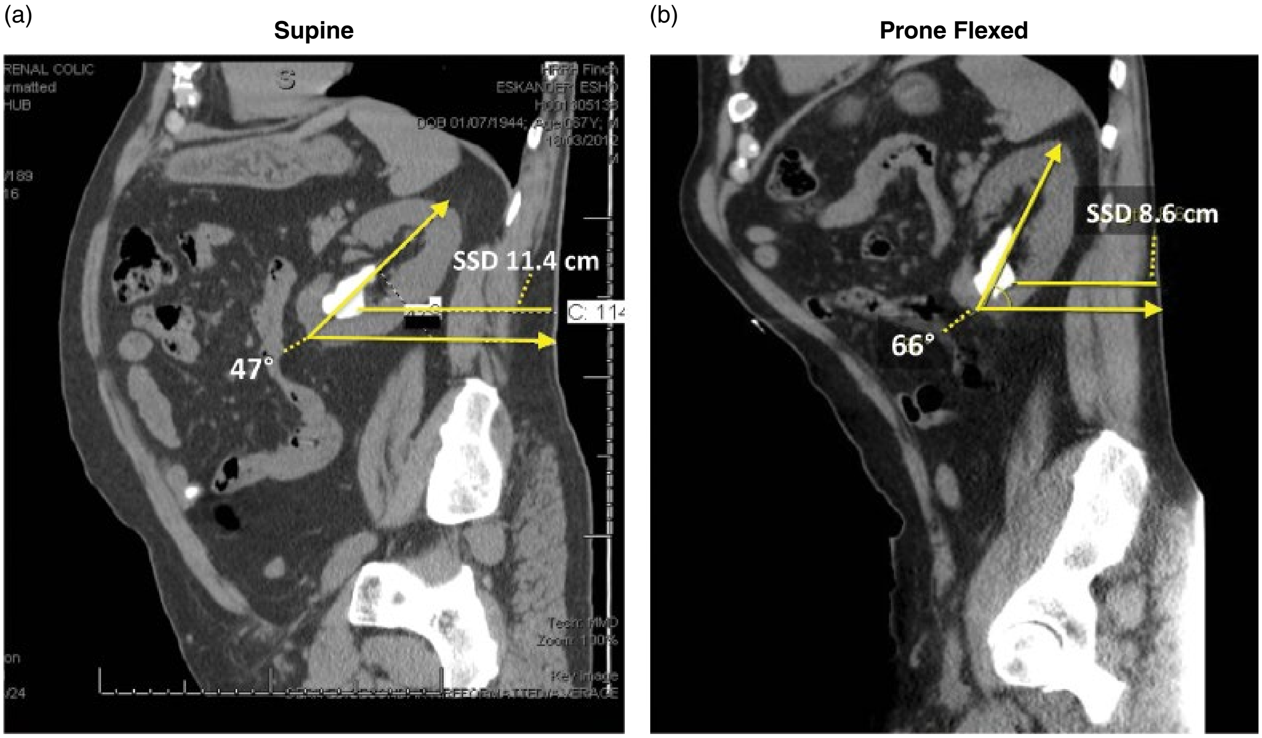
There are several implications to these findings. First, puncture of the lower pole may be slightly more difficult as the freely mobile lower pole tends to move away from the needle and dilators. Second, lower pole tracts tend to be longer and at a right angle to the axis of the kidney, making stone removal from upper calyces with rigid instruments more difficult. Compared to supine, the prone-flexed position shortens the distance from the skin to the upper and lower pole calyces and the renal angle is flattened, improving access to the upper pole through a lower pole puncture (Figure 12.11). Percutaneous access into the upper pole is simplified by the more dense attachments of Gerota's fascia, reducing mobility, and the shorter distance from the skin compared to into the lower pole.

## Complications of PCNL

Preventing and reducing complications of PCNL requires proper technique, adaptation, and attention to detail (see also Chapters 33–35). In our latest series of 318 consecutive PCNLs, our overall complication rate was 11.6% with no transfusions or angioembolizations [15]. This rate is lower than studies from a similar period published by de la Rosette et al. (37.2%) and Tefekeli et al. (29.2%) [38, 39].

### Intra-abodominal organ injury: colon, spleen, liver, and gallbladder

Several anatomic studies have attempted to define the relationship of organs to the target kidney and nephrostomy tract. However, the position of the kidneys within the retroperitoneum is dynamic, changing with both respiration and body position. We, and others, have demonstrated that when the patient is positioned in the prone or prone-flexed positions, the spleen and liver rotate laterally, away from the kidneys and nephrostomy tract, compared to when the patient is positioned supine [40, 41]. This would make it less likely that either of these organs would be injured with



- **Prone-flexed changes the renal angle, bringing lower pole closer to the skin (skin to stone distance SSD)**
- **Improves access to the lower pole**
- **Shortens the distance from the skin to the upper pole calyx**

**Figure 12.11** Sagittal CT reconstruction of the right kidney demonstrating puncture of upper and lower pole posterior calyces. Upper pole punctures are shorter and more in line with the ureteropelvic junction and renal pelvis, whereas lower pole punctures are longer and have more acute angles, leading to more torque and renal shear. (a) Supine and (b) prone-flexed positioning: this demonstrates how prone-flexed shortens the distance from the skin to the upper and lower pole calyces and flattens the renal angle, improving access to the upper pole through a lower pole puncture.

a puncture 30° from the vertical [12]. A study using images from reconstructed magnetic resonance imaging (MRI) scans reaffirmed the preference for more medial puncture to avoid iatrogenic injury to the spleen and liver [42].

Several studies have utilized both CT and MRI to study these changes and estimate the relative risk of iatrogenic organ injury during renal puncture. The colon is most at risk from lower pole access [43–45]. One group found the incidence of retrorenal colon was 4.7% in the prone position and 1.9% in the supine position [44]. However, in a study of reformatted CT scans, Tuttle et al. demonstrated that axial CT scans may dramatically overestimate the risk of colon injury associated with lower pole puncture [43]. On axial CT reconstructions, compared to oblique and parasagittal CT, there was a 15.1 and 3% risk of colon injury in the prone position, respectively, with no risk to liver, spleen, or lung. These findings are more in keeping with clinical series demonstrating low rates of organ injury. In a large clinical series, of almost 1600 prone PCNLs, the rate of bowel injury was 0.06%, with no cases of splenic or liver injury [46]. Similarly, in another series of 5039 prone PCNLs, the colon injury rate was 0.3% [45]. Multivariate analysis determined that older age and presence of horseshoe kidney were independent risk factors for colon injury.

Organs at risk from upper pole puncture include the liver, spleen, and pleural space [42, 47, 48]. Risk of organ injury varies considerably amongst published reports. In one study, the predicted risk of injury to the liver or spleen with upper pole puncture between the 11th and 12th rib was approximately 15% in the supine position, but decreased to zero by changing body position from supine to prone [47]. However, prone access between the 10th and 11th rib increased the risk of liver or spleen injury to 14% on the right and 94% on the left. Fortunately, these complications are exceedingly rare. A systematic review of PCNLs reports published between 1985 and 2013, included only 11 splenic, one liver, and eight gallbladder injuries [49]. This study emphasises that early identification and management are crucial to prevent patient morbidity and mortality.

Falahatkar et al. state that the colon “floats away from the kidney when the patient was in the supine position” [19]. Our CT studies did demonstrate that the colon was more medially situated and theoretically more prone to injury in the prone and prone-flexed positions compared with the supine position; however, the overall effect was minimal. Anatomically the colon is attached laterally to the peritoneum of the side wall of the abdominal cavity at the level of the kidneys and movement is restricted. The more lateral approach of the supine position would therefore still be more likely to result in the rare complication of colonic injury, which has been reported in this position [38].

### Thoracic complications

The risk of pleural injury is of considerably greater concern where significant complications include pneumothorax, hydro/hemothorax, damage to lung, and empyema. The diaphragm inserts onto the 12th and 11th ribs with the pleural reflection running horizontally and crossing the midpoint of the 12th rib in the majority of patients. The risk of pleural injury is therefore related to the position of the kidney in the retroperitoneum, the level of the pleural reflection, and the calyx chosen for access, and the phase of respiration. The majority of pleural complications occur with upper pole access. Hopper and Yakes showed that the predicted risk of injury to the lung from an upper pole puncture dramatically decreases from inspiration to expiration (86 to 29%, respectively) [47]. The same study did not show a difference in risk to pleura; however, the findings emphasize the importance of inserting the trocar needle in the upper pole with expiration. Significant complications include pneumothorax, hydrothorax, hemothorax, and empyema. In a study by Munver et al., the incidence of thoracic complications was 23.1% above the 11th rib, but dropped to just 1.4% above the 12th rib. The overall complication rates ranged from 4.5% for subcostal access to 9.7% above the 12th rib, and 34.6% above the 11th rib [50]. We have previously demonstrated that prone-flexed positioning results in inferior displacement of the kidneys inferiorly within the retroperitoneum, an effect which could result in fewer thoracic complications [12]. In an update of our previous report including data from the last 318 consecutive patients in our unit to be treated in the prone-flexed position, of which 16 (5.4%) of the tracts were above the 11th rib, 120 (40.8%) were above the 12th rib, and 158 (53.7%) were infracostal, there were only four pleural complications requiring chest drain insertion, representing 2.6% of the supracostal cohort [15].

### Hemorrhage and transfusion rates

Bleeding during PCNL, as well as delayed postoperative bleeding, is another complication that deserves attention. To prevent bleeding, the most important aspect is the end-on puncture of a posterior calyx. Using 3D polyester resin endocasts, Sampaio et al. demonstrated that the risk of arterial injury was highest from infundibular puncture and that the calyceal fornix provided the safest route of access [51]. Normally, the upper pole of the kidney is more medially and posteriorly located than the lower pole. Consequently, an upper pole posterior calyceal puncture lateral to the paraspinal muscles will result in access being more in line with the axis of the kidney. This is more likely to result in puncture along the avascular line of Brödel and less torquing of the kidney to reach the lower calyces and, consequently, less chance of the parenchyma splitting and bleeding. An angled tract that is not in line with the infundibulum or renal axis, or a puncture of the lateral calyces, will require more torque to reach the stone, which may result in unnecessary bleeding and increased transfusion rates. Choice of the appropriate percutaneous tract through a posterior calyx in line with the infundibulum will allow the operator to achieve a transfusion rate for PCNL of approximately 1% [46]. In an update of our previous report reviewing data from 318 consecutive PCNLs at our center, including patients with staghorn calculi and multiple tracts, no patient required blood transfusion or angioembolization [15].

### Neurologic complications: cerebrovascular accident, spinal cord ischemia, and nerve injury

Cerebrovascular accident, coma, and paralysis during PCNL are rare with a combined incidence below 0.1% [52]. The majority of these cases have been contributed to paradoxical air embolism from the use of air to perform retrograde pyelogram [53, 54]. However, inadequate spinal cord perfusion is also suspected to be due to stretch in the prone position, having the face turned or face down, and hypotension [52]. As such, use of air for retrograde pyelograms should be minimized and perioperative care taken to avoid these potentially devastating complications.

Injury to spinal nerve roots as they exit the spinal column as a result of percutaneous access in the prone position is rare but there are published case reports of two patients with renal anomalies [55, 56]. These complications can have permanent and catastrophic consequences but, in patients with normal renal anatomy, can usually be prevented by using a puncture site lateral to the paraspinal muscles and avoiding medial angulation towards the spine.

## Complications specific to patient positioning

### Anesthetic considerations

Anesthetic concerns garner much attention in prone percutaneous surgery and have been the driver of much of the renewed interest in supine PCNL. Another concern has been the maintenance of prone anesthesia in obese patients or those with cardiovascular or respiratory compromise. Although we have found that the prone-flexed modification may further increase airway pressures in obese patients, necessitating a reduction in patient flexion, we have not found it necessary to revert to conventional prone positioning [57]. As with other authors, in the morbidly obese patient we favor lateral or lateral-flexed positioning as this avoids abdominal compression and allows the anesthesiologist free access to the patient's airway [2, 3]. Others have reported using the lateral decubitus position in high-risk patients under regional anesthesia [58], as well as awake endotracheal intubation with prone self-positioning [59] as ways to overcome these difficulties. In two large reviews of complications during prone PCNL, no complications were attributed to the physiologic changes associated with prone positioning [46, 48, 60].

The greatest risk of airway loss is when the patient is positioned prone. For this reason, secured endotracheal anesthesia is preferred [61]. However, even with a cuffed endotracheal tube problems may occur. Obstruction of the tube may occur due to kinking or secretions draining under gravity in this position [62]. Fortunately, such concerns remain largely theoretical and complications are limited to case reports.

In rare circumstances, insertion of central venous monitoring or cardiac compression and defibrillation is necessary in the prone patient. When possible, it is advisable to return the patient to the supine position and to have a stretcher standing outside the OR for this purpose. However, when there is need for a prolonged delay in repositioning due to instrumentation protruding from the flank, successful insertion of central venous line and cardiac resuscitative efforts with the patient positioned prone have been reported [63–65].

### Cardiovascular changes

The greatest body of research related to the effects of prone and prone-flexed patient positioning comes from spinal surgeries, where the impact of patient position on both physiology and surgical outcome has long been recognized. Hemodynamic changes related to patient positioning remain controversial and likely depend on the underlying cardiovascular status of the patient, the precise body position, and the use of saddles/bolsters. It is generally agreed that prone positioning causes a decrease in cardiac index. However, this is not felt to be clinically significant as mean arterial pressure in the prone and prone-flexed positions is maintained due to an increase in systemic vascular resistance [61, 66, 67]. In a study of 19 patients, Hatada et al. concluded that the drop in cardiac index presented no significant challenge to the maintenance of anesthesia [68]. Other groups have also reported this finding [66, 67]. In the prone and prone-flexed positions, mean arterial pressure appears to be maintained due to an increase in systemic vascular resistance [66].

Prone positioning may also lead to transient inferior vena cava obstruction. In spinal surgery, this has led to speculation that impeded venous drainage may contribute to increased bleeding during surgery [69]. Whether this may also play a role in blood loss during renal surgery remains unknown but our data would suggest that this is not a concern. It has been shown that relieving abdominal compression by placing a bolster under the patient's chest and padding of the anterior superior iliac crests can dramatically decrease the effect [70].

### Respiratory changes

As with cardiovascular changes, changes in pulmonary physiology vary considerably with patient position, body habitus, and the amount and type of padding/support used. Although tidal volumes and inspiratory flow rates are preserved in the ventilated patient, functional residual capacity consistently increases with a change from supine to prone position [61]. One study found that prone positioning did not significantly affect compliance and that respiratory resistance increased only slightly in nonobese patients [71]. As both functional residual capacity and $P_aO_2$ markedly increased from the supine to the prone position, the authors concluded that, during general anesthesia, prone positioning did not have a negative effect on respiratory mechanics, instead improving both lung volumes and oxygenation [71, 72]. Interestingly, these improvements were maintained in a similar study in anesthetized and paralyzed obese patients in the prone position [71]. Siev et al. also found that the peak inspiratory pressure does not increase significantly with prone positioning [73]. It has been hypothesized that improvements in gas exchange may be due to changes in pulmonary blood flow and redistribution of lung ventilation, resulting in better ventilation/perfusion matching [61]. Importantly, the requirement for free abdominal and chest-wall movement cannot be overemphasized in the surgical patient.

### Ophthalmic complications

Eye injuries resulting from surgery are extremely rare, with an incidence of approximately 0.1% following nonocular surgery [74]. Corneal abrasions account for the majority of these injuries, but rarely result in vision loss. In the prone position there is also a theoretical risk of blindness, due to increased intraocular pressure which can result in blindness due ischemic optic neuropathy or central retinal artery occlusion [60, 75]. Fortunately, this complication is rare and has mainly been reported during spinal surgery, especially with prolonged OR times in excess of 6 hours in the prone position [76, 77]. We are unaware of any cases following PCNL. For patients with one eye at increased risk of elevated pressure, rotating the head at 45° decreases the intraocular pressure measured after the procedure in the upper eye, compared to the more dependent eye [75].

### Peripheral nerve injury

Positioning-related peripheral nerve injuries occur secondary to stretch, ischemia, or compression. The combined factors of time, mechanical pressure, and immobility place patients at risk for these complications. Recovery can be variable and is directly related to the severity of the injury.

Special care must be taken with patients in the prone position as they are susceptible to brachial plexus injuries [78]. Such injuries are most commonly due to nerve stretch from extreme shoulder abduction; however, external compression can also play an important role. Prolonged surgical procedure has also been suggested as a contributing factor. Typically, these injuries present as painless motor dysfunction. To prevent this complication, some authors recommend tucking the arms at the patient's side during the procedure. We find that abduction of the shoulder to approximately no more than 90°, with elbow flexion, relieves undue stress. Ideally, the arm should be well padded and rest below the level of the patient's chest. Additionally, for patients in the prone and prone-flexed positions, the head must be maintained in a neutral position, to preventing lateral flexion. Fortunately, the prognosis for these injuries is usually good. In one study, following a cohort of 22 patients with brachial plexus injury, including 14 following noncardiac surgery, complete recovery was achieved in 79% [79].

Nerve compression injuries may also occur in other operative positions. In the lateral position, the ulnar nerve is at risk from the edge of the OR table. The majority of these injuries can thus be prevented by adequate padding at the elbow and supination of the dependent arm [80]. In particular, flexion of the elbow of greater than 90° is a known risk factor and is due to shrinkage of the cubital tunnel, resulting in compression of the ulnar nerve [81].

Injury to the peroneal nerve has commonly been described in association with the dorsal lithotomy position. Many surgeons use Bierhoff leg holders when placing patients in this position. Long duration of the procedure has been implicated in this type of injury [82]. General guidelines for use of these supports include: (i) slow and simultaneous placement of the legs into their final position and (ii) limiting the amount of hip flexion, abduction, and lateral rotation [78]. In the lateral decubitus position, compression of the unpadded fibular head against the OR table during nephrectomy resulted in peroneal nerve injury in one patient [83]. Sciatic nerve compression between the OR table and the ischial tuberosity has also been known to occur in patients in the semilateral position as well as in the lithotomy position [78, 82].

Fortunately, the great majority of intraoperative nerve injuries are preventable. A high level of suspicion is important when recognizing these injuries as patient complaints in the early postoperative period may be easily dismissed. Careful attention to patient positioning, the use of adequate padding, and awareness of patient comorbidities such as skeletal deformity are all essential components. When peripheral nerve injuries do occur, prompt referral to a neurologist who specializes in these types of injury is required.

## Prone versus supine PCNL

### Studies comparing supine and prone PCNL

Several randomized studies have compared prone versus supine positioning for PCNL [18, 19, 84–87]. DeSio et al. randomized 75 patients with stones treatable with single percutaneous access, stone(s) >2.5 cm, and BMI <30 kg/m$^2$ to prone or modified supine PCNL [18]. Falahatker et al. randomized 80 patients with stones treatable with single percutaneous access and stone(s) >2 cm to prone or complete supine PCNL [19]. More recently, Abdel-Mohsen et al. randomized 77 patients with BMI <40 kg/m$^2$ to prone or free-flank modified supine PCNL [84]. In a similar study, Wang et al. randomized 122 patients with renal (>2 cm) or ureteric (>1.5 cm) stones to prone or modified supine PCNL [87]. Karami et al. randomized 150 patients to prone or complete supine, both with fluoroscopically guided access, or lateral PCNL with ultrasound-guided access [85]. Al-Dessoukey et al. randomized 203 patients with stones renal stone(s) >2.5 cm or upper ureteric stones >1 cm or smaller stones with previously failed shock-wave lithotripsy to prone or oblique supine lithotomy PCNL [86]. Unfortunately, these studies have relatively small sample sizes and many have different results, therefore preventing definitive answers about the differences between prone and supine PCNL.

In addition, these studies compare different supine positioning techniques. Despite these differences, three studies have combined data on prone and supine PCNL and performed meta-analyses [59, 88, 89]. Liu et al. combined two randomized and two case controlled studies including a total of 389 patients [88]. Wu et al. combined four comparative studies and 27 case series, comparing 4837 prone and 1469 supine PCNLs [59]. Zhang et al. combined two RCTs and seven non-RCTs comparing 4956 prone and 1457 supine PCNLs [89]. Over a 2-year period, the registry-based prospective CROES collected nonrandomized data for the PCNL Global study and has produced many important findings. One subgroup analysis used this registry to compare PCNL in 4637 prone and 1138 supine procedures [90].

## Hemodynamic and ventilatory changes

Al-Dessoukey et al. showed that oblique supine lithotomy positioning PCNL compared to prone had less change in mean blood pressure (−2 vs. −14.06 mm, respectively), heart rate (−0.82 vs. +13.28 beats per minute, respectively), and peak airway pressure (+1.08 vs. +7.56 $cmH_2O$, respectively) [86]. However, the clinical relevance of these differences has not been studied.

## Access and failed PCNL

Due to the anatomic changes while supine, the number of potential access sites is decreased compared to prone PCNL. Yazici et al. found that the access field was shorter in supine compared to prone and prone-flex positions (80.8, 86.3, and 86.7 mm, respectively) [91]. As such, more limited field access in supine may result in more failed access. In the CROES PCNL Global study there were more failures in the supine PCNL group compared to the prone (2.4 vs. 1.5%, respectively) [90]. However, lower pole puncture in the supine position may offer greater accessibility to the upper pole calyces compared to prone [92].

## Stone-free rates

Stone-free rates are highly variable based on center and definition. An argument given by proponents of the supine technique has been that it is more ergonomic and facilitates stone clearance through spontaneous evacuation from the dependent nephrostomy tract. However, in the supine position stone fragments also collect in the dependent posterior calyces rather than the renal pelvis, as is the case when the patient is prone, allowing for easy removal.

Four RCTs and two meta-analyses failed to show a difference in stone-free rates between prone and supine positing [18, 19, 27, 84, 85, 88]. One RCT found that prone PCNL was associated with a greater stone-free rate compared to modified supine (89 vs. 73%, respectively) [87]. Similarly, the meta-analysis by Zhang et al. found that prone positioning was associated with a higher stone-free rate (odds ratio 1.36) [89].

The CROES PCNL Global study also found that prone PCNL was associated with a higher stone-free rate compared to supine (77% vs. 70%, respectively) [90]. However, the authors note the substantial difference between these rates and those previously reported in comparative studies. In a subset of 1311 patients in the CREOS registry with staghorn calculi, prone PCNL had a higher stone-free rate compared to supine (48.4 vs. 59.2%, respectively) which persisted after multivariate analysis adjusting for number of access sites and method of determining stone-free status [93].

## Intraabdominal organ injury

In an attempt to overcome some of the difficulties associated with prone positioning, there has been a resurgence of interest in PCNL performed with the patient supine. The first report on supine PCNL, by Valdivia Uria et al. in 1998, included 557 patients [10]. In this position, puncture is performed under fluoroscopic or ultrasound guidance either in or anterior to the posterior axillary line (see Chapter 10). This distinction is important as the resulting tract is significantly more lateral than the access used in prone or lateral PCNL. In their original report, Valdivia Uria et al. expressed a preference for puncture of anterior calyces, with low complication rates; however, transfusion rates were not reported. Other authors have similarly found that puncture of anterior calyces is often necessary in the supine position [15, 63]. As noted, rates of adjacent organ injury are rare when performing PCNL. As noted above, the colon floats away from the kidney with the patient in the supine position [19]. Our data from axial, triphasic CT scans performed with the patient prone, prone-flexed, and supine supported this statement. However, the overall effect was small and would likely be diminished by the more laterally placed tracts necessary with supine PCNL. Of 1720 supine procedures in the literature, reported in the literature to date, only one case of bowel injury has been reported (0.00058%) [94]. Anatomically the colon is attached laterally to the peritoneum of the sidewall of the abdominal cavity at the level of the kidneys and movement is restricted. The more lateral approach of the supine position would therefore still be more likely to result in the rare complication of colonic injury, which has been reported in this position [94].

In all of the randomized studies there was no difference in organ injury between prone and supine positioning [18, 19, 84–87]. In total there were two colon perforations in the prone position and two pleural effusions in the supine position [85, 86]. However, with 707 patients in total, given the rarity of these events, the power to detect a difference may be insufficient [18, 19, 84–87]. The CROES PCNL Global study found similar organ perforation rates in the supine (3.4%) and prone (3.3%) groups [90].

### Blood loss and transfusion rates

Bleeding following PCNL is another area that deserves attention. A review of all studies published to date demonstrated an overall transfusion rate of 4.6% (range 0–20%) with PCNL performed in the supine position [15, 16, 38, 63–72]. The higher transfusion rates may be partly due to renal shear, as puncture of an anterior or lateral calyx in the lower pole would result in more manipulation when using a rigid endoscope to access the full length of the collecting system. Additionally, end-on fluoroscopic views of the calyces in this position are obstructed by the patient's spine and side rails of the OR table, particularly in oblique views. As a result, the triangulation method of fluoroscopic puncture may be necessary or, more commonly, ultrasound-guided access. In the latter case, special expertise may be necessary to perform end-on calyceal puncture to avoid the intrarenal arterial injuries that can be the cause of profuse bleeding during PCNL [41].

Four studies have performed a direct comparison of prone and supine positioning during PCNL by the same surgeon [15, 16, 38, 63]. Due to small sample sizes, no significant difference in transfusion rate was noted by any group. There is mixed results regarding blood loss in supine versus prone PCNL. Randomized trials by De Sio et al. and Falahatker et al. did not find a difference in mean blood loss or transfusion rates [18, 19]. However, in another randomized trial Aldessoukey et al. found supine PCNL to have less mean hemoglobin loss compared to prone (−1.03 and −2.18 g/dl, respectively) [86]. The CROES PCNL Global study also found a higher blood transfusion rate in the prone position versus supine (6.1 vs. 4.3%) [90]. However, this study did not correct for differences in renal anomalies, number of percutaneous access sites, and American Society of Anesthesiologists (ASA) classification score, all of which could have contributed to the higher blood loss.

### Operative times

Despite repositioning, some studies suggest that prone PCNL may be associated with shorter operative times. Randomized studies by Abdel-Mohsen et al. and Wang et al. found that compared to supine the operative time for prone PCNL was 16 and 10 minutes shorter, respectively [84, 87]. The CROES PCNL Global study also found that prone PCNL is associated with a shorter operative time compared to supine in all patients (82.7 vs. 90.1 minutes, respectively) [90] and a subset of 1311 patients with staghorn calculi (103.2 vs. 123.1 minutes, respectively) [93]. However, the Liu et al. meta-analysis found prone PCNL to take longer than supine by 25 minutes [88].

### Obese patients

Despite concerns regarding hemodynamic stability and ventilation, prone PCNL may be the best option for most obese patients. A recent study found that although obese patients have higher peak inspiratory pressures in the supine and prone positions compared to non-obese, peak inspiratory pressures does not change from supine to prone positioning [73]. Furthermore, as supine positioning has an increased tract length compared to prone by as much as 2 cm, obesity further complicates the procedures in an already challenging subgroup of patients [91]. In a review, de la Rosette et al. examined the effect of patient positioning, concluding that for obese patients, or those with staghorn calculi, the prone position was associated with similar bleeding rates, but decreased operative times, and slightly improved stone-free rates compared to the supine position [38]. However, a review by Mazzucchi et al. of 42 obese patients undergoing PCNL found that prone positioning was associated with higher transfusion rate, as well as longer operative times and hospital stay compared to supine [95].

## Conclusions

Appreciation of the calyceal anatomy and the ability to choose the appropriate posterior calyx for percutaneous access in the prone position will allow the operator to perform the procedure with minimal morbidity. Prone-flexed positioning is a simple modification that is well tolerated by the patient and offers significant surgical advantages. The lateral position is well suited to the morbidly obese patient, while the lateral-flexed position adds further advantages and is familiar to all urologists. Treating urologists must be familiar with the potential complications of PCNL and ways to prevent and manage them. Compared to supine, prone positioning has similar complication rates but may increase chances of successful access and stone-free status and is likely better suited for obese patients and treating staghorn calculi.

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# Part 3 Imaging for Access

## 13

## Percutaneous Nephrolithotomy Access Under Fluoroscopic Control

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The last years of the 1970s and the early 1980s will probably be remembered by urologists as a time of tremendous changes, in particular the whole concept of minimally invasive surgery and the development of percutaneous surgery, which have shown spectacular clinical results and reduced the morbidity of open surgery [1]. Percutaneous stone extraction was first described more than 40 years ago and has become an increasingly common intervention for patients with stone disease [2, 3], evolving into a safe and effective treatment for patients with large or otherwise complex stone disease. However, despite the increasing use of percutaneous renal surgery, Lee et al. reported that only a minority of urologists (27% of those who have trained in percutaneous access) actually gain their own access for percutaneous nephrolithotomy (PCNL) [4]. One of the more common reasons given by respondents for not doing so was inadequate skills in the techniques of access.

The placement of percutaneous access into the intrarenal collecting system is one of the most critical aspects of percutaneous renal surgery. Image guidance is a critical factor for the performance of percutaneous minimally invasive procedures, which are being used with ever increasing frequency. Procedures such as PCNL are not performed without image guidance. The puncture of the kidney, insertion of guidewires, establishment of the percutaneous tract, and the disintegration and removal of stones are based on appropriate image guidance. For percutaneous renal surgery using fluoroscopy, access must be gained: different forms of access have been developed, all with the indispensable assistance of the image intensifier [5].

The first percutaneous nephrostomy to decompress an obstructed kidney was described by William Goodwin in 1955 [6]. However, removal of a renal calculus via a percutaneous tract established specifically for that purpose was not performed until 1976, when Fernstrom and Johansson used the technique successfully in three patients [7]. In their series, the tract was slowly dilated under fluoroscopic control over a 7-day period to a size sufficient for stone extraction. Similarly, Alken et al. in their experience with PCNL established access to the renal collecting system over the course of weeks, by repeatedly dilating it with hand-shaped polyethylene tubes of increasing size [8]. He subsequently developed metal telescope dilators to solve the problems met during the treatment of his first 21 patients, which accelerate the procedure and allow percutaneous stone removal to be performed in a single session with a delicate set of instruments. In 1982, Smith et al. described the rapid dilation of the nephrostomy tract in minutes with no untoward effects, which revolutionized the field of percutaneous stone surgery and contributed to the demise of open surgery [9]. Since that time the percutaneous approach has generated wide interest among the pioneers of endourology, and they developed and popularized most of the basic principles in this area in the late 1970s.

## Fluoroscopy

Imaging equipment in percutaneous renal surgery typically uses radiation for image formation and guidance during access and tract dilation.

Fluoroscopy is useful during the advancement of guidewires, tract dilation, stone removal, and nephrostomy placement, providing real-time depiction of the collecting system and the stones therein. Percutaneous renal surgery is performed with a combination of fluoroscopic

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and endoscopic visualization of the collecting system. Fluoroscopy is a two-dimensional method and provides limited information regarding the surrounding soft tissue. Nevertheless, it has proven to be an invaluable tool for the performance of percutaneous procedures of the kidney and collecting system.

## Radiation exposure

All parameters of fluoroscopy affecting image quality, reproducibility, and radiation output from each radiographic unit must be evaluated routinely to ensure optimal image quality while minimizing the radiation dose [10]. The endourologist can improve their imaging techniques and minimize both their and the patient's radiation exposure with no concurrent loss of image quality.

When attempting to obtain a diagnostic-quality image and the image is underpenetrated, and given the choice between increasing the total number of X-rays (mA) or the penetrability of the X-rays already present (kVp) to improve the image, the kVp should be increased initially as this will not increase the radiation output [11]. Collimating the image to the minimum size necessary for performing the work will reduce the amount of unnecessary radiation to which the patient and anyone else in the room is exposed. The radiation output from the X-ray tube should have been evaluated within the past year by a radiologic physicist, who determines whether the unit's radiation output is within legal limits as well as optimal for each examination.

There have been various reports evaluating the typical radiation exposure from fluoroscopy during PCNL, with an estimated effective dose between 7.63 and 8.66 mSv. Certain risk factors increase radiation exposure during PCNL. These include high body mass index, increased stone burden, and increased number of access tracts [12]. In a prospective study of PCNL and obesity, total operative time and radiation exposure increased as patients' body mass index increased, in part due to technical challenges. Obesity increased fluoroscopy time by 36% and mean effective dose by 177% [13].

Radiation "spreads out" in a three-dimensional (3D) space with a discrete or fixed number of photons spreading out into successively larger spaces. As a result, the area increases geometrically as a function of distance from the source. Increasing the distance from the source is one of the least expensive and most dramatic ways to reduce the dose of radiation to which operating personnel are exposed. By doubling the distance from the source, the radiation is reduced to one-quarter of its original intensity because the same number of photons is in a space that is four times larger. Similarly, by tripling the distance, radiation is reduced to one-ninth. Moving 1 m further away from an initial distance will reduce the dose by 89%.

The principle of radiation exposure to be as low as reasonably achievable (ALARA) should be followed during procedures that require fluoroscopy. A drape placed over or under the patient helps reduce scatter radiation [12]. Shielding, whether provided by lead aprons or thyroid shields, is a method of last resort. It provides excellent protection and should always be worn by those who work near the fluoroscopy table to limit the dose of radiation to which they are exposed. When fluoroscopy is performed, the radiation dosimeter badge is worn on the collar, outside the apron. As a result of this technique, the actual effective whole-body exposure is up to 99% lower than the dose measured by the badge [14].

Component positioning on the C-arm can significantly influence scattered radiation fields. The image intensifier should be as close to the patient as possible and the image should be collimated as much as possible over the area of interest. When the image intensifier is placed above the patient, and the tube is shielded by the table, both leakage and scatter radiation are minimized. Foot control must be entrusted to the operator and not to a third party, allowing better coordination, and audible alarms with a fluoroscopy locking system are very useful.

The introduction of digital radiography has contributed to the reduction of radiation exposure as well as to the improvement of image quality [15]. The combination of digital radiography with image storage systems and use of image processing systems resulted in the prevention of unnecessary image duplication and facilitated preoperative planning. A new generation of equipment has been designed with patient and operator dose reductions central to its development. Pulsed fluoroscopy and digital imaging have become available that reduce the dose of radiation delivered to the patient. Pulsed fluoroscopy should be set at the lowest possible frames per second that provide an image quality adequate for performing PCNL. Digital equipment eliminates the need for film; the information is electronically captured and manipulated on computer. As a result, the image can be enhanced, providing a sophisticated tool for dynamically evaluating patient organ function using editing techniques.

Radiation exposure can be a deleterious problem in percutaneous surgery, especially for the surgeon [16, 17]. There are two types of generalizable effects from radiation exposure: deterministic and stochastic effects. Deterministic effects are dose-related; therefore, if you have received a high-enough dose equivalent, certain types of effects will appear. For example, if dose exceeds 2 Gy, skin erythema will be observed. Stochastic effects are characterized by the absence of a threshold dose. Increased levels of exposure do not affect the type or severity of the effect, but do increase the probability of an effect. Risk of malignancy from radiation exposure is a stochastic effect. Common malignancies include leukemia, multiple myeloma, and thyroid, bladder, breast, lung, ovarian, and colon cancers. The National Council on Radiation Protection and Measurements has recommended an annual occupational limit of 50 mSv [18]. In medicine, there are no suggested limits for patient exposure. Instead, the risks from radiation must be balanced with the clinical necessity and benefit of the imaging study or procedure [12]. The use of ultrasonography can eliminate the side effects of radiation exposure during fluoroscopy-guided PCNL, and it can be used as a reliable method for localization of renal stones, especially nonopaque stones that are not visible with fluoroscopy. Also B-scan sonography can be used as a tool for localization of intrarenal arteries and avoidance of puncture by a Chiba needle.

### Ultrasound versus fluoroscopy-guided access

The advantages of ultrasound- over fluoroscopy-guided access into the collecting system include reduction of exposure to radiation for the urologist and operating room personnel (see also Chapter 16 in this volume). In pregnancy and in patients with transplanted, horseshoe, or ectopic kidneys, ultrasound represents the modality of choice [19, 20]. Another advantage is proper localization of the adjacent organs for prevention of injury. The main disadvantage of this modality is the difficulty and the need for greater care when the collecting system is only mildly dilated.

Ultrasound has been used by several groups for the guidance of PCNL, especially during the puncture of the collecting system [21].The performance of puncture with ultrasound guidance and without use of fluoroscopy has also been reported [22]. While ultrasound can be a useful complement to access the kidney, it should be emphasized that fluoroscopy is an indispensable component of safe percutaneous surgery.

## Preoperative images

Conventional computed tomography (CT) has been used for diagnosis of urologic diseases for many years. Recently, unenhanced helical CT has become a serious alternative to intravenous urography [23]. For preoperative planning, helical CT depicts the extent, orientation, and location of renal calculi, which are useful for access selection in percutaneous procedures. In addition, the anatomic relationships of the collecting system with surrounding organs are delineated, and the performance of a safe puncture is possible [24]. Nevertheless, the inability to provide real-time imaging capability has prevented wider application of CT in interventional procedures [25].

The 3D reconstruction of CT images for planning of percutaneous procedures has been reported to be feasible and accurate. With the use of 3D rendering software, the anatomic relationships of the collecting system are provided, and access selection is facilitated. The usefulness of 3D-reconstructed CT images, however, is not widely accepted [26]. 3D CT-rendered images that combine axial CT, CT urography, and angiography have been used for preoperative planning of urologic procedures, such as nephron-sparing surgery. Renal lesions and vessels can be accurately detected [27, 28]. Recent improvements in CT technology provide rapid and continuous reconstruction of CT raw data and provide real-time CT imaging (CT fluoroscopy) [29, 30].

Systems as Uro Dyna-CT (Siemens Healthcare Solutions, Erlangen, Germany) installed in the endourologic operating suite provides not only standard X-ray and fluoroscopy but also interventional 3D imaging and cross-sectional image reconstructions. It also offers a 3D planning and laser-guiding puncture tool called the syngo iGuide. It may be an additional instrument that allows the urologist to handle complex punctures [31].

Magnetic resonance imaging (MRI) provides better depiction of the soft tissue in comparison with fluoroscopy and CT, but remains unreliable for the identification of stones in the collecting system or ureter. MRI can be obtained without exposure to ionizing radiation. Thus, the technique may be considered as an alternative to ultrasound in selected cases such as the pregnant patient. Nevertheless, the strong magnetic field used interferes with ferromagnetic foreign bodies or electronic medical devices that are frequently carried by patients, although improvements in electronic medical devices have minimized this problem [32]. Newly introduced multisensor detector and faster image processing systems, as well as more advanced MRI scanners, have rendered real-time imaging a reality (MR fluoroscopy). The latter technique has been used in interventional cardiology [33]. Percutaneous nephrostomy placement has been performed with the use of open configuration MRI. MR urography represents an evolving imaging modality that allows optimal noninvasive evaluation of many abnormalities of the urinary tract. The application of several technical modifications provides adequate information for preoperative planning and postoperative assessment [34].

Each of these new technologies offers several potential advantages over the traditional percutaneous approach under fluoroscopic control. It should, however, be stated that all of these technologies are in a nascent stage of development. For that reason it is necessary to reinforce the basic concepts governing the realization of a conventional procedural approach to the kidney under fluoroscopic control. While this conventional approach is appealing, only a small percentage of urologists are

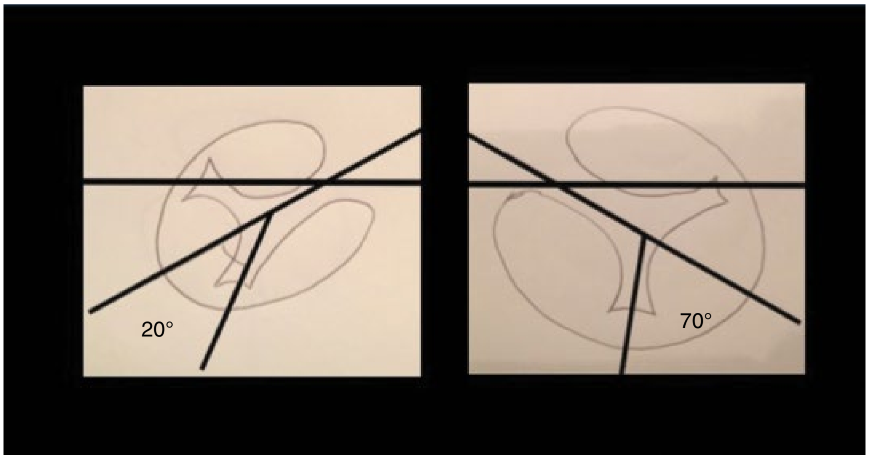

**Figure 13.1** Schematic view of both kidneys. Right kidney: posterior calyces positioned 20° posteriorly to the its own frontal plane. Left kidney: posterior calyces positioned 70° posterior to its frontal plane.

familiar with it [4], and various training models are essential for consolidating the use of this surgery [35, 36].

## Percutaneous renal access under fluoroscopic control

The information provided by preoperative helical CT is very valuable at the time of puncture under fluoroscopic control [37], as it identifies the most suitable place to set the path of the needle from the skin to inside the calyx that has been chosen for tapping. A CT scan can assess the presence of adjacent organs brought into the path of the needle. In this case, there is the option to change that path at the time of puncture under fluoroscopic control or to decide that percutaneous access is contraindicated.

When deciding where to make the puncture, areas of parenchyma should be considered that are thick enough to maintain a stable needle path and prevent subsequent development of a fistula. Also, it is desirable to identify those calyces for which surrounding thickness of parenchyma will promote their spontaneous closure of the puncture. Areas of kidney with an extremely thin parenchyma should be avoided.

Also, the information provided by helical CT will allow paths to be planned that avoid simple cysts, which sometimes are present in the renal parenchyma and are frequently not picked up on fluoroscopy.

The collecting system is opacified with direct injection through the ureteral catheter of contrast. A posterolateral transparenchymal puncture minimizes the chance of injury to the major renal vessels. The chosen posterior calyx is visualized with the C-arm fluoroscopy unit in the posteroanterior direction initially. The posterior calyces are positioned 20° posteriorly to the frontal plane of the kidney in most right kidneys, and 70° posterior to the frontal plane of the kidney in most left kidneys. In a normally rotated kidney, the frontal plane of the kidney is 30° posterior to the coronal plane of the body (Figure 13.1). In general, all patients undergoing any percutaneous renal procedure are given a general anesthetic.

### PCNL in prone position

The patient is placed in a lithotomy position for cystoscopy, with insertion of a 6 Fr open-end ureteral catheter under fluoroscopy guidance. A retrograde urogram then delineates the ureteral anatomy, as well as the exact stone location, degree of hydronephrosis, and the image of the selected calyx in order to plan the approach to the collecting system if this is deemed necessary [38].

The rigid cystoscope is used to place a 0.038 inch Teflon-coated guidewire into the upper collecting system. When a tortuous area blocks the progress of the guidewire, a wire with a hydrophilic coating must be used. This wire is composed of an alloy core, a polyurethane jacket, and a thin hydrophilic polymer as the outermost layer. When in contact with fluid, the polymer binds water to create a lubricious coating with greatly diminished friction, avoiding excessive edema and creation of a false passage. When the guidewire is in position, the 6 Fr catheter is advanced over it to the renal pelvis, and the endoscope is removed.

A 16 Fr Foley catheter is inserted and attached to a drainage bag at the same time. Both catheters are tied with 2-0 silk to secure them in place. It is helpful to connect an empty syringe to the Luer Lock adapter at the end of the ureteral catheter to prevent urine leakage.

The patient is positioned prone to allow posterior access. The patient is moved slowly and gently to allow the body to adjust to the position change. A foam rubber pillow is placed under the head to prevent it from being angulated excessively in relation to the trunk. The endotracheal tube is placed in the side slot of the foam pillow, making sure that the tube is unobstructed and free from kinks. To reduce resistance to breathing, the chest and abdomen are elevated on two foam rubber rolls that extend from the shoulder to the hip. Knee donuts padded with sheepskin inside the ring are positioned between the knees and the operating table to protect the bony prominences. A foam rubber roll is placed anterior to the ankles. The arms are flexed and secured on padded arm boards, and the elbows are protected with sheepskin pads. At this time, the 2-0 silk tie securing the two catheters together is cut and discarded. The intravenous extension tubing is connected to a 60 ml syringe containing 25% diatrizoate (Hypaque) solution, and the tubing is primed. The nurse removes the empty syringe from the ureteral catheter and attaches the syringe and tubing to the Luer Lock adapter of the ureteral catheter.

The percutaneous access is created via an upper, middle, or lower calyx. Thorough evaluation of the renal collecting system anatomy is essential prior to definitive percutaneous puncture for access tract creation.

Percutaneous access to the upper urinary tract through a calyx must meet five conditions that guarantee safe access and avoid complications:

1) performed from a posterolateral position
2) performed through the renal parenchyma
3) toward the center of the calyx posterolaterally
4) toward the center of the renal pelvis
5) as a result of these four conditions, the trajectory does not damage any major blood vessels.

There are two primary methods used to gain fluoroscopy-guided percutaneous renal access: the bullseye technique and triangulation [39, 40]. Both techniques need a target, most commonly generated by opacification of the collecting system with iodinated contrast that is administered retrograde via a ureteral catheter. A calyceal entry point is selected to avoid the larger vascular structures that are found at the level of the infundibulum.

As with most percutaneous access techniques, the bullseye technique requires fluoroscopy to monitor and guide the procedure. To this end a ureteral catheter is placed and the patient is positioned as described above. With the C-arm in the 30° position, an 18G diamond tip access needle is positioned, so that the targeted calyx, needle tip, and needle hub are in line with the image intensifier, giving a bullseye effect on the monitor. In effect the surgeon is looking down the needle into the targeted calyx. The needle is advanced in 1–2 cm increments using a hemostat to minimize radiation exposure to the surgeon. Continuous fluoroscopic monitoring is performed to ensure that the needle maintains its proper trajectory. Needle depth is ascertained by rotating the C-arm to a vertical orientation. If the needle is aligned with the calyx in this view, the urologist should be able to aspirate urine from the collecting system, confirming proper positioning.

The triangulation technique is based on simple geometric principles and is guided by biplanar fluoroscopy; one plane is anteroposterior to the line of puncture and the other is oblique. The anteroposterior view may be considered to be in a plane parallel to the axis of puncture and is used to monitor mediolateral (left–right) adjustments. The oblique view gives information regarding depth to the site of puncture and is used to monitor needle adjustments in the cephalad–caudad (up–down) orientation.

The tip of the needle is oriented towards the calyx to be punctured in both the anteroposterior and oblique planes. Left–right adjustments are limited to the anteroposterior view only, and cephalad–caudad adjustments are limited to the oblique view. When making adjustments in the mediolateral axis, care should be taken not to inadvertently move the needle in the cephalad–caudad axis, and vice versa. In most cases, it is helpful for the surgeon to rest their arm on the patient during the access part of the procedure, as this minimizes unintended drifting of the needle away from the targeted axis and also provides additional needle stabilization.

To decrease the radiation exposure to the surgeon's hands, the C-arm should be oriented with the image intensifier angled toward the head of the patient. Whenever possible, the iris of the fluoroscope should be kept as small as possible, to further minimize stray radiation exposure. Once the needle is aligned with the targeted calyx in both the mediolateral and cephalad–caudad orientations, it is advanced with continuous fluoroscopy. The needle should always be advanced in the oblique view, which will allow for the assessment of the depth of the needle's penetration. It is helpful for the anesthesiologist to hold the patient's respirations while the needle is being advanced, to avoid having to "hit a moving target," as well as to minimize the risk of an inadvertent transthoracic puncture. After advancing the needle several centimeters in the oblique view, the anteroposterior view should be examined to confirm that the mediolateral trajectory of the needle is still properly aligned to the target. If necessary, the needle trajectory can be readjusted to maintain proper targeting. Again, it is critical not to alter the access needle's orientation in one plane while making adjustments in the other plane, particularly when advancing the needle.

Several groups have reported refinements in techniques, incorporating elements of the bullseye and triangulation methods, proposing new approaches, describing adjuncts, and using new technology. Mues et al. described a geometric model to create a plane of coincidence between the C-arm and the needle, each at the same angle of 20–30° from the targeted calyx, but in opposite directions [41].

For lower pole access, the C-arm is rotated cranially 30° from the vertical plane, and a needle is advanced from a position distal to the calyx, rotated caudally 30° from the vertical plane. For mid-renal and upper pole calyceal access, the C-arm is rotated 20° away from the surgeon, and a needle is advanced from a position lateral to the calyx, at an angle of 20° toward the surgeon from the vertical plane. In either case, the C-arm remains fixed, and the needle is advanced until the point of coincidence between the calyx and the needle tip is reached. This technique purportedly eliminates the need for C-arm rotation, thus potentially reducing C-arm manipulation and fluoroscopic exposure time. This technique, however, requires a plumb, protractor, and ruler to calculate and confirm the necessary measurements.

Another proposed modification by Sharma and Sharma represents a hybrid of the bullseye and triangulation techniques [42]. The posterior calyx that provides the best access for stone clearance is selected. The initial puncture needle is held at this point. The needle with its overlying hub in the same line as the calyx creates a bullseye effect on the C-arm monitor. The site on the skin corresponding to the target calyx is thus determined, and its position is marked with a hemostat as point A (see Video 13.1). We place an intramuscular needle at this point instead of a hemostat. Then, under direct vision, the needle is placed vertically and the puncture is made at this point in the subcutaneous cellular tissue at a depth of about 1 cm (Figure 13.2a). The visual control of the needle in the vertical position reduces fluoroscopic exposure to a few seconds. Subsequently, a brief fluoroscopic exposure is used to check the position of the needle and it is shown on the screen as a point. The trajectory of the line of puncture of the needle into the dorsal area represents an imaginary line through the selected calyx in the anteroposterior direction. However, this trajectory does not meet all five requirements for optimum puncture, described above, as the needle is not directed toward the center of the renal pelvis.

The C-arm is then angled toward the surgeon, 30° from the vertical in the axial plane. With the ventilation suspended in end expiration, the second puncture needle is held over the targeted calyx in such a way that the needle with its hub is in the same line with the calyx, which leads to a bullseye effect on the C-arm. This particular point on the skin is punctured with an intramuscular needle and is taken as point B (Figure 13.2b) (see Video 13.2). This position represents an imaginary line that is projected onto the center of the selected calyx. Again, all five requirements for safe renal puncture are not met because the trajectory is not toward the center of the renal pelvis. This position is checked in relation to the 12th rib. Visually observing the trajectory of the two small needles placed in the lumbar area, the intersection of two lines coincides with the desired calyx.

The distance between the two needles is measured (Figure 13.3a). The C-arm is then brought back to its vertical position. Now the line of puncture is determined in alignment with the infundibulum from point A. Along this point line, the point B1 is marked. The distance between points A and B1 is equal to or greater than the distance between the intramuscular needles (points A and B) (Figure 13.3b). The point B1 is the point where the skin is punctured for renal access. A small incision is then made at point B1 and the 18G needle is introduced for 1–1.5 cm (Figure 13.4). Now, with the C-arm in the 90° vertical position (i.e. parallel to the line of puncture), the mediolateral (right to left) adjustments are made. Then the C-arm is tilted toward the head of the patient by 30° and adjustments are made in the cephalad and caudal orientation of the line of puncture. The needle orientation is maintained in one plane while making adjustments in the other plane. With the C-arm in the oblique orientation, the needle is advanced with ventilation suspended in full expiration. Under fluoroscopic control and from this position, the 18G needle is advanced towards the point of intersection of the two lines that project both intramuscular needles to reach the selected calyx (see Video 13.3). This is the ideal path and the only one that meets the five requirements described above of a safe percutaneous renal puncture.

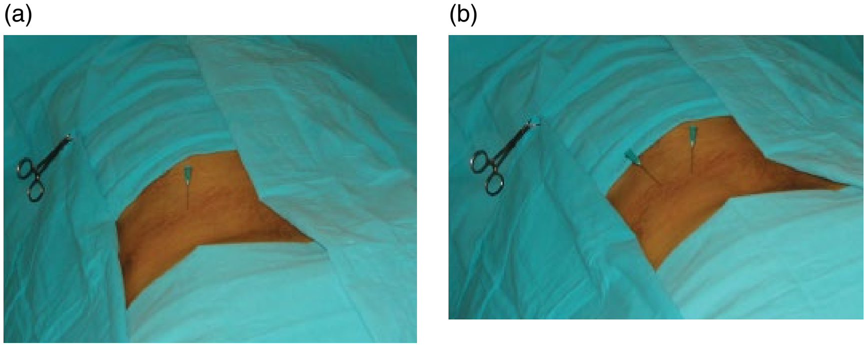

**Figure 13.2** (a) The intramuscular needle with its overlying hub in the same line as the calyx creates a bullseye effect on the C-arm monitor. The needle is placed upright and puncture is done at this point at a depth of about 1 cm in the subcutaneous cellular tissue. (b) The C-arm is angled 30° toward the surgeon. The second needle is held over the targeted calyx in such a way that the needle with its hub is in the same line with the calyx, which leads to a bullseye effect on the C-arm.

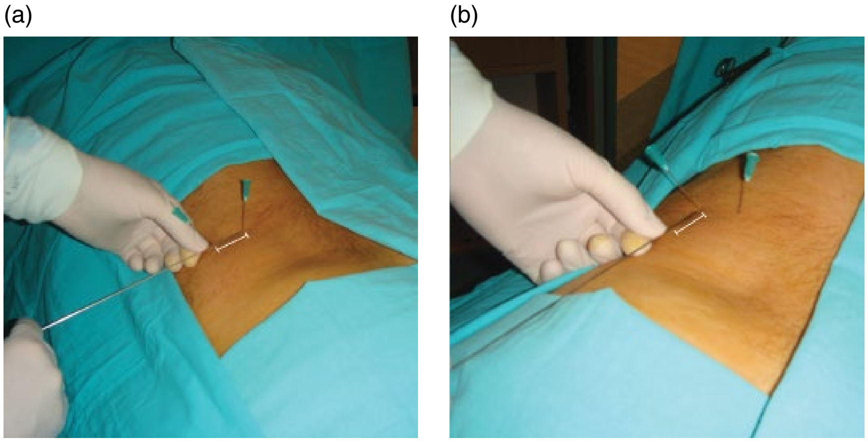

**Figure 13.3** (a) Distance between the two needles is measured (points A and B). (b) B1 is the point where the skin will be punctured for renal access. The distance between points A and B1 is equal to or greater than the distance between the intramuscular needles.

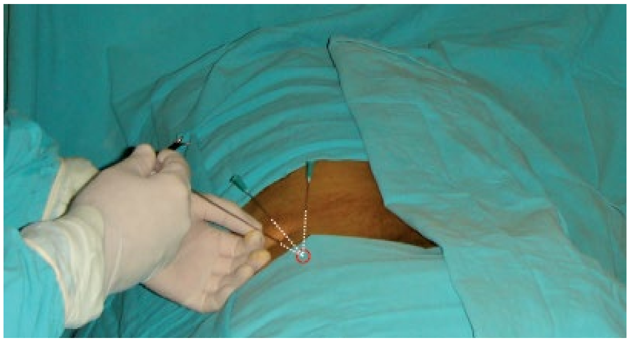

**Figure 13.4** The intersection of the two lines of small needles placed in the lumbar area coincides with the desired calyx. The 18G needle is advanced under fluoroscopic control towards the point of intersection of the lines that project from both intramuscular needles in order to reach the selected calyx.

When the tip of the needle appears fluoroscopically to be within the collecting system, the needle trocar is removed, leaving only the needle cannula in place, and a small amount of urine is aspirated to confirm the needle's intraluminal position.

Definitive puncture of the renal collecting system with an 18G diamond needle permits the immediate introduction of a 0.038 inch guidewire into the collecting system. The rigidity of this needle is advantageous for accurately directing the needle diamond tip as it is advanced through the fascial planes.

If at the point of withdrawing the trocar of the needle a spontaneous output of urine has not been observed, it is advisable gently to try to introduce a hydrophilic guidewire, observing the advancement of the guidewire under fluoroscopy. Typically, it moves into the cavity of the calyx and progresses towards the renal pelvis. If for some reason the guidewire does not easily advance, it is advisable to inject an additional volume of contrast through the initially placed ureteral catheter with the intention of filling the calyx cavity and thereby facilitating the progression of the hydrophilic guidewire.

If no urine exits from the 18G needle, it is not advisable to inject contrast through the needle, since contrast can extravasate, creating a lake of radio-opaque material and making it difficult to visualize the shape of the kidney cavities. Should this occur, the procedure must either be abandoned and returned to at another time, or the urologist must wait until there has been adequate absorption of the contrast material (see Video 13.4).

Several reports have been published of percutaneous renal surgery in the supine, modified supine, or lateral position [43, 44]. This has potential advantages over the prone position for PCNL but it has not been adopted by most urologists (see Chapters 11 and 12). The modified supine position preserves cardiovascular and ventilatory dynamics and allows better access to the respiratory tract. Additionally, the bowel slips away from the puncture area, lowering the risk of it being damaged. PCNL with the patient in a modified supine position may be considered for most patients, especially if concomitant ureteroscopy is planned [45].

## PCNL in supine position

With this technique it is possible to puncture the calyceal papilla without having to rotate the C-arm fluoroscope. Fluoroscopic control is maintained perpendicular to the needle and renal access. Initially a long metal instrument, as the nephroscope, is overlaid on the patient's abdomen and under fluoroscopic control its distal tip is placed over the selected calyx. This point is marked on the sterile drape as it indicates the orientation of the needle.

After having crossed the skin and muscular layers with the needle in an ascending direction to the selected calyx, if depth orientation is wrong it is necessary to retract the needle from the kidney and try to palpate it again in a higher or lower direction. When the selected calyx has been reached and the first urine drops are obtained through the needle, the guidewire is introduced and the tract can be dilated [46, 47].

### PCNL in lateral position

When PCNL is performed in lateral position it is important to consider the different degree of rotation presented by the posterior chalices of each kidney, as previously mentioned. In most right kidneys, the posterior calyces are positioned 20° posteriorly to the frontal plane of the kidney, and in most left kidneys they are 70° posterior to the frontal plane of the kidney (Figure 13.1). This shows that in left stones the needle will be inserted in a direction almost parallel to the operating table, whereas in right stones the needle will be inserted in downward position.

The triangulation technique is used, determining the cephalad–caudal axis with the C-arm in anteroposterior configuration, and determining the anteroposterior axis with the C-arm in oblique configurations [48]. Once the calyx is reached, the wire is introduced and we can proceed to dilation.

## Challenging situations

In situations where the volume of the stone occupies the entire volume of the calyx selected to be punctured, the needle is advanced until there is the tactile sensation of the needle tip touching the hard surface of the stone. In this situation the tip of the trocar of the needle is in contact with the stone but the cannula of the needle is at a distance of 1–2 mm from the surface of the stone. It is advisable to then move the cannula on the trocar toward the stone until contact with the surface of the stone is felt. Then the trocar needle is removed and the hydrophilic guidewire is gently inserted into the narrow space between the urothelium of the calyx and the surface of the stone. Sometimes this allows the advancement of the guidewire to the renal pelvis, but in other situations it is only possible to locate the guidewire in the punctured calyx and attempting otherwise is risky because of the short length of the guidewire in the upper urinary tract. The guidewire is advanced carefully across the calyceal infundibulum.

## Dilation

To perform tract dilation, a 1 cm skin incision is made around the needle with a no. 10 blade and the needle is removed. Then, in order to enlarge the defect in the lumbar fascia, a fascial incision needle can be used (no. 090070, Cook Urological). This instrument consists of an 18G needle fixed to a small, blunt, diamond-shaped blade that is passed over the puncture wire under fluoroscopic control and through the abdominal wall until it crosses the lumbar fascia (Figure 13.5). It is then withdrawn while gentle traction is placed on the puncture wire, and the tip of the blade is rotated 90° and then advanced again over the puncture wire in order to open the lumbar fascia more extensively. This action will facilitate the introduction of any of the available dilation systems.

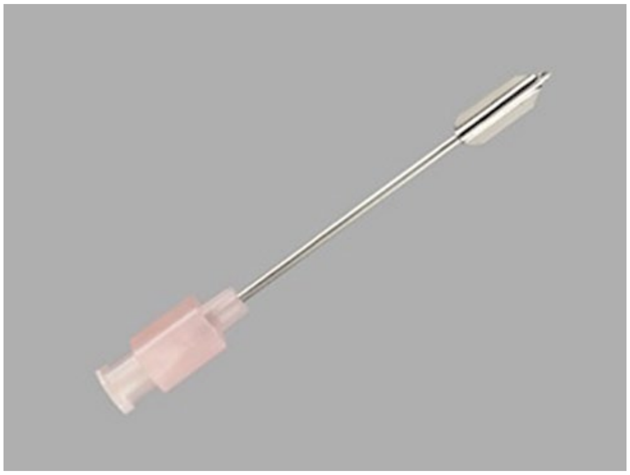

**Figure 13.5** Fascial incising needle. This instrument facilitates the introduction of any of the available dilation systems. It is used to open the lumbar fascia.

Acute dilation of nephrostomy tracts can be performed with a variety of instruments. These instruments are inserted over a working guidewire. Because of the risk of the perinephric guidewire kinking with loss of the nephrostomy tract and laceration of the renal parenchyma, all percutaneous dilator systems require fluoroscopic guidance [49–51].

The nephrostomy tract is dilated up to 30 Fr, according to the nephroscope to be used. In the serial dilation system, an 8 Fr Teflon catheter is used as an obturator. Progressively larger dilators are then serially inserted over this guidewire and catheter combination. This additional obturator stiffness greatly reduces the risk of perinephric guidewire buckling.

With the access tract dilated, a working sheath is introduced into the collecting system under fluoroscopic guidance over the 30 Fr (or the chosen diameter) dilator, which is then removed. The renal pelvis is examined nephroscopically to identify the obstructed segment of the ureteropelvic junction and locate the previously placed ureteral catheter. If necessary, either the ultrasonic probe or the grasping forceps are passed into the renal pelvis to clean out clots.

The catheter is grasped and brought out through the nephrostomy tract. A 0.038 inch super-stiff wire, which is a fixed core guidewire with an extra-stiff shaft and a flexible tip, is advanced through the catheter. A surgical assistant removes the ureteral catheter, leaving the guidewire in place at the urethral meatus. Once the ureteropelvic junction has been bridged (i.e. the guidewire is in position from the flank through to the urethral meatus), the nephroscope is removed and a hemostatic clamp is placed about 5 cm proximal to the distal end of the guidewire. It is pulled through the nephrostomy tract to position the clamp near the urethral meatus. This maneuver ensures the preservation of the nephrostomy tract, so that if the access route to the kidney is accidently lost it is easily recovered by following the guidance described above. Additionally, if for some reason the procedure has to be interrupted, placement of the nephroureteral stent will allow both drainage and subsequent easy access.

### Special situations: multiple access

In the treatment of complex renal lithiasis with branches in multiple calyces, it is sometimes necessary to make multiple punctures through different calyces. The multiple punctures can all be made initially, or alternatively one puncture can be made, through which most of the stone is removed and, if necessary, additional punctures can then be made.

If the planned multiple punctures are made at the beginning of surgery, the injection of contrast through the initially placed ureteral catheter facilitates visualization of all calyces and those most suitable for punctures can be chosen in accordance with the silhouette of the stone. The injection of contrast distends the upper urinary tract and this facilitates insertion of the needles into the calyces.

In contrast, if multiple punctures are made in addition to establishing a unique initial nephrostomy tract, the calyceal distention of the cavities may be hampered by the leaking of contrast that is injected by a 6 Fr ureteral catheter through the Amplatz sheath tract nephrostomy. In this situation it is advisable to place a Foley catheter and to inflate the balloon inside the Amplatz sheath to occlude its caliber. Thereafter it is possible to inject contrast either through the ureteral catheter placed at the beginning of surgery or the Foley catheter, and to place a clamp to prevent leakage of contrast from the distended renal cavity. This maintains the distention of the calyces, facilitating additional punctures under fluoroscopic control.

Liatsikos et al. have described the technique of a single subcostal skin incision with multiple angular punctures to approach the superior, middle, and lower pole of the kidney for the management of staghorn calculi [52]. Singla et al. have evaluated the safety and efficacy of an aggressive approach to staghorn calculi using multiple-tract PCNL, and reported a greater stone clearance rate without increasing the risk of significant complications [53].

## Conclusion

Percutaneous endourologic procedures require an advanced level of skill. The techniques used should be understood by those treating patients with complex renal stone disease to improve their ability to manage these often challenging clinical problems. The bullseye and triangulation methods are the most commonly used approaches, but refinements in technique and applications of new technology offer the potential for improved access with reduced patient and surgeon morbidity. Percutaneous puncture, tract dilation, and antegrade nephrostomy sheath placement into the desired calyx can be achieved rapidly and with precision when fluoroscopy is adequately used. For this reason and for patient comfort, access is best achieved in the operating room by the urologist, even in special situations like staghorn stones requiring multiple or supracostal accesses, calyceal diverticulum, and horseshoe kidneys.

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## 14

# Dyna-CT-Guided versus Standard CT-Guided Renal Access

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## Background

The standard techniques for gaining access to the renal pelvis for percutaneous stone treatment are usually based on ultrasound and fluoroscopy. The exact technique depends on the imaging modalities that are available in different countries and medical centers. Both techniques have some drawbacks, especially in complex cases. Although ultrasound is a perfect real-time imaging tool, image resolution and contrast are limited, even in modern systems. Fluoroscopy provides a detailed depiction of the renal calyceal system using a contrast agent, but it does not offer the possibility of soft tissue imaging. Consequently, the risk of organ injury during the puncture or bleeding might be increased [1, 2]. Furthermore the two-dimensional (2D) depiction of the renal calyceal system obviously harbours difficulties for surgeons to visualize the anatomical three-dimensional (3D) situation during the puncture. The combination of both 2D techniques, ultrasound and fluoroscopy, might overcome this problem up to a certain degree, but 3D imaging has been proved to facilitate the procedure [3].

In the case of unsuccessful punctures of the renal calyceal system by standard techniques, computed tomography (CT)-guided access offers the possibility of depicting the kidney's surrounding structures and organs and with a high spatial resolution and therefore allows for gaining access even in special anatomical situations such as horseshoe kidneys, malrotation, or obese patients [4–6].

However, the procedure itself is more time consuming, expensive, and may cause higher radiation exposure to the surgeon and especially the patient. Due to these drawbacks CT-guided punctures of the kidney should be *restricted to special indications*. However, in cases of difficult anatomy, unclear ultrasound findings, or unsuccessful fluoroscopy-guided attempts, CT-guided punctures may be necessary [7]. The technique was first described in 1977 [8] and further developed over subsequent decades [9, 10]. The indications for CT examination of patients that undergo percutaneous nephrolithotomy (PCNL) might be puncture planning, puncture guidance, and control of puncture success [10]. Furthermore, CT scans after PCNL allow for fast and exact diagnostics of complications and provide the highest sensitivity for the detection of residual fragments. Routine application of post-PCNL CT provides additional advantages compared with other imaging modalities: namely, the identification of the presence and location of even small residual fragments, which has been shown to cause significant trouble and necessitate secondary procedures in a significant cohort of patients after PCNL [11]. As limited access to the patient inside the CT gantry and the need for several scans during a puncture are somehow limitations of punctures guided in multidetector-computed tomography (MDCT), cone-beam CT systems are now beginning to be used for gaining renal access not only by radiologists but also by urologists themselves [12]. Both techniques – standard CT-guided access and the 3D-planned, laser-guided access with a Uro Dyna-CT – are presented in this chapter.

## CT-guided access

### Patient positioning

For standard CT-guided access of the kidney, the patient is required to be in the prone position. For patients with respiratory difficulties a supine oblique position is possible but offers less working space for the interventional radiologist. The insertion point of the needle is marked

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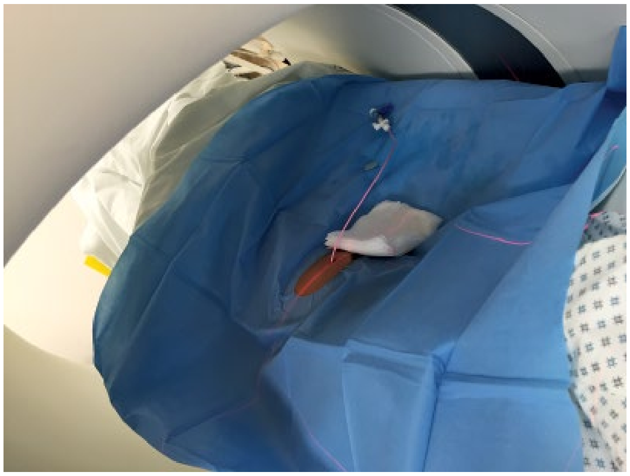

**Figure 14.1** Setting of a standard CT-guided puncture of the renal collecting system. Reproduced with permission of Dr. N. Rathmann.

by a laser point (Figure 14.1). Angulation of the needle usually is not marked, unlike a cone-beam system. Therefore recurrent scans of the puncture area are necessary to check the needle direction during the puncture. Although the latest generation of CT scanners allows these recurrent scans with a relatively low radiation exposure it still leads to higher exposures than any other puncture technique. If the CT scan is used preoperatively for planning the puncture with a different technique, the patient should be placed in the same position that is used during surgery. CT scans that are performed in supine position do not provide sufficient anatomical information if the PCNL is to be performed in prone position.

## Puncture planning

The advantages of CT scanning over intravenous urography is the ability to assess the spatial relationship of the kidney relative to the stone, depict the calyceal anatomy in 3D format to choose the access site, assess the risk of pleural or bowel injury, and even predict success of subcostal fluoroscopic access for upper pole puncture [13, 14]. The preoperative detection of heptaosplenomegaly or the presence of retrorenal colon allows serious complications related to tract placement to be avoided [15]. Recent findings suggest that the preoperative use of CT angiography may reduce the risk of bleeding during PCNL. Patients who underwent CT angiography prior to PCNL had lower drop of hemoglobin and needed fewer transfusions [16]. However, similar results can be achieved with ultrasound-guided puncture techniques without any radiation exposure [17]. In patients with anatomical deformities, ectopic or transplant kidney, or suspicious ultrasound findings preoperative CT evaluation reduces the risk of intraoperative injuries and complications. Vasculature, retrorenal, or overlying bowel as well as pleural position in inspration and expiration are well indicated. In case access to the upper pole of the kidney is required as a result of stone position, CT examination helps to predict the success of subcostal and supracostal approaches [18]. Preoperative CT imaging enables the surgeon to measure the skin-to-stone distance and the ideal puncture tract. Especially in obese patients, knowledge of the expected tract length helps with choosing the right instruments (overlength) and avoids costly preparation of unnecessary devices.

## Radiation exposure

Radiation exposure is seldom reported in the published studies on CT-guided percutaneous renal access or nephrostomy placement. Published data are within a wide range due to different generation of CT systems and puncture techniques with and without CT fluoroscopy. The use of CT fluoroscopy increases the radiation exposure of the radiologist compared to the standard technique when the radiologist is outside the intervention suite during repeated scans and advances the needle between scans. Furthermore, modern generations of CT systems allow for fast evaluation of the area of interest during the procedures with relatively low radiation doses. Procedure time ranges from 7 to 50 minutes, with the dose area product being between 43 and 56 $\text{Gy/cm}^2$ and the effective dose 6.9–13.6 mSv [9, 19, 20]. The authors conclude that the procedure is not only time consuming but exposes the patient to significant radiation, too. Thus, the intervention requires a strict indication and should be performed exclusively when routine approaches have failed and preferably in older or oncology patients [19]. Another group evaluated the clinical impact of the use of a dose-reduced examination protocol for CT-guided cryoablation of renal tumors. They found no significant change in the effectiveness of the dose-reduced protocol but significantly less radiation exposure to the patient [21]. These findings suggest a *high potential* for reducing radiation exposure during CT-guided nephrostomy placement.

## CT-guided puncture

After positioning of the patient in the possible position depending on respiratory capacity, scouting tomography of the area of interest is performed. Dilated collecting systems are well depicted already in noncontrast examinations. If dilatation is not detectable or if there are any suspicious findings in the kidney area like a renal mass then further scans using contrast agent might be performed for better visualization of the region of interest.

Depending on the anatomical relation between the collecting system, stone position, and surrounding structures such as vessels, liver, spleen, or colon the ideal puncture tract is planned. If a laser marker of the planned entry site is not provided by the CT system a skin marker may be placed. The ideal position of the marker is found by repeated scans until a direct transverse tract into the chosen calyx seems possible.

Once the entry point of the needle is defined the puncture site is disinfected and covered by a sterile fenestrated drape. Local anesthesia is administered and the puncture needle is advanced subcutaneously. Repeated scans of the area with usually only three or four 5 mm slices help correcting the needle trajectory until the collecting system is entered and urine can be aspired. A further scan proves the correct position of the needle tip. Afterwards antegrade filling of the collecting system with contrast agent or direct placement of a guidewire is possible. If CT fluoroscopy is available, dilation of the tract and placement of the nephrostomy tube can be performed under direct visual control. Otherwise, further scans prove the correct position of the nephrostomy tip. The tube is secured by a suture. When starting the PCNL a guidewire is placed through the indwelling nephrostomy before dilating the tract and placement of an access sheath. PCNL can be performed directly after CT-guided nephrostomy tube placement or during the days after.

### Outcome

Failure of CT-guided renal access is very rare and some studies even report success rates of 100% [9, 20]. About 80% of the punctures are successful with the first attempt [7, 9, 20, 22]. The need for three attempts is reported in less than 8% [9, 22]. Severe complications such as organ injuries are not reported and bleeding complications are rare. Due to the fact that the cross-sectional imaging enables exact tract planning depending on stone location even in patients with special anatomical situations, CT-guided access was reported in a small series to enable a stone-free rate of 83% after PCNL even with these challenging indications [6].

## Dyna-CT-guided renal access

Most of the punctures performed by urologists can be accomplished safely and quickly by ultrasound alone or in combination with fluoroscopy [23–25]. Ultrasound provides inexpensive, fast, and real-time imaging, but problems include availability in the endourologic suite in some countries, the need for extensive training, and relatively low spatial contrast depending on the abilities of the available system. Common ultrasound machines enable only 2D imaging. Fluoroscopy systems, either C-arm-based or stationary units, are available almost everywhere worldwide to support the performance of endourologic procedures. The main disadvantage of the technique is the lack of soft tissue imaging, the use of ionizing radiation, and only a 2D depiction of the structures of interest. To overcome these problems, new techniques based on 3D imaging have been developed. The Uro Dyna-CT (Siemens Healthcare Solutions, Erlangen, Germany) installed in the endourologic operating suite provides not only standard X-ray and fluoroscopy but also interventional 3D imaging and cross-sectional image reconstruction [23]. It also offers a 3D planning and laser-guiding puncture tool called the syngo iGuide [26]. After having proved the applicability for urologists in cases of complex punctures in a standardized *ex vivo* model [26] the technique was performed sucessfully in complex clinical cases [1].

### Uro Dyna-CT system

The Uro Dyna-CT suite is equipped with an Artis Zee® Ceiling System (Siemens Healthcare Solutions) combined with a customized, full carbon urological examination table and a rotatable flat-panel detector (30 × 40 cm, 48 cm diagonal, 2 k matrix). Post-image processing and 3D reconstruction are performed on the dedicated workstation using syngo MMWP VE 40A 3D reconstruction software (Leonardo, Siemens Healthcare Solutions) [23].

### Urological imaging table

The urological intervention table of the Uro Dyna-CT is a free-floating full carbon table measuring 262 × 52 cm. Additionally, the table enables lateral and cranio–caudal buckling by ±15°. The surgeon can easily control all movements of the table by means of a wireless foot pedal or via the operation terminal that can be covered to render it sterile. The table consists of two parts: the removable distal part (95 × 52 cm) is fixed by an easy-to-use plug socket and can be replaced by stirrups for the lithotomy position. To avoid any interference of metal structures during the imaging process, all parts of the table are made of carbon. The main table and the removable distal part have maximum loading capacities of 250 and 80 kg, respectively. At 19 cm from the distal end of the main table, 23 × 7 cm nephrostomy slots are cut out on both sides to provide perfect access to the renal area in supine position [23].

### Image quality

The ceiling-fixed X-ray system comes with a 30 × 40 cm flat panel detector and moves freely in all directions.

Its maximum rotation speed of 60° per second with up to 495 images per rotation enables complete cross-sectional imaging of the urinary tract and the surrounding tissue within 5–20 seconds depending on the protocol settings. The complete procedure for 3D reconstruction takes less than 2 minutes at any setting [23].

While high concentrations of contrast agent provide excellent imaging quality in fluoroscopic and standard X-ray examinations, they lead to increased streak artifacts in cross-sectional and 3D reconstructions which would reduce the image quality of a Uro Dyna-CT during the intervention. Furthermore, the detection of residual stone fragments can be limited by interference of the contrast agent. Therefore the use of diluted contrast agent is essential to provide good image quality especially for cross-sectional images. Following experimental findings a *20% contrast agent dilution* proved to be perfect for imaging of the urinary tract and radiopaque kidney stones with the Uro Dyna-CT even in obese patients [27]. Similar to undiluted contrast agent, metallic endourological devices are able to cause streak artifacts during cross-sectional and 3D imaging. However, the system can be used for all interventional endourological procedures using the common armamentarium and instruments without significant limitation of image quality. There are only minor limitations according a PCNL working sheath and the rigid URS. These instruments should be removed from the examination field before performing the CT and replaced afterwards using a safety wire [28]. If a plastic Amplatz sheath is used for PCNL it can stay in place for the Dyna-CT scan. In contrast to standard MDCT the image quality of a Uro Dyna-CT depends on the MDCT convolution kernel. As compared with MDCT using a medium-hard convolution kernel, the Uro Dyna-CT produces images at medium noise levels and, simultaneously, medium spatial resolution at approximately the same dose. It is well suited for visualizing hard-contrast objects in the abdomen with relatively low image noise and patient dose. For the detection of low-contrast objects at standard tube voltages of approximately 120 kVp, however, MDCT should be preferred [29].

## Radiation exposure

Although urologists can minimize the radiation dose by tighter collimation and reduction of fluoroscopy time during interventions, the new technical possibilities of the Uro Dyna-CT with CT-like imaging require customized examination protocols for urological needs. On the one hand these protocols have to enable the intraoperative detection of small residual stone fragments and on the other hand they must give surgeons the possibility to detect soft tissue structures such as renal tumors to enable focal therapies or laser-guided biopsies in the future. Therefore customized protocols for urological needs have been developed in a phantom study [30]. The developed and clinically implemented protocols allow for better application of the as low as reasonably achievable (ALARA) principle of radiation protection. The soft tissue protocol causes an effective dose of 7.76 mSv, the stone standard protocol 1.96 mSv, and the stone low-dose protocol 0.33 mSv. The urology stone standard protocol provides excellent hard-contrast imaging with adequate soft tissue depiction, whereas the urology stone low-dose protocol enables sufficient hard-contrast depiction with extremely low radiation dose. Finally this phantom study proved that interventional soft tissue 3D imaging can be performed with an acceptable radiation dose. The image acquisition uses higher radiation doses than the standard fluoroscopy technique. However, it is in an acceptable range compared with standard MDCT examinations. For hard-contrast depiction radiation exposure by the Uro Dyna-CT is even lower than with MDCT.

## Dyna-CT guided puncture

The complete process of a Dyna-CT guided puncture is shown in a video associated with a separate publication [1].

### Image acquisition and puncture planning

For image acquisition, the Artis Zee Ceiling System with a modified imaging protocol is used. Maximum inspiration triggered by the cooperative patient or the anesthesiologist is recommended to enable a reproducible kidney position during the puncture. The Dyna-CT scan is possible with the patient fully covered with sterile drapes as the system's C-arm can be covered, too. Planning of the puncture and image windowing are performed at the dedicated 3D workstation. The most suitable puncture tract to avoid interference with surrounding organs is planned using cross-sectional images and can be checked in the 3D reconstruction for the ideal direction to reach the target, especially for entering a renal calyx (Figure 14.2). The planning software shows the exact length of the planned puncture tract. It also provides an analysis of the ideal C-arm positions to depict the required planes for the puncture.

### Laser-guided puncture

To start the laser-guided puncture, the table is adjusted, and the C-arm is placed in the bullseye position to indicate the puncture site and direction with a laser cross (Figure 14.3). The needle is inserted, keeping the laser cross permanently in an inline position to the needle. During the puncture the anesthesiologist reproduces the same inspiration level as during the initial scan. This is

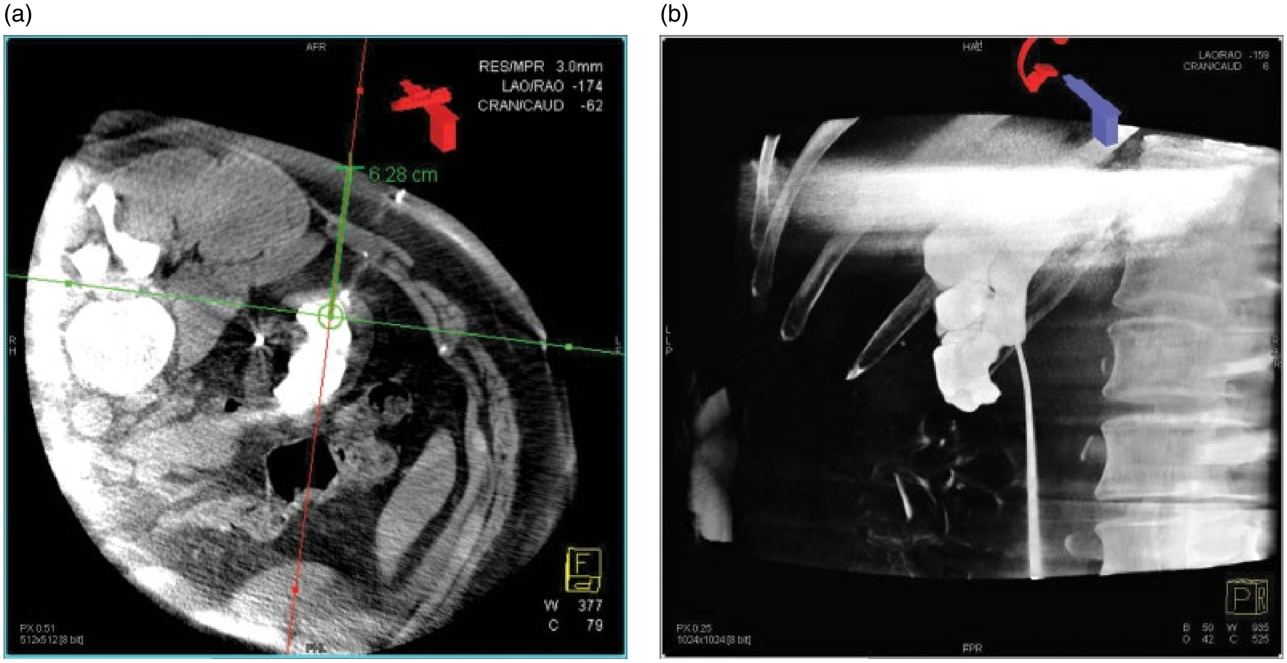

Figure 14.2 Planning of puncture tract with the Uro Dyna-CT in (a) cross-sectional images and (b) 3D reconstruction of the collecting system after retrograde filling with a balloon catheter.

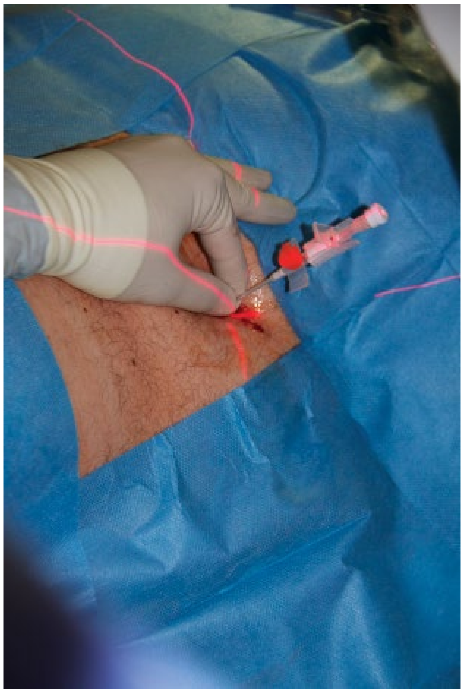

Figure 14.3 Laser cross indicating puncture site and direction during the puncture.

usually controlled by adjusting the same positive airway pressure. The correct placement of the needle can be checked by fluoroscopy. The placement of the needle can be corrected as required by matching it with the indicated road map on the fluoroscopy screen in the bullseye, oblique, and lateral views until the target is reached (Figure 14.4). This road map is provided by the system in any position of the C-arm that might be necessary during the puncture because the Dyna-CT system knows the exact position of the table in relation to the C-arm at any time [1, 23, 26]. When puncturing a renal calyx, fluid excretion through the needle indicates puncture success. This can be additionally checked by antegrade pyelography. When puncturing solid structures as for tumor biopsy, the correct position of the needle can be verified by a customized low-dose Dyna-CT imaging protocol with the possibility of modifying the puncture direction by image overlay with the initial planning data.

### Outcome

Median puncture time for a laser-guided puncture from insertion of the needle to reaching the target with the Uro Dyna-CT is 30 seconds. Median fluoroscopy time during and after the puncture to check the needle position in different angles by the indicated road map on the fluoroscopy screen is 0.7 minutes. Radiation dose caused by the procedure leads to a mean dose area product (DAP) of 96.9 μGy per $m^2$ by fluoroscopy during the procedure and 6113.1 μGy per $m^2$ by the Dyna-CT scan for puncture planning. A total of 24 of 27 punctures (89%) were successful. In two cases a second puncture was necessary and in one case puncture success was achieved after three attempts [1].

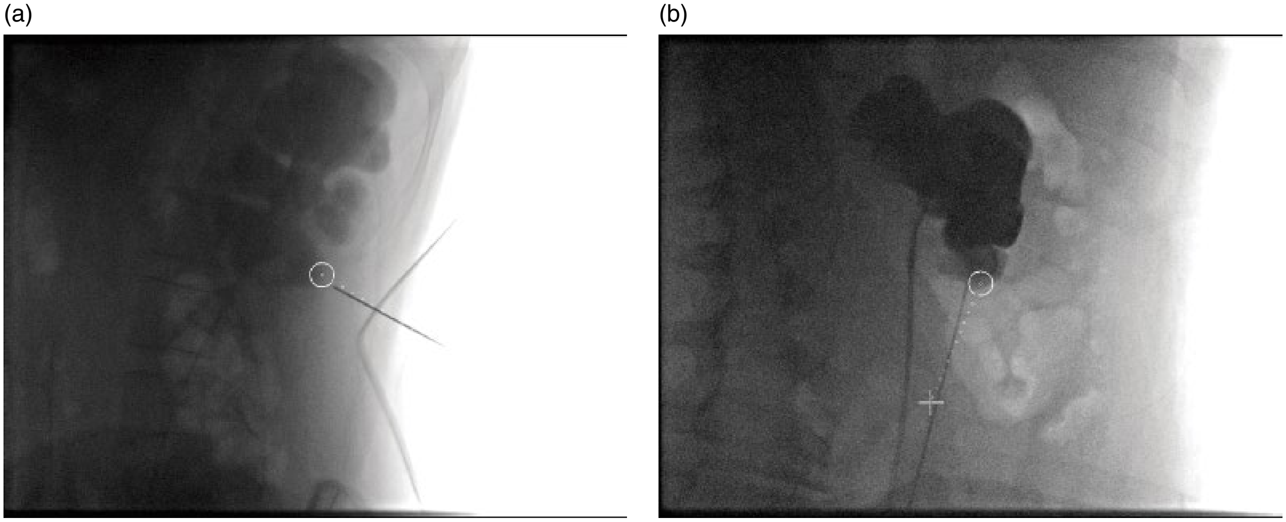

**Figure 14.4** (a, b) Indicated road map of the planned puncture tract on the fluoroscopy screen during the puncture in different planes.

### Limitations

Targets with no or only little movement due to respiration in particular can be punctured successfully with high accuracy. Structures with extensive movement might profit from additional live image acquisition such as with ultrasound or the additional use of electromagnetic tracking of previously placed sensors inside the kidney, for example. Both techniques could be easily combined with the described Uro Dyna-CT puncture technique. The technique is applicable not only for the urinary tract but for any target that can be depicted by the Dyna-CT scan with excellent image quality such as lymph nodes, metastases, tumors, or an abscess. This enables the diagnostic use of the system for gaining histology or therapeutic use for drainage or focal therapy. Image quality of these scans, especially for soft tissue imaging, correlates with the radiation dose exposure of the patient. The radiation dose is naturally higher than with standard fluoroscopy. However, compared with complex punctures with standard MDCT, the radiation dose even might be lower in cone-beam CT-guided procedures as with Uro Dyna-CT. Handling of the system and the guiding software requires specific training, just as other puncture techniques do; therefore, we first evaluated the applicability of the technique in an *ex vivo* biological model. These *ex vivo* experiments are shown in the first part of the supplementary video in [1].

## Conclusion

Both puncture techniques described for gaining access to the collecting system of the kidney before percutaneous stone treatment provide high success rates when they are performed by experienced interventional radiologists (CT-guided) or endourological surgeons (Uro Dyna-CT-guided). As both techniques cause higher radiation exposure to the patient and potentially to the performing surgeon the indication for both techniques should be limited to patients with special anatomical conditions, suspect ultrasound findings, or a history of frustrane punctures with standard techniques. However, with the increasing number of hybrid operating rooms with integrated cone-beam imaging systems, the Uro Dyna-CT technique might become widely available in such medical centers. In these centers the presented technique might be used for selected patients with an increased risk of rare but severe complications such as bowel perforation. For routine procedures the available standard techniques of ultrasound and fluoroscopy should be used. Dyna-CT scans of the patient are possible in the supine position, which might also enable the application of our puncture technique for supine percutaneous lithotomy in complex cases [1, 6, 17, 24, 31, 32].

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# 15

# Endoscopically Guided Percutaneous Renal Access

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## Introduction

There has been a dramatic increase in the incidence and prevalence of urolithiasis over the past two decades [1]. Accordingly, there has been a concomitant rise in surgical intervention for urolithiasis [2]. Percutaneous nephrolithotomy (PCNL) is the gold-standard treatment for large kidney stones (>2 cm) [3, 4]. Data from the Nationwide Inpatient Sample (NIS) from 1999 to 2014 demonstrated an increase in the use of PCNL for the treatment of upper urinary calculi [5–8]. Similarly, an analysis of 6 month case logs submitted to the American Board of Urology revealed a 117% increase in PCNL usage from 2004 to 2013 among applicants for Part II board certification [9].

The first description of percutaneous drainage of the renal collecting system dates back to 1865, when Dr. Thomas Hillier reported using repeated renal decompression to relieve symptoms of congenital ureteropelvic junction obstruction in a 4-year-old boy [10]. Ninety years later, in 1955, while attempting an aortogram, Willard Goodwin unintentionally performed the first antegrade nephrostogram by inadvertently injecting contrast into the renal collecting system [11]. Goodwin, turning a "perceived" error into a breakthrough advance, later published his novel image-guided nephrostomy technique in 16 patients with severe hydronephrosis [12]. Over the ensuing decades, the technique for percutaneous nephrostomy has been continuously refined and has thus become widely adopted for both temporary and permanent drainage of the obstructed kidney. In 1976, under fluoroscopic guidance, Fernström and Johannson described the first percutaneous stone removal [11, 13]. In 1984, Smith and colleagues, in a seminal article, described their technique for PCNL in a series of 100 patients, reporting a 5% complication rate and 91% stone-free rate [14]; this cohort was updated in 1985, by which time there were 400 patients with a stone-free rate of just over 94% [15]. Over the past 30 years, PCNL has been further advanced due to the advent of laser and pneumatic lithotripsy, digital endoscopy, and developments in flexible nephroscopy as well as ureteroscopy.

### Endoscopic guided percutaneous access

Obtaining percutaneous renal access presents the greatest challenge during a PCNL. Indeed, de la Rosette and colleagues noted that for a resident to become competent in performing percutaneous nephrostomy, a minimum of 60 cases were needed [16]. Given this requirement, it is not surprising that fewer than 20% of urologists actually gain their own access. However, it is clear that the most crucial part of the procedure is the proper placement of the nephrostomy tract as it determines whether or not the stone can be effectively encountered and cleared.

Due to its challenging nature, multiple modifications for facilitating percutaneous access have been proposed beyond the standard antegrade fluoroscopic approach. Lawson and colleagues were the first to establish a percutaneous tract in a retrograde fashion by puncturing outward from the collecting system to the skin; however, this method proved to be difficult to perform in the presence of a large obstructing pelvic stone and the length/direction of the resulting nephrostomy tract was difficult to control [17]. In 1995, Grasso and colleagues modified the retrograde technique by using ureteroscopic guidance in combination with fluoroscopy to place a percutaneous nephrostomy tract when antegrade fluoroscopic access failed. The technique was subsequently used as a salvage procedure in seven patients [18]. Subsequently, in 2003,

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

Kidd and Conlin reported similar results using the combined fluoroscopic-endoscopic approach to successfully gain access in three patients for whom the traditional antegrade fluoroscopic method was complicated [19]. Both groups concluded that direct endoscopic visualization of the needle puncture simplified obtaining percutaneous access. While initially considered only as a salvage technique, Clayman and colleagues began to use the combined ureteroscopic-fluoroscopic technique as a first line approach for all PCNL procedures [20].

In this chapter, we describe the combined ureteroscopic-fluoroscopic percutaneous nephrostomy technique as currently employed at the University of California, Irvine. This approach assures a highly precise entry into the targeted calyx. It also may decrease time to access the collecting system, reduce the number of needle passes, lower the radiation dose, and diminish complications associated with purely fluoroscopic antegrade percutaneous renal access.

## Preoperative patient preparation

In all patients, a sterile urine culture is documented within 2 weeks of the procedure. Further, all patients are placed on ciprofloxacin 250 mg twice daily for a week prior to their percutaneous procedure as recommended by Tolley and associates [21]. It is of interest that with this regimen, El Tayeb and colleagues noted a marked decrease in their incidence of postoperative bleeding and need for angioembolization [22]. Also, all patients are placed on a week of tamsulosin 0.4 mg daily to possibly induce a state of ureteral relaxation in order to facilitate deployment of an ureteral access sheath (UAS).

A computed tomography intravenous pyelogram with three-dimensional reconstruction is obtained within 1–6 weeks of the procedure. This is performed with and without contrast, preferably with the patient in a prone position. The transverse, sagittal, and coronal views are carefully reviewed; stone measurements (in three dimensions) and Hounsfield units are recorded. Using the sagittal views, the planned nephrostomy tract to the stone is mapped out such that it will provide the broadest angle of entry to the stone burden; in this regard, the angle between the planned nephrostomy tract and the location of the stone should be greater than 117° to allow passage of the rigid nephroscope and more than 68° to insure calyceal access by the flexible nephroscope [23].

### Box 15.1 Five surgical steps of endoscopically guided renal access for PCNL.

1) Patient in prone position on spreader bars, legs abducted 30°
2) Retrograde preparation:
   a. prone flexible cystoscopy and ureteral guidewire insertion
   b. Foley catheter (12 Fr)
   c. UAS deployment
   d. flexible ureteroscopy
3) Nephrostomy puncture
4) Establishing a through-and-through guidewire
5) Balloon dilation of the nephrostomy tract and placement of a 30 Fr Amplatz sheath

### Box 15.2 Instrumentation list for endoscopically assisted fluoroscopy-guided percutaneous nephrostomy tract establishment

**Permanent operating room equipment**

1) Fluoroscopy-compatible operating room table
2) Spreader bars for the operating room table
3) C-arm fluoroscopy with monitor
4) Video tower setup with light source and television monitor
5) Irrigation system
6) Flexible cystoscope (16 Fr standard)
7) Flexible ureteroscope (7.5 Fr tip and shaft [Karl Storz, Culver City, CA, USA][a] allows use of the Fr UAS; for all other ureteroscopes where the shaft tapers up to 9 Fr or larger a 14 Fr UAS is usually needed)
8) Standard surgical tray (with #11 scalpel blade and Kelly clamps)
9) Holmium laser lithotriptor

**Disposable equipment**

1) UAS
2) 18G nephrostomy needle
3) 5 mm fascial incising needle (Cook Urological, Bloomington, IN, USA) [a]
4) 5 Fr open-ended ureteral catheter (optional)
5) 0.035 inch 150 cm nitinol hydrophilic guidewire
6) 10 Fr Amplatz introducer catheter with 8 Fr obturator (Cook Urological)[a]
7) 0.035 inch 145 cm super-stiff guidewire
8) 0.035 inch 260 cm floppy tip exchange guidewire (male patients only)
9) 1.5 Fr nitinol stone basket for the ureteroscope
10) 30 Fr nephrostomy dilating balloon with 30 Fr renal access sheath
11) 12 Fr Foley catheter
12) 10 ml syringe

[a] Company names have been provided only for products for which there is a single source producer.

## Surgical technique

There are five steps in establishing a successful endoscope-assisted antegrade fluoroscopic percutaneous nephrostomy tract (Box 15.1). Box 15.2 provides a complete list of the instrumentation required for performing an endoscope-guided PCNL.

## Step 1: patient positioning

The procedure begins with the induction of general anesthesia in a supine patient; the patient is then turned prone with his/her legs on spreader bars abducted to 30° (Video 15.1). This position allows the surgeon to have simultaneous access to the affected flank and perineum. In male patients, it is important that the pubis is aligned with the bottom end of the table, which allows the phallus and scrotum to hang free of the table, thereby facilitating male flexible cystoscopy. Cylindrical gel pads are placed on either side of the patient's chest. The patient's legs are padded, fitted with intermittent compression leggings, and then fixed in place with silk tape. The affected flank, external genitalia, and perineum undergo surgical preparation and draping.

## Step 2: retrograde preparation

### Prone flexible cystoscopy and guidewire Placement (Video 15.2a)

The irrigant is attached to the working channel of the flexible cystoscope and irrigant is run through the endoscope to flush all air out of the working channel. Flexible cystoscopy is performed; however, the trigone and ureteral orifices now lie in a superior orientation and one has to "look up" to view them. Accordingly, the cystoscope is deflected upward to identify the intraureteric ridge, which is then followed laterally to identify the affected, ipsilateral ureteral orifice. Provided there is no stone in the ureter, a 0.035 inch super stiff guidewire is advanced into the ureteral orifice and, under fluoroscopic guidance, is passed to the level of the renal pelvis or further cephalad, into the upper pole calyces. It is important to not push the wire to the extent that it coils in the upper pole or else some bleeding may occur. An 8/10 Fr obturator and introducer sheath is then passed. The 8 Fr obturator is removed and a retrograde ureteropyelogram is performed through the 10 Fr sheath in order to outline all of the calyces, and their respective infundibulae. This provides a clear outline of the collecting system and assists in planning the access route to the stone.

If any resistance to passage of the super-stiff guidewire is encountered or if there is a stone in the ureter, then a 0.035 inch hydrophilic nitinol guidewire is used instead of the super stiff guidewire. Once this guidewire is manipulated beyond the ureteral stone and into the renal pelvis, the flexible cystoscope is removed and a 5 Fr angiographic or 8 Fr catheter (from the 8/10 Fr introducer set) is passed over the guidewire until it reaches the renal pelvis. The nitinol guidewire is removed and a retrograde pyelogram is obtained via the 5 or 8 Fr catheter. Next, the 0.035 inch super-stiff guidewire is passed through the 5 or 8 Fr catheter, and the catheter is removed, leaving only the super-stiff guidewire in place. No second guidewire is passed into the system (i.e. there is no designated "safety guidewire").

### Foley catheter placement

A 12 Fr Foley catheter is placed in the bladder alongside the guidewire to ensure proper drainage of urine from the contralateral kidney throughout the procedure.

### UAS placement (Video 15.2b)

For dealing with calculi in the kidney, a 35 cm UAS is selected for the female patient and a 55 cm UAS is selected for the male patient, as the goal is to have the end of the sheath extend into the renal pelvis. The UAS is deployed over the super-stiff guidewire under fluoroscopic control. Initially a 16 Fr UAS (Cook Urological, Bloomington, IN, USA) is passed; if this does not pass easily, then a 14 or 11 Fr sheath is used. The key is to not exert any excessive force on the sheath; "if it don't go easy, it don't go at all" (Louis Kavoussi, personal communication). By adhering carefully to this approach, any significant ureteral damage can be avoided. The UAS facilitates rapid and repeated passage of the ureteroscope, excellent fluid drainage from the kidney, low intrarenal pressure, and spontaneous expulsion of stone fragments during lithotripsy.

### Flexible ureteroscopy (Video 15.2c)

After the UAS is in position, its internal obturator is removed; the surgeon may or may not elect to remove the super-stiff guidewire at this point. If the guidewire has been coiled in the upper pole, it is advantageous to leave it in place as a guide to the upper pole provided that the sheath is large enough to accommodate the guidewire and the flexible ureteroscope. The flexible ureteroscope is advanced through the UAS into the renal pelvis and up into the upper pole calyces. If a stone is blocking the way to the upper pole, then the holmium laser is used to fragment a portion of the stone until a path to the upper pole has been created along which the flexible ureteroscope can then be manipulated into the upper pole calyces.

## Step 3: nephrostomy puncture

### Air nephrogram (Video 15.3a)

Air (3–5 ml) is slowly instilled through the irrigation port of the flexible ureteroscope under fluoroscopic control. Since the patient is in a prone position, the air will flow into a posterior upper pole calyx. The ureteroscope is moved into the air-filled upper pole posterior calyx that is most in line with the upper pole infundibulum and the renal pelvis. In some situations a posterior calyx in the lower pole or a posterior calyx in the midzone of the kidney may be targeted if the situation warrants it (i.e. a bifid system with a lower pole branched calculus).

### Nephrostomy puncture under direct endoscopic visualization (Video 15.3b)

With the C-arm in a cephalad–caudal position (10–15°) for an upper pole puncture (or 10–15° caudal–cephalad for a lower pole approach), the tip of a hemostat or Kelly clamp is fluoroscopically positioned over the tip of the previously positioned ureteroscope in the targeted posterior calyx; if a rib appears to be obstructing the intended path, then the fluoroscope may be moved to a more anteroposterior position or it can be moved further oblique until the rib is no longer overlying the needle's path. A 3 mm horizontal incision is then made in the flank.

Now an 18G percutaneous nephrostomy needle is manipulated under fluoroscopic guidance until it lies "hub over tip" directly in line with the tip of the flexible ureteroscope, which rests in the targeted air-filled posterior calyx. The entire shaft of the needle should appear as a "radiopaque dot" since the entire length of the needle should now be in alignment with the fluoroscopic view. The needle is then advanced toward the tip of the ureteroscope; the goal is for the needle to enter the collecting system directly in front of the tip of the ureteroscope. After the needle has been passed 5–6 cm into the body, the fluoroscope can be rotated 25–30° laterally (i.e. "rainbowed") thereby visualizing the shaft of the needle such that the point of the needle can be monitored as it is advanced toward the tip of the ureteroscope. The entry of the needle into the collecting system should occur as the needle's point crosses the tip of the ureteroscope. If the needle's point is not visualized by the ureteroscope at that time, then there is no reason to advance the needle any deeper; instead the needle is withdrawn, repositioned, and passed a second time, again aiming directly at the front edge of the tip of the ureteroscope. Ideally, the needle's point should be seen to enter the collecting system at the periphery of the papilla or through the fornix. If the needle traverses the infundibulum, it should be left in place and a second needle passed such that it enters the collecting system properly. (Note: if the transinfundibular needle is removed, bleeding sufficient to obscure the field may occur. Also, dilating an infundibular tract runs the risk of significant hemorrhage.)

## Step 4: establishing through-and-through flank to urethral meatus guidewire access

The obturator of the needle is removed. Next, as described by Hoenig et al., a 2.4 Fr nitinol stone basket is passed through the ureteroscope, opened, and advanced over the tip of the nephrostomy needle [24]. A 145 cm guidewire in females, or a 260 cm exchange guidewire in males, is advanced through the nephrostomy needle; the basket is slowly slid off of the needle and then closed on the tip of the guidewire. The guidewire and ureteroscope are then withdrawn through the UAS thereby establishing the through-and-through guidewire.

An alternative method (i.e. the St. Petersburg maneuver as suggested to us by Dr. Nariman Gadzhiev; Video 15.4) is to pass the 145 cm (in females) or 260 cm (in males) 0.035 inch guidewire directly through the ureteroscope and into the open lumen of the nephrostomy needle and then out the flank. This technique eliminates the use of the stone basket, avoids having to withdraw and pass the ureteroscope through the sheath again alongside the guidewire, keeps the ureteroscope aligned on the nephrostomy site for subsequent monitoring of placement of the balloon dilator and the 30 Fr Amplatz sheath, and has the flexible end of the guidewire exit the needle, thereby allowing it to be used for placement of the stent at the end of the procedure.

## Step 5: tract dilation (Video 15.5)

Once through-and-through guidewire access is established, the initial flank incision is extended to 1 cm to accommodate the 30 Fr Amplatz working sheath. A 5 mm fascial incising needle (Cook Urological) is passed over the through-and-through guidewire to incise the lumbodorsal fascia; this precludes buckling of the dilating balloon. Next, under endoscopic visualization, a 10 mm dilating balloon catheter is advanced over the through-and-through guidewire until the balloon just enters the calyx. The balloon is inflated to 16 atm using the Leveen syringe; this too is monitored endoscopically along with a single shot of fluoroscopy to make sure the entire length of the balloon has been fully inflated. The 30 Fr Amplatz working sheath is advanced over the pressurized inflated balloon until the full circumference of the edge of the sheath is seen to enter the collecting system. The dilating balloon is deflated and removed. Now the ureteroscope is removed from the UAS to allow maximum drainage of fragments and irrigant. The rigid nephroscope is passed via the Amplatz sheath into the collecting system and, if stone is not blocking the nephroscope, the position of the UAS is checked. If the opening in the UAS is not in the renal pelvis, then the UAS's obturator is replaced, and under nephroscopic control the sheath is manipulated upward until it rests in the renal pelvis. The surgeon can now proceed with the PCNL.

## Discussion

The combined endoscopic-fluoroscopic approach has the potential to enable the majority of urologists to obtain their own percutaneous access with the highest degree of precision. Previous studies have shown that exclusively using an image-guided approach, be it fluoroscopy or ultrasound, a resident would need to perform 25 and 60 procedures to overcome the learning curve and achieve technical proficiency, respectively [16, 25, 26]. As such, it is not surprising that only 11–16% of urologists in the United States routinely obtain their own access for PCNL [27].

### Advantages

Establishing an antegrade percutaneous nephrostomy using a combination of limited fluoroscopy and endoscopic guidance has many advantages (Box 15.3). First, the surgeon is able to be certain that the needle enters a posterior calyx through the periphery of the papilla or at the edge of the fornix, which are the least vascular points of access. Also the endoscope-assisted technique allows for precise placement of the dilating balloon and positioning of the Amplatz sheath, thereby minimizing parenchymal injury/bleeding due to past-pointing of the balloon dilator or the Amplatz sheath. Further, this approach facilitates placement of a through-and-through guidewire. In addition, by using the ureteroscope and holmium laser, stones blocking or filling the targeted calyx can be cleared prior to needle placement thereby avoiding the situation where the Amplatz sheath is short of the collecting system and irrigant is flooding the retroperitoneum. Moreover, the UAS provides for easy passage of the ureteroscope as well as for drainage of stone fragments and the maintenance of low intrarenal pressures. Ureteroscopy can also be used to inspect those calyces juxtaposed to the nephrostomy tract that would be inaccessible to the flexible nephroscope; this obviates the need for placing a second nephrostomy tract in many cases. Indeed, the flexible ureteroscope is capable of accessing over 95% of the calyces allowing for movement of stones from a remote calyx into the renal pelvis for rapid removal with the rigid nephroscope [28–30]. Lastly this approach is also optimal for obtaining access in the face of a nondilated or markedly distorted collecting system.

Several publications have corroborated the foregoing advantages of the endoscopically assisted approach to nephrostomy tract placement and dilation. Scoffone and colleagues demonstrated the utility of combined retrograde intrarenal surgery with PCNL, reporting needing only single tract access in 98.4% [31]. Similarly, Sountoulides and colleagues demonstrated that compared to fluoroscopic access, combined endoscopy-/fluoroscopy-guided PCNL required significantly fewer access tracts to remove the stone and required fewer subsequent second-look procedures to achieve the same stone-free rate [32]. More recently, Isac and colleagues similarly reported significantly fewer access tracts and secondary procedures when endoscopic guidance was used to obtain renal access [33].

### Reducing radiation exposure

Both patients and healthcare providers are exposed to a significant dose of ionizing radiation during diagnosis, management, and follow-up of stone disease [34]. The endoscopically guided PCNL reduces radiation exposure in comparison to standard PCNL. A contemporary retrospective review of 55 endoscopically guided PCNL cases by Lantz and colleagues revealed that the radiation

**Box 15.3 Advantages of endoscopically assisted fluoroscopic guided percutaneous renal access.**

1) Endoscopic visualization allows for direct visual confirmation that the targeted papilla is posterior.
2) The ureteroscope tip is readily visible on fluoroscopy, providing a clear target for the nephrostomy needle.
3) Increased success of supracostal renal access [32].
4) Reduced fluoroscopy time [33].
5) Visual confirmation of needle placement through the periphery of the papilla or the edge of the fornix.
6) Accurate monitoring of balloon dilation and 30 Fr sheath placement, thereby eliminating injury to the anterior collecting system or to the infundibulum (i.e. no past-pointing).
7) Facilitates securing through-and-through guidewire access.
8) Ability to combine antegrade and retrograde endoscopic manipulations within the collecting system.
9) Retrograde endoscopic access allows entry to portions of the collecting system that cannot be attained readily through the antegrade access.
10) May reduce the learning curve for percutaneous renal access.
11) Decreased risk of pleural effusions requiring drainage [40].
12) Decreased bleeding complications requiring transfusion [32].

dose was reduced by 50–75% versus standard PCNL, regardless of body mass index [28, 35]. Two similar retrospective studies corroborated these findings, revealing a 50–90% reduction in radiation exposure compared with a standard PCNL [23, 32]. These reductions may be further augmented by using low-dose, pulsed fluoroscopy [29, 30]. In 2014, Baldwin et al. reported successful fluoroscopy-free ureteroscopy, showing that tactile feedback, direct visualization, and external visual clues may act as a reliable substitute to fluoroscopy during routine ureteroscopy in selected patients [36]. Applying this approach to PCNL, Alsyouf and colleagues used ultrasound-guided endoscopically assisted PCNL in 20 patients; their results showed comparable operative times, blood loss, and stone-free rates to standard PCNL while reducing radiation exposure by 99% and in some cases eliminating the need for fluoroscopy entirely [37].

### Limitations

There are several drawbacks to endoscope-guided renal access. First, one person (e.g. another surgeon, resident, surgical assistant, etc.) is needed to hold the ureteroscope in position while the operating urologist passes the nephrostomy needle into the collecting system. Second, the use of a UAS and a flexible ureteroscope adds to the equipment and thus the expense of a PCNL procedure. Furthermore, use of an UAS has generated some concern as its passage may result in iatrogenic ureteral injuries [38]. However, large cohort prospective studies have demonstrated that when the appropriately sized access sheath is positioned without excessive force, the incidence of acute injury is minimal [39]. Further there has been no documented increase in post-ureteroscope strictures when the UAS was used [40]. Finally, endoscopically guided PCNL increases the overall operative time by an average of 10–19 minutes [32, 33].

### Complications

The most common complications following PCNL include pleural injury, bleeding, urinary tract infection, fever, and sepsis. Most of the bleeding events are associated with poor placement of the nephrostomy needle followed by tract dilation (i.e. infundibular or lateral to the calyceal fornix). The endoscope-guided percutaneous renal access assures a more precise placement of the needle and hence has led to reduced blood loss and transfusion requirements [32, 41]. Also, while supracostal access is associated, in some series, with a higher stone-free rate, concerns over pleural effusions has limited its use [42, 43]. In this regard, recent studies have shown that pleural effusions with the need for chest tube placement occur significantly less after endoscopically guided PCNL [32]. To date, there are no studies, to the best of our knowledge, examining the infectious complications after an endoscope-assisted versus a totally fluoroscopic percutaneous nephrostomy.

## Conclusion

PCNL is a well-established and effective treatment modality for the management of large kidney stones. Endoscope-assisted fluoroscopic guided percutaneous nephrostomy can enhance the safety and efficacy of PCNL by reducing radiation exposure, improving stone clearance rates and reducing complications while making the procedure more accessible to the urologic community. However, these benefits come at the cost of increased instrumentation, work force, and operative time.

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# 16

# Percutaneous Nephrolithotomy Access Under Ultrasound

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## Introduction and indications for ultrasound-guided renal access

Percutaneous renal access can be achieved with either ultrasound or fluoroscopy guidance. The method of choice depends on training and personal preference. The side effects of extensive radiation during therapeutic procedures are wellknown, which is the main drawback of fluoroscopy [1]. Ultrasound has several strengths as an interventional tool. It is readily available, relatively inexpensive, and portable. It emitsno radiation and provides guidance for access in multiple, transverse, longitudinal, and oblique planes. Its greatest advantage is use for real-time monitoring of the needle tip, which guides proper placement of the needle and avoidance of important viscera. An added advantage is that it can be used in conjunction with Doppler to avoid important vascular structures lying along the needle path.

Percutaneous ultrasound-guided access is the simplest and most direct technique to drain a hydronephrotic collecting system. It is most often utilized to place a temporary urinary diversion because of an obstructing stone or pyonephrosis. It has also been used successfully to relieve upper tract obstruction secondary to malignancy. Ultrasound-guided nephrostomy puncture is preferred for patients in whom retrograde ureteral access is unsuccessful. It is also a method of choice in pregnancy when there is a need for deobstruction. Allergies to topical or injectable local anesthetic and coagulopathy are the only relative contraindications to ultrasound-guided renal access [2].

The ultrasound-guided approach has proven to be safe and efficacious in the pediatric population [3], for renal stones in transplanted kidneys [4], and in pelvic renal ectopia [5].

Contemporary issues regarding ultrasound as a method to guide access are:

- Who should achieve access:urologists or radiologists?
- How should they be trained?
- Is there is any difference in the outcome for ultrasound- and fluoroscopy-guided access?
- What should be the technique forachieving access? Ultrasound versus fluoroscopy?

In this chapter, we discuss these issues in light of the existing literature. We also describe our technique of achieving percutaneous renal access with ultrasound.

## Instrumentation

### Types of transducer

The "transducer," or "scanning probe" as it is known, is the most important and expensive component of the ultrasound machine. The transducer emits ultrasound pulses and receive echoes during scanning. Ultrasound access requires a dedicated transducer with an ultrasound frequency ranging from 3.5 to 5.0 MHz. The monitor used for intervention should ideally be equipped with an electronic dotted line which shows the needle path. The needle guide that is attached to the ultrasound transducer helps preventdisplacement of the needle from its proper trajectory.

**Sector probes**

The scans from these probes are fan shaped. These scanners can be used when the space for scanning is narrow as they show a very small acoustic window, and are primarily used in gynecologic and cardiac ultrasound. They can be useful when performing nephrostomies in the pediatric age group.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

#### Convex probes

These probes produce rectangular scans and are most commonly used for gaining percutaneous renal access.

#### Linear array probes

These probes are most commonly used for scanning the breast and thyroid.The ideal transducer for renal access is a convex transducer of 3.5 MHz, focused at 7–9 cm. If such a transducer is not available, then either a linear or sector transducer of 3.5 MHz is necessary. If children or thin patients are to be scanned, then a 5 MHz smaller transducer with a focus at 5–7 cm is required. Alternatively, a sector probe can be used in this situation (Figure 16.1).

### Access needles

Using an 18G needle to access the renal collecting system helps with the introduction of a 0.035 or 0.038 inch guidewire into the collecting system. When ultrasound-guided access is to be achieved, the rigidity of the 18G needle compared to the 21G needle is advantageous for accurately directing the needle tip as it is advanced through the fascial planes. The 18G needle tip is also readily identifiable with realtime ultrasonography guidance.

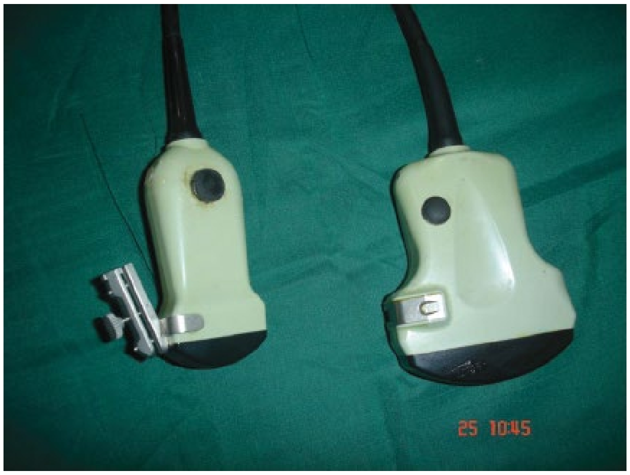

**Figure 16.1** Smaller probes help in gaining access in children. The puncture guide attachment helps direct the needle.

Although routine needles can be used for this purpose, the echo tip needle (Cook Medical, Bloomington, IN, USA) is helpful in achieving ultrasound-guided access; the needle tip is scored and this increases the reflectivity and visualization on ultrasound. The needles are available in three or two parts (Figure 16.2). The three-part needle is useful for instilling contrast after ultrasound-guided puncture as the needle does not need to be removed from the puncture guide. Another variant of the needle has a Teflon sheath which allows instillation of contrast and a guidewire.

## Ultrasound technique

### Orientation and calibration of the image

Before starting, it is necessary to visually check which side of the transducer produces which side of the image. Although most of the times there is an indicator on the ultrasound probe for orientation, this is best done by placing a finger at one end of the transducer and seeing where it appears on the screen; if the orientation is incorrect, the transducer should be rotated through 180°. On a renal scan the liver or spleen helps in orienting the upper pole.

The machine should be calibrated properly before use and in such a way that there is a black background with white echoes [6].

### Needle visualization

Clear visibility of the needle is key to the success of ultrasound-guided needle access (Figure 16.3). The most common reason for nonvisualization of the needle tip is nonalignment of the needle tip and transducer. This can be achieved by proper alignment. Although alignment is challenging when done freehand, it will improve with experience and occasionally a mechanical attachment can be used [7].

If the needle is not visualized it may be either off-center or angled away from the transducer. A “bobbing” or “in–out jiggling” movement of the tissue in the superficial

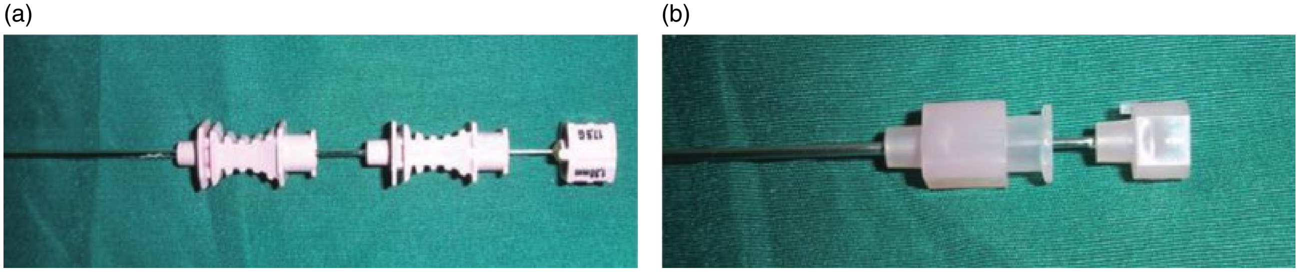
(a) (b)

**Figure 16.2** (a) Three- and (b) two-part needle.

plane helps decide the path of the needle. This movement also helps push the soft tissue away from the needle path and clear visualization of the needle[7].A few other ways in which the needle can be better visualized are by increasing the reflectivity by using large caliber needles, scoring the needle tip (see above), and keeping the bevel of the needle facing upwards.

### Ultrasound-guided access with a needle guide

This is the method of choice for ultrasound-guided access at our center. We use the 3.5/5 MHz probe (Profocus™, B & K Medical, Denmark) with a Doppler attachment. We typically keep one bolster under the patient's lower chest and the other at the level of the iliac crest. We consider that with the patient in the prone position and bolsters in these positions, the bowels and viscera tend to drop down, thus minimizing the chance of bowel injury.

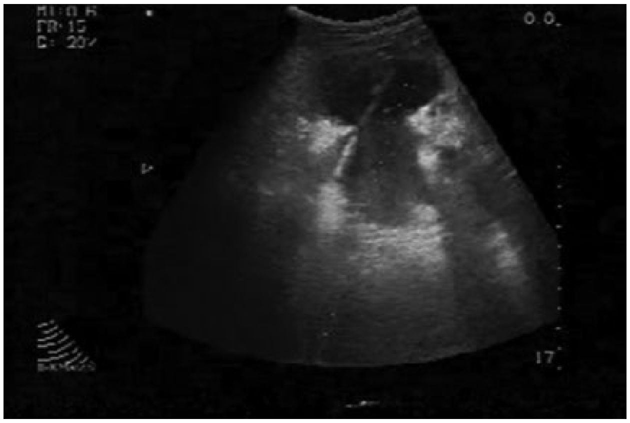

**Figure 16.3** If the needle is aligned properly, then the shaft of the needle is visualized throughout its course.

Ultrasound scanning commences posteriorly and proceeds until the posterior axiliary line. If scanned in this way, the first calyx to be seen will be the posterior calyx. The site of needle entry is marked and the puncture performed with an 18G echo tip (Cook Medical) needle. The key point at this crucial step is that there should be minimal respiratory and ultrasound probe movement. In order to ensure an accurate puncture, the needle tip should be seen along the electronic dotted line throughout its course. The position of the needle in the desired calyx is confirmed with return of clear fluid.

The attributes of a perfect renal access are shortest possible route and a straight tract, traversing the skin, cortex of the kidney, and cup of the desired calyx of puncture (Figure 16.4). We consider that ultrasound-guided access maximizes the chances of this. We have been successfully performing access with ultrasound guidance in percutaneous nephrolithotomy (PCNL) with patients in the supine position; this has also been performed in the pediatric population [8, 9].

### Ultrasound access without a needle guide

Someultrasound transducers do not possess an electronic dotted line or puncture guide. The operator places the probe and scans the relevant renal unit. The probable path of the needle is marked and access is gained. Alternatively, in grossly hydronephrotic kidneys, the ultrasound probe helps with access in the paraspinal area, which is used for opacification of the pelvicalyceal

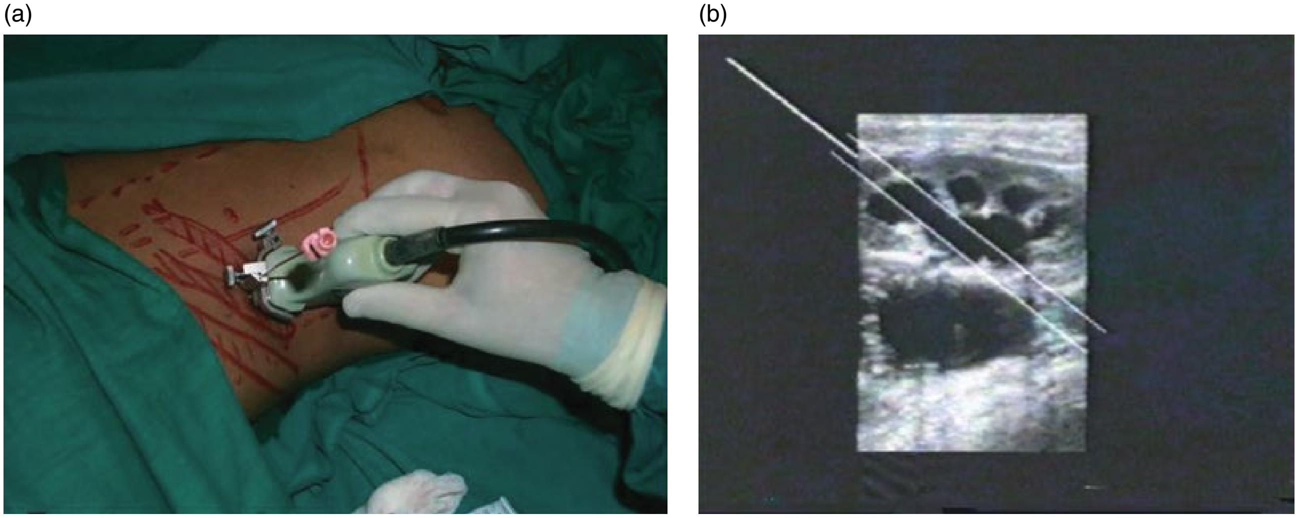

**Figure 16.4** (a) The puncture guide helps in directing the needle in the desired plane and to the correct depth. (b) The ultrasound probe should be aligned in such a way that the tract provides the shortest access from the skin through the cup of the calyx, infundibulum, and finally into the pelvis.

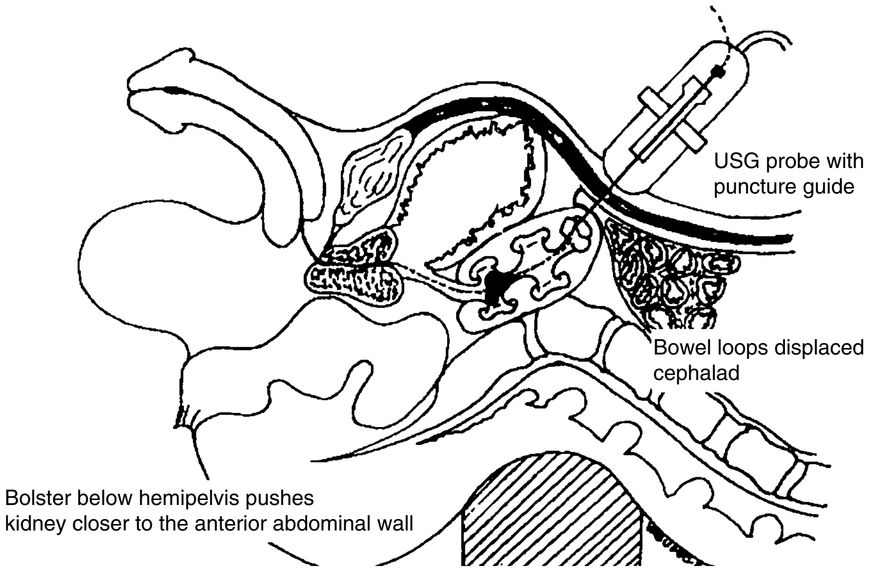
USG probe with puncture guide
Bowel loops displaced cephalad
Bolster below hemipelvis pushes kidney closer to the anterior abdominal wall

**Figure 16.5** Technique of ultrasound-guided puncture of a pelvic ectopic kidney. USG, ultrasound guided. Reproduced with permission of Mary Ann Liebert, Inc. Publishers.

system and subsequent fluoroscopically guided puncture in a appropriate calyx.

The serious limitation of the technique is that although the ultrasound probe shows the kidney and calyces, the image is devoid of depth and does not show the plane of the path that the needle traverses; as a result the chance of visceral injury increases. Ultrasound-guided puncture with a Doppler guide is of help in abnormal renal anatomy, such as horseshoe kidney and malrotated kidneys.

## Application of ultrasound in special situations

The various drawbacks of PCNL in the conventional (prone) position include the need to turn the patient from the supine to prone position, risk of tube dislodgments, and neuropraxias. In addition to severe kyphoscoliosis, morbidly obese patients with heart and lung conditions do not tolerate the prone position well. Ultrasound-guided renal access is of value in such situations. Ultrasound-guided punctures are also of value in emergency situations, such as percutaneous nephrostomies in obstructive uropathy in pregnancy [8, 10].

### Ultrasound punctures in ectopic kidneys and transplanted kidneys

The management of calculi in ectopic kidneys is a hotly debated topic, given that a number of treatment modalities, including laparoscopic-guided PCNL, are available. At our center we have been performing PCNL in these cases under ultrasound guidance. Preoperatively the side-to-side mobility and ability to displace the kidney in relation to the abdominal wall is assessed. The site of the puncture is the iliac fossa. A supine oblique position with a bolster under the ipsilateral hemipelvis is used. A mechanical bowel preparation with a low enema is used in all the cases. This helps in identification of gas in the sigmoid colon, which helps identify the bowel and prevents possible injury. Pressure on the ultrasound probe helps to displace the intervening bowel loops between the puncture line and targeted calyx. Similarly, contralateral pressure applied by the assistant helps displace the kidney close to the abdominal wall. All these maneuvers improve the chances of achieving a straight, short, and direct tract to the desired calyx (Figure 16.5).

PCNL is feasible in transplanted kidneys with the help of ultrasound-guided access and this decreases the amount of radiation and intravenous contrast required. With the patient in a left-sided oblique position with a bolster under the ipsilateral hip, the bowel is displaced and a puncture into the superior calyx provides easy access to the ureteropelvic junction and stone in the pelvis [4].

## Preceptorship and mentoring

Competence in ultrasound-guided renal access requires a learning curve to be overcome. The mentoring should start from the residency training itself. At our center training is structured. The trainee initially performs the ultrasound in the outpatient department; later, in the first year of training, they perform ultrasound-guided percutaneous nephrostomies in grossly hydronephrotic systems, and by the end of third year they perform ultrasound-guided punctures for PCNL for renal calculi. We believe this approach shortens the learning curve by giving the trainee insight into the intricacy of aligning the needle with the transducers.

A variety of models have been described for training in ultrasound. Häcker et al. have developed the biologic model using a chicken carcass and fresh *ex vivo* porcine kidney. The laboratory model used routine PCNL equipment. For imaging, ultrasound (7.5 MHz) and a fluoroscopy unit are necessary. This model simulates realistically the clinical procedure of PCNL under ultrasound guidance. In addition, it is low cost and takes little time to prepare, and there are no legal issues involved. The drawback of this model is that it gives no tissue feel and lacks simulation of respiratory movement [11]. Mozer et al. described a system in which the ultrasound image was projected on fluoroscopy. The system consisted of a computer and localizer, allowing spatial localization of the position of the various instruments. Without any human intervention, the ultrasound nephrostomy tract is superimposed in realtime onto fluoroscopic images acquired in various views. In this study the possibility of fusing images derived from two imaging sources was explored[12].

## Urologist or radiologist?

Many urologists do not perform percutaneous access routinely, especially in the United States and some parts of Europe. Despite evidence that urologists can safely acquire percutaneous renal access for PCNL, many centers still rely on interventional radiologists to obtain renal access. In our opinion, the urologist is better suited for making the access. Apart from being technique oriented, their insight into the disease process helps improve outcome.

El-Assmy et al. studied access achieved by a urologist with that by a radiologist; both groups of patients were comparable demographically except that the group treated by the urologist had a higher risk of multiple stones and multiple tracts. The stone-free rates and complication rates were comparable. Multivariate analysis showed that bleeding was not related to whether access was performed by a urologist or radiologist. They concluded that urologists can safely and effectively obtain percutaneous renal access for PCNL as a single-stage procedure [13]. Another study revealed that despite similar access difficulty between groups, access-related complications were less and stone-free rates were improved when a urologist acquired percutaneous access. Urologists trained in percutaneous access may be able to provide improved stone-free rates during PCNL while minimizing access-related complications [14].

To accomplish this, it is essential that the urology residency program should include training in the technique of percutaneous access, as recommended by El-Assmy et al. [13]. It is important to recognize that PCNL has a relatively long learning curve. The fact that kidney puncture and access is a major step for PCNL success highlights the importance of training urologists in this surgical step [15].

## Ultrasound versus fluoroscopy

Access to the renal collecting system with fluoroscopy has the disadvantage of inability to visualize surrounding structures, such as bowel or solid organs, and need for cystoscopy and retrograde contrast instillation for opacification of the system (see also Chapter 12). Percutaneous access with fluoroscopic guidance is more challenging than with ultrasound guidance [16]. The ultrasound-guided approach is safe with a very low risk of major complications. We consider ultrasound is more precise in achieving access, at times, as all the calyces are not filled on opacification.

Level 1 evidence comparing ultrasound and fluoroscopy is scant. In a clinical trial, 100 patients with no abnormality of the upper urinary tract were selected from among candidates for PCNL and randomly assigned to two 50-patient groups: ultrasound-guided access (group 1) versus fluoroscopy-guided access (group 2). Duration of the access procedure was 11 ± 3.5 minutes and 5.5 ± 1.7 minutes in groups 1 and 2, respectively ($P = 0.0001$). Duration of radiation exposure, on average, was 0.69 ± 0.26 minutes and 0.95 ± 0.44 minutes, respectively ($P = 0.0001$). They concluded that access for PCNL using ultrasound guidance is an acceptable alternative to fluoroscopy and decreases radiation hazards [17].

Zegel et al. compared 55 patients with ultrasound access with 33 patients with fluoroscopy access. A significantly reduced number of puncture attempts was noted with ultrasound-guided access (1.2 vs. 4.1) [18], thus significantly reducing the length of time for the procedure.

In our study comparing the two methods of access, the decrease in hemoglobin and hematocrit was significantly less in the ultrasound group [3]. The number of attempts required to achieve a successful puncture was also significantly less in the ultrasound group.

Ultrasound-guided access has also been described in the nondilated system [19, 20]. The fluid infusion

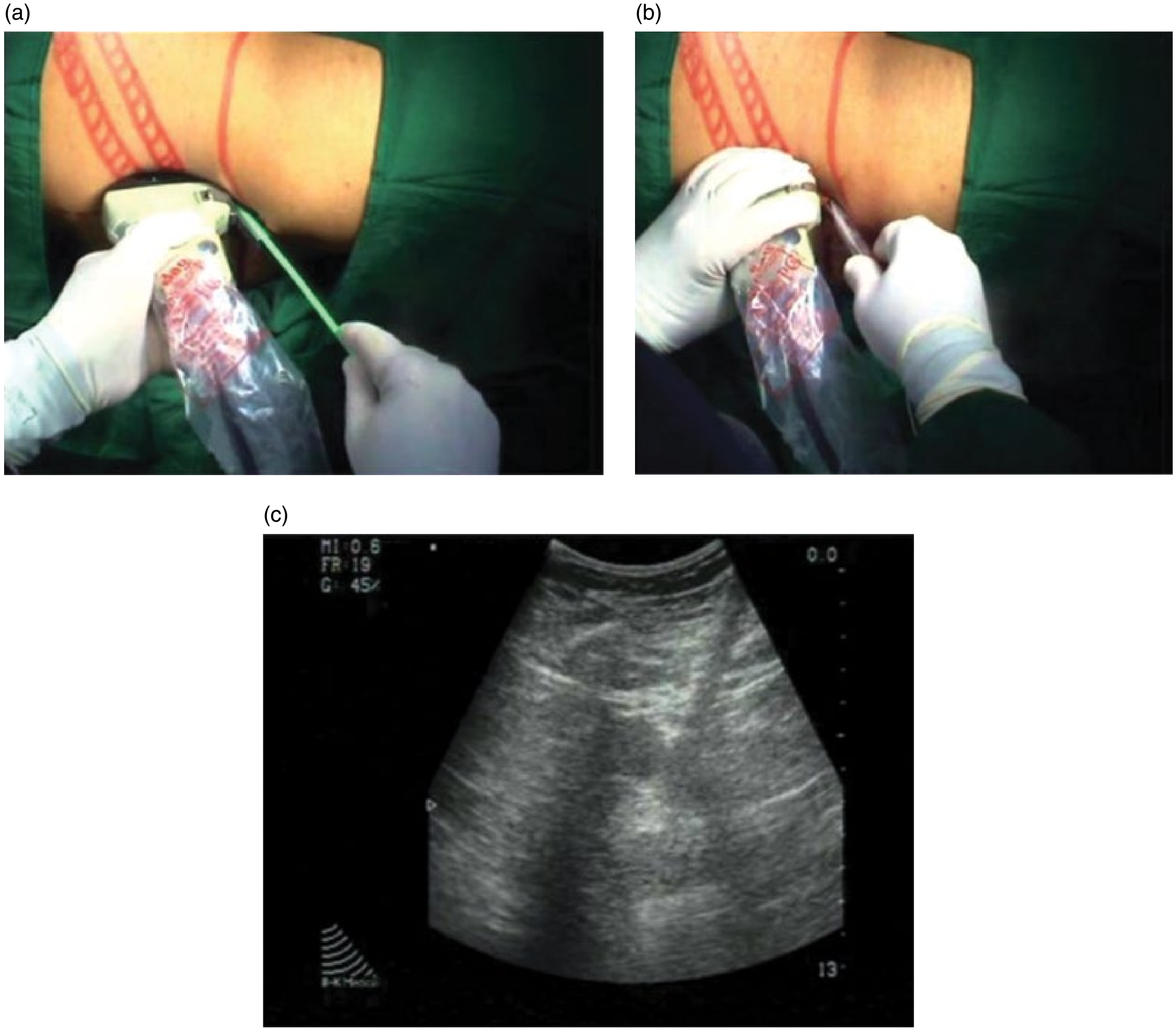

**Figure 16.6** (a) Puncture is performed under ultrasound guidance. (b) The tract is dilated under real-time ultrasound guidance with a balloon dilator. (c) The balloon can be seen under real-time ultrasound guidance.

technique used to make the pelvicalyceal system more prominent has been described to achieve access in such situations [21]. Total ultrasound-guided PCNL has been described [22]. The authors describe that while gaining access the transducer is placed posteriorly whereas during dilation it is placed on the anterior abdominal wall for better visualization of the dilators. Anterior placement is possible as the patients are placed in the flank position. Although feasible, this procedure requires significant experience and the dilators must be visualized throughout the procedure to avoid under- or overdilation (Figure 16.6).

## Conclusion

The role of ultrasound and fluoroscopy are synergistic. Ultrasound-guided access is the method of choice in deobstruction of the upper tract in failed retrograde access, malignancy, and pregnancy. It also helps in PCNL in transplanted or ectopic kidneys. This technique requires considerable experience and training in it should be structured and begin in residency.

Video 16.1 demonstrates the technical aspects of gaining ultrasound-guided access to the collecting system.

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## 17

# New Concepts of Renal Access: iPad, GPS, and Others

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## Introduction

Nephrolithiasis is a common clinical problem, and its prevalence has increased over the last 30 years [1]. In the United States, it has a prevalence of 8.8%, affecting one in 11 people, being more prevalent in males (10.6%) than in females (7.1%) [2]. Given the high prevalence of this disease, various forms of treatment have been developed and applied over time [3], such as open surgery, percutaneous nephrolithotomy (PCNL), extracorporeal shock-wave lithotripsy, and, more recently, flexible ureterorenoscopy [4, 5]. However, of all these forms of treatment, PCNL, first described in 1976 by Fernstrom and Johansson [6], is the best for bulky kidney stones [7, 8]. The guidelines of the European Urology Association recommend PCNL for the treatment of renal calculi larger than 2 cm and lower pole renal calculi larger than 1.5 cm [7]. PCNL comprises several main steps: insertion of a ureteral catheter in the renal pelvis with dilation of the pyelocaliceal system, percutaneous puncture of a renal calyx, passage of a guidewire, tract dilatation, placing of Amplatz sheath, nephroscope introduction and ultimately, calculi fragmentation and fragments removal [9]. In all these surgical steps, percutaneous puncture of the renal collecting system is the most difficult step, which causes more complications and which influences more the subsequent success of the procedure [10, 11].

Fluoroscopy and ultrasound, alone or combined, are the most used methods to guide the puncture of the renal collecting system [12]. However, these methods have a steep learning curve and continue to be a major cause of morbidity [10, 11]. To overcome these important limitations, new methods and techniques have been introduced to improve the quality of renal puncture during PCNL, since the modification of patient position to the use of new instruments to guide the puncture [13]. These methods include an optical system incorporated into a needle [14]; marker-based Apple iPad-assisted puncture [15–17]; puncture assisted by electromagnetic sensors [15, 16, 18, 19]; laser-assisted puncture through three-dimensional (3D) computed tomography (CT) using Uro Dyna-CT [15, 16, 20]; and ultrasound using the SonixGPS navigation system [21, 22]. The increasing use of computer programs to assist in the use of these new approaches should be noted.

This chapter will review the new techniques developed for puncture of the renal collecting system, in order to verify the advantages and disadvantages of each and understand which technique has the greatest potential to become the future gold standard of PCNL.

## Classic techniques for renal collecting system puncture: fluoroscopy and ultrasound with direct endoscopic visualization

Classic percutaneous access techniques to the renal collecting system in PCNL comprises, most commonly, the use of fluoroscopy and ultrasound [8]. Fluoroscopy and ultrasound can be used alone or in combination, acting as if in synergy [23–25]. When using fluoroscopy, the procedure begins with placing a urethral catheter in the renal pelvis to opacify and extend the pyelocaliceal system [23]. The image obtained by this method allows an excellent characterization of the renal excretory tree in real time, but has the disadvantages of giving a view

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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only in two dimensions (2D), causing exposure to ionizing radiation, and being highly dependent on the technical skills of the surgeon [23, 26]. Ultrasonography is a technique that allows real-time direct visualization of the structures involved in the puncture, being useful to prevent damage to adjacent structures in addition to serving as a guide to the needle, and it has also the advantage of there being no exposure to ionizing radiation. However, as with fluoroscopy, it is highly operator-dependent, requiring great experience for its correct use, especially in situations involving a lack of expansion of the pyelocaliceal system. In addition, the images are displayed in 2D, and correct visualization of the needle can be impossible in cases of obesity or a patient's anatomical deformities [24, 26]. In an attempt to improve access in PCNL, these two techniques (fluoroscopy and ultrasound) were combined. a combination of these techniques allows a higher success rate. This combination does not eliminate exposure to ionizing radiation, but reduces significantly the radiation exposure time [25].

In an attempt to minimize exposure to ionizing radiation and improve the accuracy of access to the renal collecting system, Alsyouf et al. [27] proposed a technique that involves combining ultrasound with direct endoscopic visualization. In this technique, the surgeon chose the ideal calyx to puncture through real-time visualization by ureteroscopy, wherein ultrasound was used to guide insertion of the needle. The ultrasound identifies the correct calyx through the movement caused by the ureteroscope deflection, and also helps avoid injury of the adjacent anatomical structures. If the needle is not centered in the calyx then small adjustments can be made under direct visualization by ureteroscope. This technique has the advantage of reducing the routine use of fluoroscopy. However, the procedure presents some disadvantages, such as the large technical capacity that is mandatory for ultrasound and the difficulty of its use in obese patients, in patients with anatomical abnormalities, and in poorly dilated pyelocaliceal systems [27].

## New technologies for puncture of the renal collecting system

### Optical system incorporated into a needle

In this system, the needle used to puncture the renal collecting system has an optical system incorporated that allows visualization of the renal collecting system in real time through a monitor, thereby eliminating the use of fluoroscopy. Access to the pyelocaliceal system is obtained by visualization of structures by conventional ultrasound. The skin is punctured in the posterior axillary line, and the punctured calyx is the posterior inferior calyx. This whole process is performed with the patient in the prone position. The optical puncture needle has been used in 15 patients and the objective was to describe the use of a micro-optical system through a specific puncture needle to confirm the quality of the chosen access. The puncture had to be repeated in four of 15 patients [14].

The great advantage (Table 17.1) of using this puncture system is that it allows secure identification of the needle's location within the renal collecting system immediately after entry, helping to clearly identify the position within the renal system, facilitating handling and learning. Thus, it enables fluoroscopy to be dispensed with, and for the procedure to be free of ionizing radiation. Visualization of needle entry is made in real time by ultrasound. On the other hand, this system does not allow the redirection of the needle in cases of path error, and it does not help in creating a correct path to the puncture and it does not improve the quality of access to the puncture, which as we have seen is a very important feature of PCNL (Table 17.1). Other disadvantages (Table 17.1) are also associated with the use of ultrasound, for example the 2D image, difficult visualization in obese patients, and being highly operator-dependent [14].

### Marker-based iPad-assisted puncture system

Prior to the surgical procedure itself, the pioneers of this technique performed a CT with multiple sections, with the patient in the prone position and at the final stage of inspiration, taking into account that this position must be equal to the position of the patient during PCNL. The CT images obtained in this way are analyzed by computer, becoming 3D images of patient anatomy. Thus, any anatomical detail of the patient is shown in 3D, and is useful for surgical planning, including the choice of the puncture site, as a guide during surgery. In order to decide upon optimal access to the collecting system, during preoperative CT five colored radiopaque markers are fixed around the target area for puncture execution [17]. During the course of PCNL, an Apple iPad is used as a camera, computer, and monitor [15, 16]. With the patient under general anesthesia and in the same position in which the preoperative CT was performed, the iPad camera is pointed toward the patient and, using a WiFi network, the images of the patient in surgery transmitted by iPad are merged with the virtual 3D images of the preoperative CT (Figure 17.1). For this merging process, it is necessary that at least four markers are visible to the camera, in order to provide a correct access position. This whole process is continuous and allows an augmented reality of the patient's anatomy, giving a virtual view from inside the patient. Since preoperative CT scan is performed at the end of inspiration, the anesthesiologist must stop the patient breathing at the end of inspiration to allow the puncture to be performed in the

**Table 17.1** Advantages and disadvantages of new renal colleting system punctures techniques.

| Technique | Advantages | Disadvantages |
|---|---|---|
| Optical system incorporated into a needle | Secure identification of the needle's location within the renal collecting system<br>Facilitated handling and learning<br>Technique is free of ionizing radiation<br>Real-time needle visualization on puncture by ultrasound | Does not allow the needle redirection in cases of error trajectory<br>Does not help in creating a trajectory<br>2D image<br>Visualization difficulties in obese patients<br>Operator dependence |
| Marker-based iPad-assisted puncture | Correct selection of the location, angle, and trajectory of the needle<br>3D images<br>Correct visualization of the patient's anatomy<br>Minimal spatial errors<br>Decreased time for puncture of training surgeons | Use of ionizing radiation<br>No real-time 3D image<br>Increased duration of puncture technique in expert surgeons<br>Only minimal adjustments in the path<br>Patient is in prone position |
| Navigation system using electromagnetic sensors | No exposure to ionizing radiation<br>3D image in real time of the needle trajectory<br>Position and orientation of the needle in real time<br>Easier technical learning<br>Significantly reduced execution time<br>Ability to redefine the trajectory<br>It allows the surgeon to make minor adjustments and complex navigation maneuvers<br>The whole procedure can be done in the supine position, thereby decreasing the operating time<br>Increases the comfort level of the patient and the surgeon | Lack of visualization of anatomical structures in the puncture path<br>Placement in the desired calyx of the ureteral catheter with an electromagnetic sensor my be difficult in situations where the calyx is fully occupied by a calculus |
| 3D CT using Uro Dyna-CT | 3D anatomical image<br>Quick, safe, and highly accurate<br>Enables success in complicated cases<br>Demonstration of the trajectory in real time<br>Possibility of trajectory change if the needle position is wrong | Ionizing radiation dose is higher than in conventional techniques<br>Technique hampered by excessive renal motility<br>The learning curve is steeper than for other techniques<br>The cost is higher than for other techniques described<br>Impaired by patient motion |
| Ultrasonography using sonixGPS navigation | No ionizing radiation<br>Needle trajectory prediction<br>Provides information about the depth, location, and needle insertion angle<br>Provides and predicts the tip position of the needle in real time on ultrasound screen<br>The operator can keep track of the needle during the procedure regardless of their location<br>Allows adjustment of the trajectory during the procedure<br>Easier to perform than conventional puncture | In patients with obesity ultrasound images are highly impaired, and the use of fluoroscopy is recommended<br>2D image |

provided space. Then, a puncture is performed using the virtual 3D image provided and a 2D digital fluoroscopy image in real time, to enable final adjustments.

This technique has been performed in a preclinical phase with human phantom with a calculated error of 1 mm. Clinically, it was performed in two patients with complicated nephrolithiasis with indications for PCNL. Both punctures were performed successfully, defined by the needle reaching the desired calyx [17]. Later, the same procedure was performed *in vitro*, which showed a significantly higher time for realization of puncture in expert surgeons, compared with the conventional techniques of fluoroscopy and ultrasound. However, in trainee surgeons the technique significantly reduced the time of exposure to radiation. After the *in vitro* trials the technique was applied in 19 patients and was performed

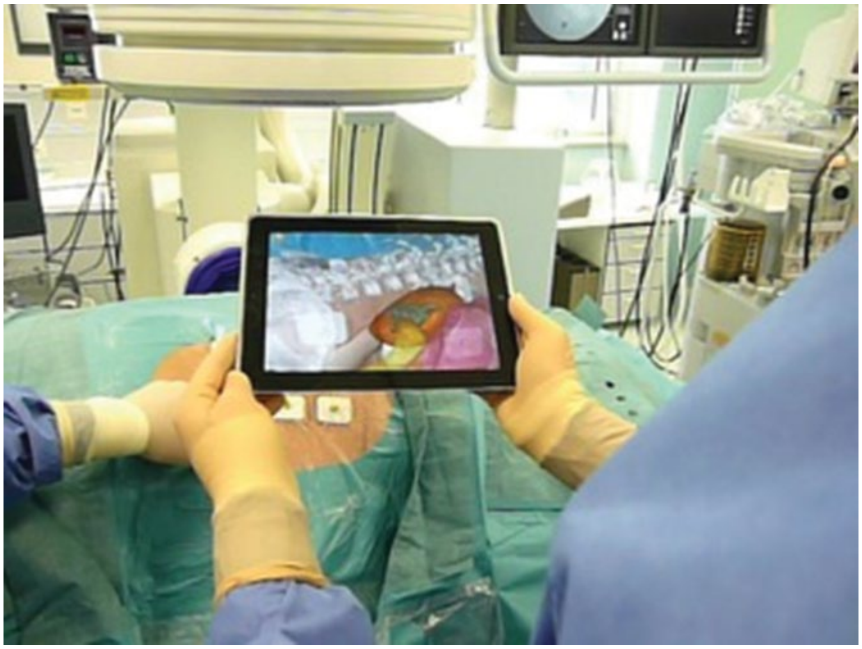

**Figure 17.1** Marker-based iPad-assisted puncture. Determination of the puncture site using an iPad and 2D fluoroscopy.

on the first attempt in 13 of 19 patients (average 1.5) with a radiation exposure dose of 377.5 μGy per m$^2$ [15, 16].

The marker-based iPad-assisted puncture system shows the following advantages (Table 17.1): correct selection of the location and angle to the puncture with good definition of the path, a better anatomical knowledge of adjacent organs with 3D image, correct visualization of patient anatomy regardless of anatomical conformation, minimal space errors, and decreased time to puncture in trainee surgeons. The disadvantages (Table 17.1) are associated with the following: use of ionizing radiation, absence of 3D image in real time, increased puncture duration in expert surgeons, only minimal adjustments in the path, and the patient being in the prone position [17].

## Electromagnetic tracking sensors

This technology was initially tested in *ex vivo* [26] and *in vivo* models [18]. In this last model, pigs were placed in the supine position, an electromagnetic field generator was placed near the pig, and a rigid cystoscope was inserted with the goal of identifying the ureteral opening of the two kidneys. Subsequently, a ureterorenoscopy was performed allowing the placement of a ureteral catheter in the desired calyx. The ureterorenoscope tip was positioned in the desired place to the puncture by direct viewing of a camera. Through an electromagnetic sensor located at the tip of the needle and an electromagnetic sensor located at the tip of the catheter, a virtual path was created from the relative orientation and position information provided in real time by needle and catheter electromagnetic sensors (Video 17.1). Using the 3DPuncture software (created for this project) the virtual path in 3D was shown to the surgeon, which confirmed that the catheter and the needle were aligned in parallel (Figure 17.2). The surgeon can redefined the orientation of the catheter when desired, and a new virtual trajectory calculated when necessary. This procedure provides real-time positioning to the surgeon, allowing a perfect orientation of the needle to be maintained constantly even in the presence of anatomical deformities. The confirmation that there are no unwanted anatomical structures at the puncture path is checked by ultrasound.

Six female pigs were subjected to the indicated procedure, and four punctures were performed by two surgeons in each animal, including one in the kidney and one in the middle ureter, on both sides. In order to certify the technical quality, the number of attempts and the time required for evaluating the virtual path and performing percutaneous puncture were monitored. A total of 24 punctures have been successfully carried out, 12 through the middle ureter and 12 in the renal calyces. To assess the trajectory of the puncture in the ureter took an average of 15 seconds, while in the kidney it took 13 seconds ($P = 0.1$). The average time for the kidney puncture was 19 second, and 51 seconds in the ureter ($P = 0.003$). Between the expert and the trainee surgeon there were significant differences in puncture planning time, with a shorter time for the expert ($P = 0.03$) [18].

Recently, the first clinical experience with a novel navigation system using electromagnetic guidance (IDEAL Stage 1) was described [19]. In this procedure, the patient

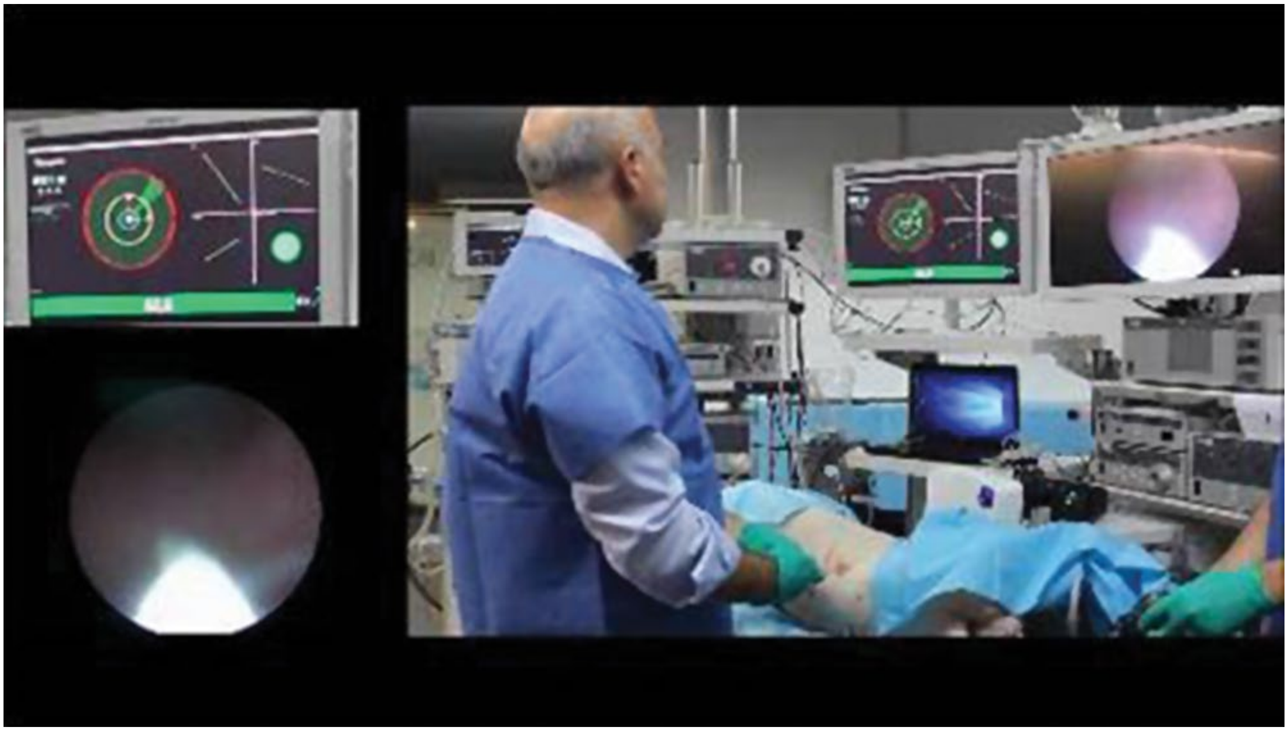

**Figure 17.2** Renal collecting system puncture using electromagnetic sensors. A research group from the University of Minho, Braga, Portugal, patented a new navigation system with an easy-to-use visual system.

is placed in the supine position to allow a combined approach with flexible ureterorenoscopy and percutaneous nephroscopy. An electromagnetic field generator is placed near to the patient to create a field that allows the position of the catheter and needle sensors to be seen. After that, an ureterorenoscope is inserted, with the identification of the ureteral meatus and insertion of a hydrophilic guidewire through it. Next, a digital videoureterorenoscope is inserted, guided by the hydrophilic guidewire to the renal pyelocaliceal system, and the guidewire is extracted. Subsequently, the ureteral catheter with an electromagnetic sensor is inserted through the flexible ureterorenoscope working channel. After choosing the most appropriate renal calyx for percutaneous puncture and carrying out an ultrasound scan in order to verify that the path of renal puncture is not obstructed by any unintended anatomical structure, percutaneous puncture of the selected calyx is done, guided by real-time 3D images observed on the monitor (Figure 17.3). Next, the percutaneous renal puncture tract is dilated, followed by placement of the dilatation balloon and the placement of an Amplatz sheath. This whole process is done without the use of fluoroscopy, only by monitoring of the videoureterorenoscope image. Finally, a nephroscope is inserted via the Amplatz sheath, followed by fragmentation and extraction of renal calculi.

This technique has the following advantages (Table 17.1): lack of exposure to ionizing radiation; real-time 3D image of the needle trajectory; correct needle placement and orientation in real time; greater ease of technical learning (learning curve of 12 cases); execution time significantly decreased; possibility of redefining the trajectory; the catheter was constantly monitored by an electromagnetic sensor and by the fiberscope camera, allowing the surgeon to make minor adjustments and complex navigation maneuvers; real-time monitoring of anatomical changes; the entire procedure could be performed in the supine position, eliminating the need of repositioning, thus reducing the surgery time in 30–40 minutes, while increasing the patient and surgeon comfort levels; no interferences were detected in electromagnetic field. The disadvantages (Table 17.1) associated with this new technique are: as in fluoroscopy, there is a lack of visualization of anatomical structures in the puncture tract, and possible difficult placement of the ureteral catheter bearing the electromagnetic sensor in the desired calyx in situations when the calyx is fully occupied by a calculus [19].

### 3D CT using Uro Dyna-CT

Uro Dyna-CT (Siemens Healthcare Solutions, Erlangen, Germany) corresponds to a modified angiography unit,

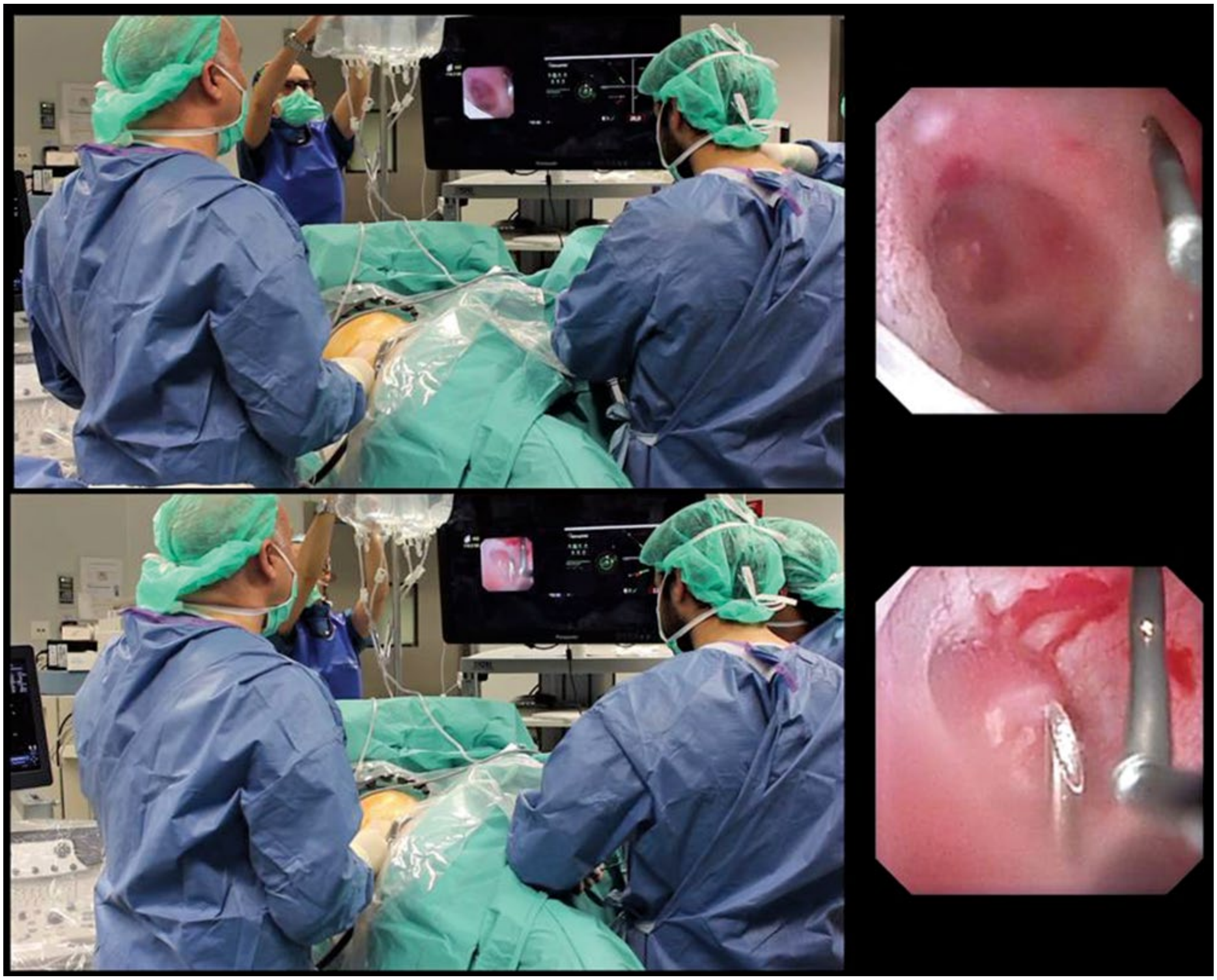

**Figure 17.3** Guided by the 3D navigation software system on the monitor and confirming simultaneously with the ureterorenoscope image, the surgeon performs a puncture of the lower calyx during human PCNL.

allowing the fluoroscopic unit to be rotated around the patient, creating a similar image to the images created by CT (Figure 17.4). The segmentation of the acquired data enables 3D multiplanar reconstruction of the renal collecting system, which is filled with contrast [15, 16]. From a reconstruction of this kind, the best puncture path, avoiding interference from other organs and coming to the desired position, can be created. The planning software shows the exact path chosen for the puncture [15, 16, 20]. The C-arm is placed in the bullseye position to indicate the puncture site and its direction, using a laser light that is oriented (based on the 3D reconstruction) for the path that the needle must take for correct execution of the puncture. Then, the needle is inserted into the predetermined site, keeping it in line with the laser light during the entire procedure to ensure the correct angle. At the end of needle insertion, positioning is confirmed by conventional fluoroscopy. The needle positioning can be corrected if necessary by combining its position with the puncture map displayed on the fluoroscopy screen, in bullseye oblique and lateral view, until the desired target is reached.

The Uro Dyna-CT system allows the surgeon to know the exact position of the table relative to the C-arm at any time, and the map is always available (Figure 17.5). During the puncture of the renal calyx, excretion of fluid through the needle indicates success. In addition, success can be further confirmed with antegrade pyelography under fluoroscopic control. This procedure was applied to 12 patients and was performed by a single surgeon [20]. The cases selected for this technique were instances where the puncture by conventional approach failed or in complex situations. Puncture success was documented and it was successfully performed in nine of the 12 patients (in two patients contrast fluid extravasation occurred and in one the procedure could not be

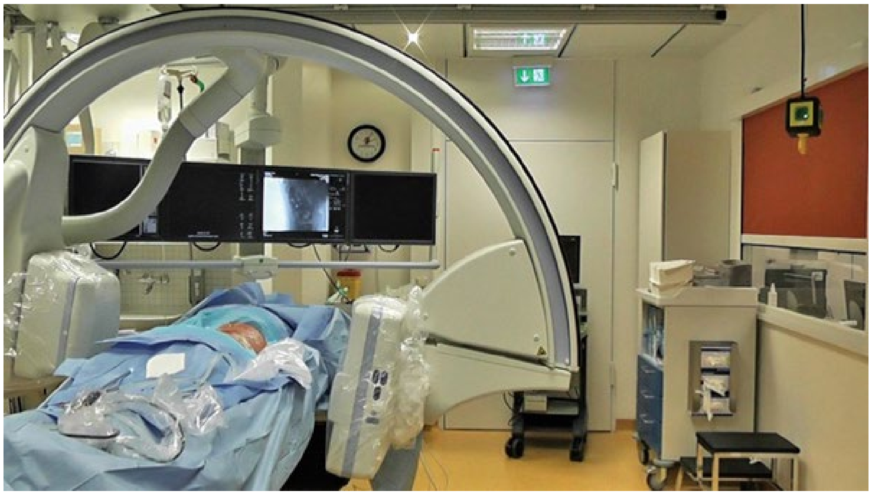

**Figure 17.4** 3D CT using Uro Dyna-CT for laser-assisted puncture during PCNL. Reproduced with permission of Marie-Claire Rassweiler.

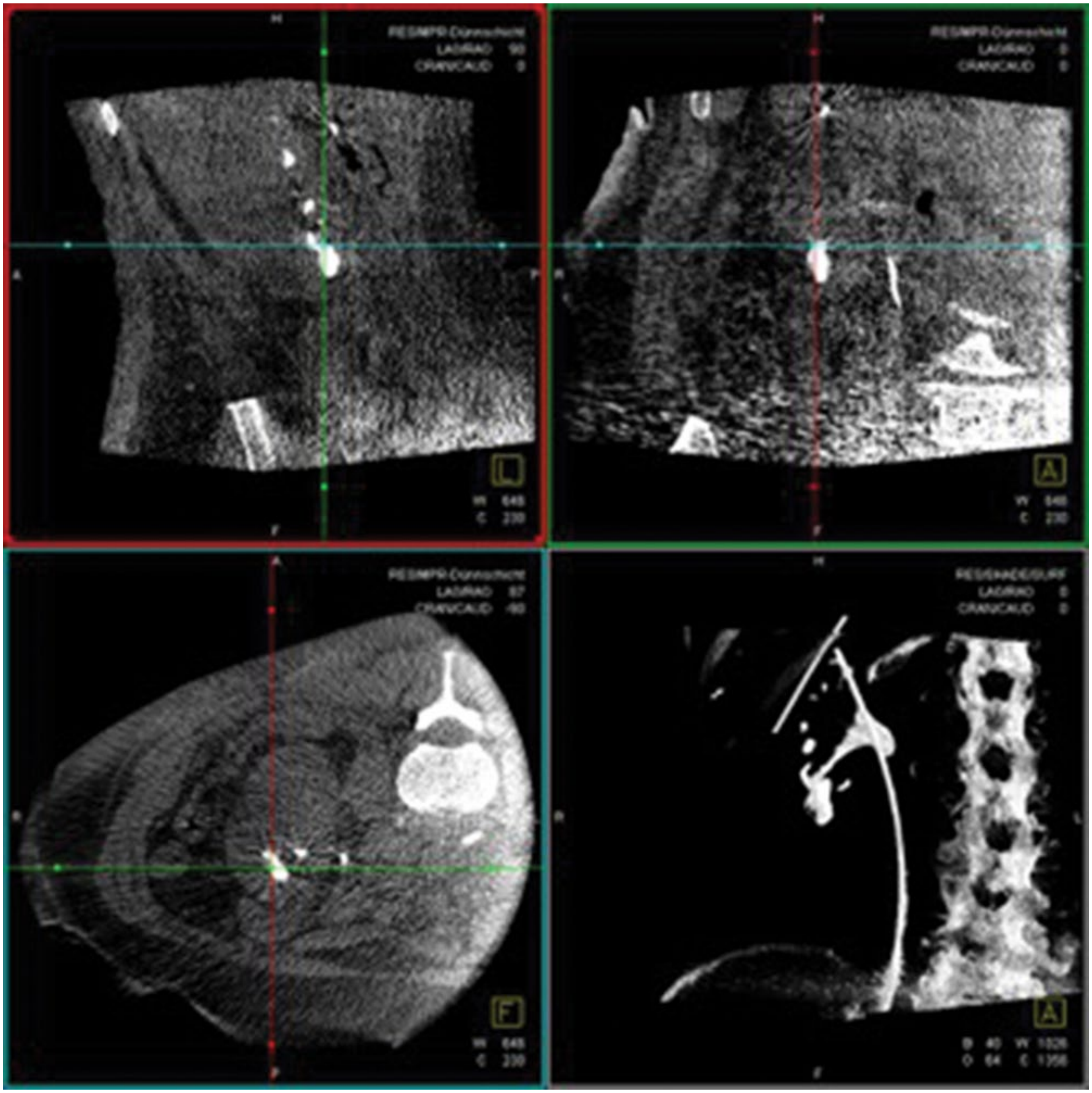

**Figure 17.5** Planned puncture tract to the renal calyx before PCNL.

performed due to renal hypermotility). In the nine in which the puncture was performed, seven punctures were done on the first attempt. The average puncture time was 60 seconds with an average planning time of 6.5 minutes, and an average dosage of exposure to radiation of 5850 µGy per $m^2$ [20]. This system was also used in an *in vitro* experiment, in which they were made 10 punctures, with nine punctures performed successfully, eight of which on the first attempt [15, 16].

This technique had the following advantages (Table 17.1): 3D anatomical image; fast, safe, and highly accurate when there is no patient movement; great definition of crossed structures, and ability to be performed in complicated cases (with a heterogeneous sample of patients); real-time path visualization; it is possible to change the trajectory if the needle is in the wrong position, because the trajectory is always available in real time; the patient can be in the supine position. However, this technique presented some disadvantages (Table 17.1): ionizing radiation dose was higher than with conventional techniques; excessive renal motility hampered the performance of the technique; the learning curve was steeper than with other techniques; and the cost is higher than with the other described techniques [20].

## Ultrasonography using SonixGPS navigation

Initially, a catheter is inserted via cystoscopy in the pyelocaliceal system with the patient in the lithotomy position. Then, with the patient placed in prone position, saline is instilled in the pyelocaliceal system to distend it. Subsequently, a global positioning system (GPS) electromagnetic transducer is placed at a location near the patient, and adjusted for good signal strength. In order to evaluate the path for the needle to follow, as well as the size and location of the stone and the kidney anatomy, an ultrasound scan is performed with the SonixGPS ultrasound probe in the area of the 11th and 12th rib edges. The observed images on the monitor acquired from the SonixGPS probe demonstrate the proper position and direction of the needle during the puncture. The direction, depth, and needle insertion angle can be adjusted as needed, according to the information available in real time through the needle sensor. Thus, using the images obtained through this technique, the needle with an incorporated electromagnetic sensor can be guided to the predetermined calyx (Figure 17.6) [21]. This technique was applied in 25 patients with a kidney stone [22]. The most important assessed outcomes were

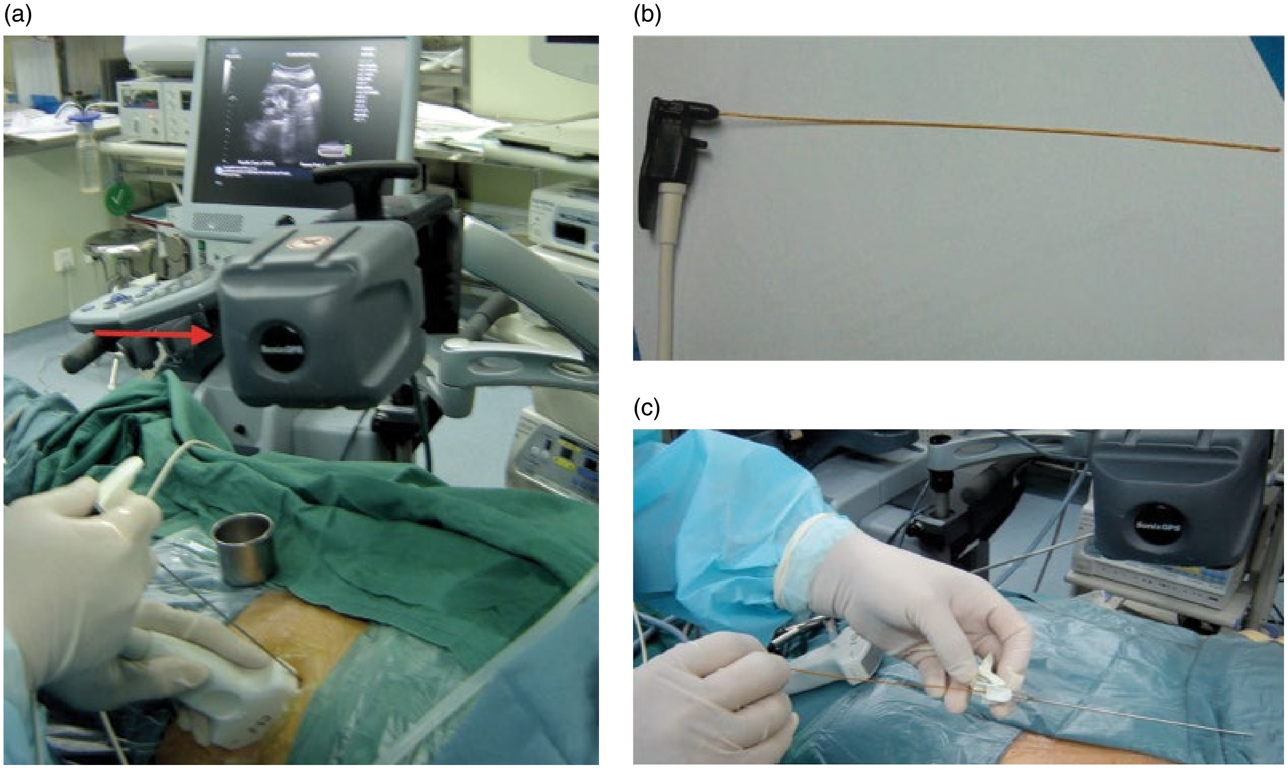

**Figure 17.6** SonixGPS needle tracking system in PCNL. (a) The transducer, which contains a positioning sensor (red arrow), is placed close to the operation area to ensure tracking and positioning of the needle. (b, c) When the electromagnetic sensor filament (b) is inserted into the GPS needle, the electromagnetic signal of the needle can be tracked and guided by the system. Reproduced with permission of Hui He.

the time required for the puncture and the success rate. It should be noted that this technique was performed successfully only with one attempt for each patient. The average puncture time was 5.5 minutes and patient stone-free rate was 92% [22].

The main advantages (Table 17.1) associated with the use of this technique are the following: absence of ionizing radiation; it can predict the trajectory of the needle prior to puncture, providing information on the depth, location, and insertion angle of the needle, allowing the operator to select the safer direction to the patient; it had provided and predicted the needle tip position at all times on the ultrasound screen, allowing the user to use ultrasound image to advance the needle correctly; the operator can keep track of the needle during the procedure even if the needle is not in the ultrasound image plane (the entire needle is shown on the display and a guidance bar present on the screen help guide the needle to correct position); it clear shows the trajectory and needle position in real time, so that the surgeon can adapt the position in order to acquire the correct trajectory; it is easier to perform than conventional puncture. Despite the advantages mentioned, the study had an important disadvantage (Table 17.1), which is the fact that none of the 25 study patients had a body mass index greater than 35 kg/m$^2$. In patients with obesity ultrasound images are highly impaired, and the use of fluoroscopy is recommended in such cases. Another disadvantage is that the patient anatomy is shown in 2D [22].

## What is the best method to access the renal collecting system during PCNL?

As we have seen, all the new renal collecting system PCNL puncture techniques discussed here have advantages and disadvantages. All aim to increase the quality of percutaneous puncture execution, so that they can be a credible alternative to the most used techniques. Thus, it becomes necessary to compare new techniques with regard to efficacy, the learning curve required, ionizing radiation utilization, security and morbidity, and the associated costs, in order to understand whether any of them is able to become the standard technique for the future.

For kidney puncture, the renal collecting system puncture technique that used electromagnetic sensors and the technique that used ultrasound with the SonixGPS navigation system had a 100% success rate in the first attempt [18, 19, 21, 22], proving them to be the most effective techniques. This high success rate can be explained by the capacity to define the needle's path and adjustment in real time provided by these two systems. These new techniques allow the operator to know the position of the needle relative to the desired renal calyx to puncture throughout the procedure. The puncture technique that uses an optical system incorporated in the needle had a first-attempt success rate of 73.3% [23]. This lower success rate can be explained by the fact that this technique does not provide an ideal path for the needle. One of the studies of marker-based iPad-assisted puncture showed a success rate on first attempt to approximately 68.4% [15, 16]. In this technique there is no possibility to redirect the needle during puncture, and furthermore the position of the patient must be the same during the preoperative CT and the procedure, and there may be some errors in the path. 3D CT using Uro Dyna-CT for laser-assisted puncture had a success rate at first attempt of approximately 58.3% [20]. Although this technique shows the direction of the needle trajectory and enables adjustment during the procedure, it is markedly impaired by renal movement caused, for example, by the patient breathing. The same technique in an *in vitro* experiment had a success rate on the first try of 80% [15, 16], which may indicate that this technique will need to be enhanced for it to be used regularly.

To a trainee surgeon, the puncture technique using guidance by electromagnetic sensors has a learning curve of 12 cases to reach the level of an expert surgeon [18], much lower than the 60-case learning curve previously reported for PCNL [11], and it is the technique with the best learning curve. Ultrasonography using SonixGPS navigation for renal collecting system puncture is easier to do than conventional techniques, especially for trainee surgeons, since the positioning of the needle can be seen throughout the procedure, unlike conventional methods [21, 22]. The technique that uses an optical system incorporated in the needle does not seem to facilitate percutaneous puncture because it only improves visualization when the needle is already in the collecting system. The model that uses an iPad and markers shows that an expert surgeon takes longer to perform puncturing than a trainee surgeon. This technique is more difficult for the expert surgeon than conventional puncture technique, in contrast to trainee surgeons [15]. The technique using Uro Dyna-CT is more difficult to perform than the others because it requires very specific learning [20].

All the ionizing radiation received during diagnosis, treatment, and follow-up of a patient is cumulative, and may contribute to an increased risk of malignant transformation [28]. Thus, the avoidance of the use of such radiation in PCNL is very important [29]. The puncture of the renal collecting system assisted by electromagnetic sensors allows urologists to dispense with ionizing radiation in an effective way, because the needle and catheter positioned in the desired renal calyx have an electromagnetic sensor which allows the trajectory of the needle to be displayed in 3D and in real time. Thus, the surgeon does not need to view the renal collecting system with fluoroscopy. Puncture of the renal collecting system with an optical system incorporated in the needle does not use ionizing radiation, because its inserted camera system at the needle tip allows visualization of the renal collecting system in real time, and it is not necessary to use fluoroscopy for that. The SonixGPS system also means that ionizing radiation does not need to be used, as it creates the path and relays information about the needle's position in real time. However, these last two techniques use ultrasound, and in complicated cases, such as obesity and anatomical abnormalities, fluoroscopy must be used because ultrasound is compromised in these circumstances. The two other techniques covered here do rely on ionizing radiation: with marker-based iPad-assisted puncture of renal collecting system there is an average dose of radiation exposure of 377.5 μGy per $m^2$ [15, 16] and 3D CT using Uro Dyna-CT for laser-assisted puncture of the renal collecting system has an average dose of 5850 μGy per $m^2$ [20]. Both systems produce a higher radiation dose than conventional fluoroscopy.

Although none of these techniques, when used in humans, have major complications or extensive morbidity associated with them, the small number of individuals included in the studies limits the definition of complications and morbidity. The technique that uses electromagnetic sensors was conducted in pigs. Thus, it will be necessary to obtain the human test results to better understand if it is associated with an increase or decrease in complications and morbidity.

Only Uro Dyna-CT is associated with a very significant increase in financial cost for the realization of PCNL [20]. The marker-based iPad technique may result in increased costs to the extent that there must be a preoperative CT performed, a procedure that is more expensive than fluoroscopy, in addition to the new equipment required for the actual technique. For the remaining three techniques, each requires new equipment, and so a survey of the costs should be carried out related to the purchase of this equipment.

The puncture technique that uses electromagnetic sensors seems to be have the most advantages over the other methods covered in this chapter, but there are currently no human studies reported in the literature.

## Conclusion

Even today, fluoroscopy and ultrasound are still the preferred techniques for performing access to the renal collecting system in PCNL. However, these methods have a steep learning curve and are a source of many complications associated with the procedure. New access methods and technologies have been developed in order to overcome the limitations of the traditional methods. Nevertheless, in the future new human studies will be required to check the efficacy and safety of these new techniques.

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# Part 4 Selection of Access and Dilation

## 18

## Percutaneous Nephrolithotomy: Upper Pole Access

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### Introduction

Stone clearance and improved patient outcomes during percutaneous nephrolithotomy (PCNL) are largely dependent on the appropriate selection of the access to the kidney. While standard PCNL is often performed through a subcostal lower calyceal approach, upper calyceal access through a supracostal approach can be ideal for many clinical situations. Traditionally, concerns for increased potential perioperative complications, particularly intrathoracic ones, have limited utilization of supracostal access [1]. However, with a good understanding of the anatomy surrounding the upper pole of the kidney and attention to a few technical considerations during the procedure, upper calyceal access through a supracostal approach can be performed safely and efficiently. In this chapter, we describe our surgical technique for upper calyceal access during PCNL and review the outcomes of this approach in the literature.

### Indications and patient selection

During upper calyceal approaches, supracostal access is performed along the long axis of the kidney. This allows for direct entry to the upper calyx and optimal visualization of the renal pelvis, ureteropelvic junction (UPJ), and upper ureter [1]. The performance of rigid nephroscopy in the direction of the long axis of the kidney minimizes the torque requirement on the kidney and results in decreased bleeding and improved clearance rates [2]. In certain circumstances, a laterally situated intercostal tract can be placed between the tips of the 11th and 12th ribs, or an infracostal approach may be used to access the upper pole (Figure 18.1). While the risk of pleural injury may be less with these techniques as compared to the more superior supracostal puncture, the benefits in visualization outside the upper pole is limited with rigid instruments and may require increased reliance on flexible endoscopy [3].

Supracostal upper calyceal access can be advantageous in several clinical situations (Table 18.1). Upper pole access can be optimal for large upper pole stones (Figure 18.2) or for complete staghorn renal calculi (Figure 18.3). Direct access to the UPJ and proximal ureter may be beneficial for treatment of large or impacted proximal ureteral calculi, particularly with concomitant renal pelvic stones, or need for antegrade endopyelotomy during UPJ obstruction management. Similarly, stones in more complicated renal systems, such as an upper pole calyceal diverticulum, or complex lower pole configurations may be more amenable to an upper calyx approach. In situations with superior kidneys located above the ribs, middle or even lower calyceal access may require a supracostal approach. Conversely, in a few patients, upper calyx puncture may be possible via a subcostal route, depending on the renal anatomy. For example, due to its incomplete ascent, horseshoe kidneys are best accessed in the upper pole [3]. However, this can usually be performed from a subcostal approach.

### Anatomic considerations

A general knowledge of the anatomy of the upper pole of the kidney in relation to the surrounding structures is necessary to minimize complications during supracostal access to the upper calyx. The intercostal nerve and vessels

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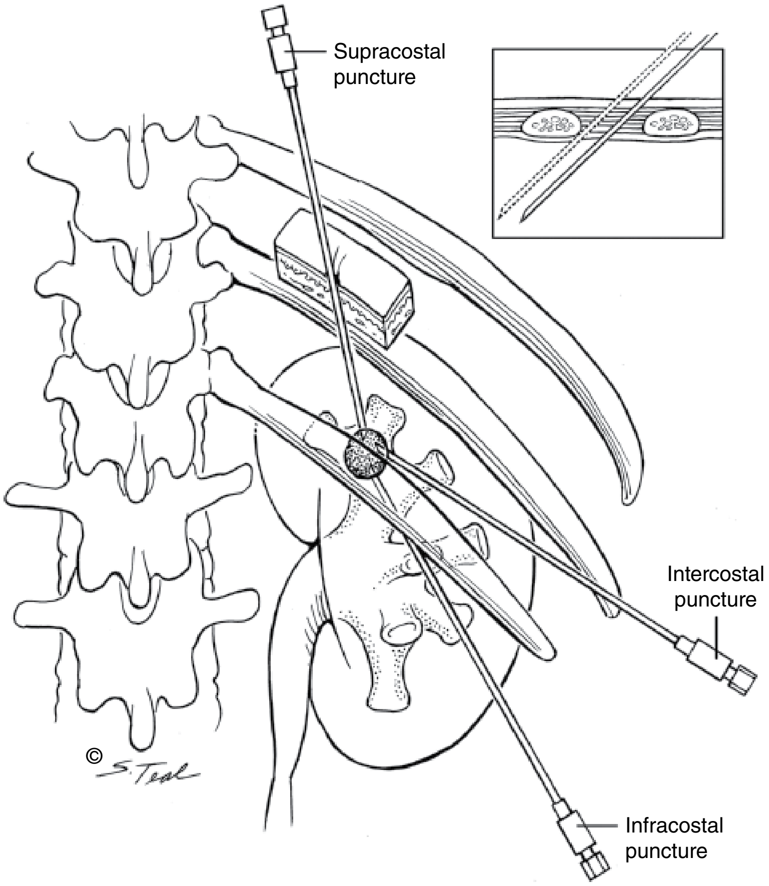

**Figure 18.1** Upper pole access can be obtained through a supracostal, intercostal, or infracostal approach. Reproduced with permission of Sharon Teal.

**Table 18.1** Indications for upper pole/supracostal access.

| Indication | Details |
|---|---|
| Large stone burden | Staghorn calculi<br>Large upper pole stones |
| Need for direct access to UPJ | Large/impacted proximal ureteral stones<br>UPJ obstruction requiring anterograde endopyelotomy |
| Complex anatomy | Upper pole calyceal diverticulum<br>Complex lower pole calculi<br>Horseshoe kidney<br>Superiorly located kidneys |

are located along the inferior portion of each respective rib. Puncture sites are directed to the middle portion of the intercostal space to avoid injury to the intercostal artery and development of a hemothorax. In most situations, lateral posterior renal calyces are targeted during percutaneous access to avoid the major branches of the renal artery. Posterior calyces generally traverse Brödel's bloodless line, the avascular renal plane between the anterior and posterior divisions of the renal artery. Additionally, posterior calyces offer the shortest access path to the collecting system [3]. Needle punctures should be directed along the axis of the renal calyx through the center of the renal papilla to avoid infundibular or renal pelvic puncture. Injury to interlobar arteries has been noted in up to 67.6% of kidneys following upper pole infundibular puncture and to retropelvic vessels in 33% following direct renal pelvic puncture [4].

The concern for intrathoracic injury following upper calyceal access is secondary to the close relationship of the upper kidney to the lungs and pleura. The upper portions of both kidneys are located anterior to the posterior portion of the 11th and 12th ribs. A review of 90 normal supine intravenous urograms during full expiration noted that 85% of upper renal calyces are located above the 12th rib [5]. In the prone position, further cephalad movement of the kidney occurs in 80% of patients [6]. Despite controlled maximal expiration, this cephalad movement results in an estimated likelihood of lung injury following supracostal access of 29% on the right side and 14% on the left [7]. The posterior diaphragm arises from the distal ends of the 11th and 12th ribs, the tip of the L1 transverse process, and the anterior aspect of the upper lumbar vertebral body [8]. During full inspiration, the posteroinferior margin of the lung expands to

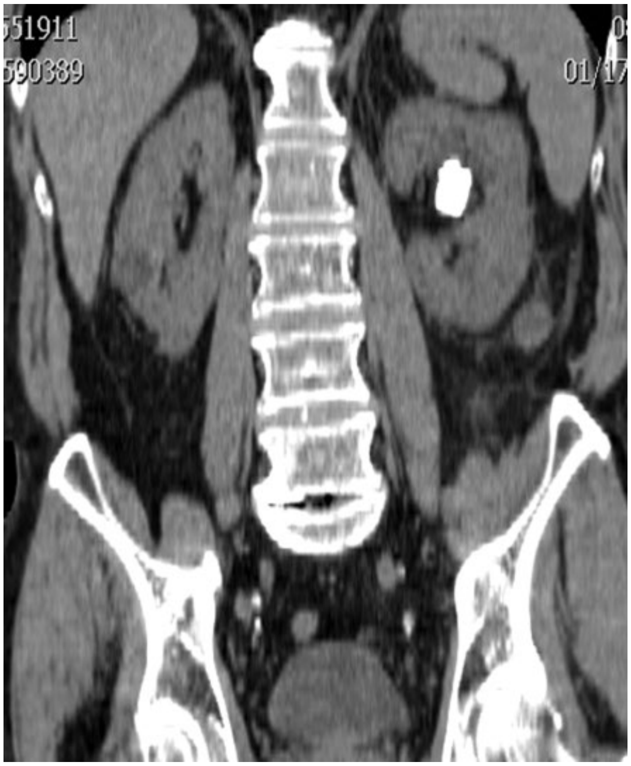

**Figure 18.2** Coronal CT imaging shows a large upper calyceal stone.

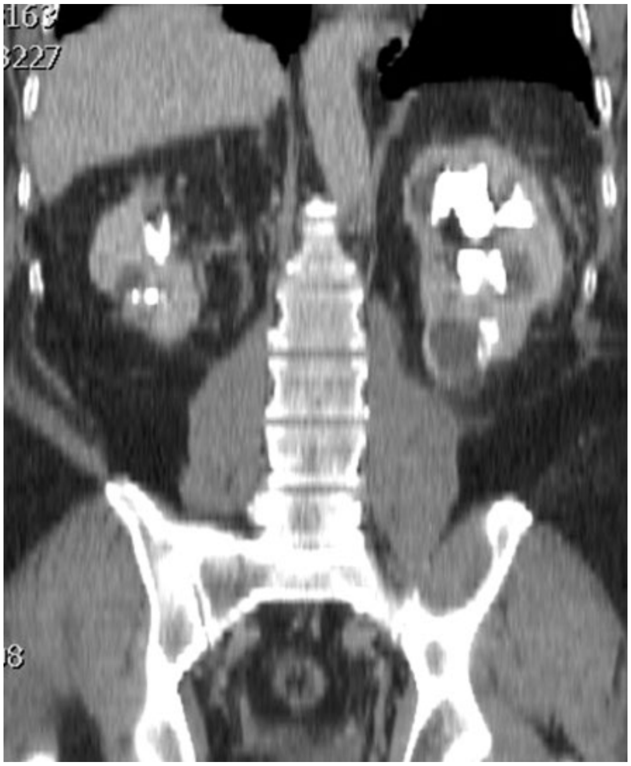

**Figure 18.3** Coronal CT imaging shows a complete staghorn renal calculus.

fill the posterior costophrenic recess. During expiration, the lung retracts and the pleura ascends cranially and laterally on the ribs [9]. The lower limit of the posterior parietal pleura crosses the 12th rib obliquely near the lateral border of the erector spinae muscles. In the midscapular line, the visceral pleura has a similar relationship at the 10th rib [10]. The initial needle puncture for a supra-12th rib access is advocated at maximal expiration and lateral to the erector spinae muscles in the 11th and 12th interspace to avoid lung and pleural injury. Supra-11th rib access can be performed in a similar fashion between the 10th and 11th rib interspace [11].

## Surgical technique

Our percutaneous approach for upper calyceal access is similar to that used for the lower pole. At the onset of the procedure, the patient is placed in the dorsal lithotomy position. Using rigid cystoscopy, we place a 5 Fr open-ended ureteral catheter to allow opacification of the renal collecting system. After subsequent placement of a Foley catheter, the patient is placed in the prone swimmer's position. A chest roll is placed horizontally to facilitate ventilation, with the neck maintained in a neutral position. An additional roll is used to slightly elevate the side of interest in order to align the posterior calyces in a more vertical position. The ipsilateral upper extremity is placed at 90° flexion, while the contralateral arm is positioned parallel to the patient. Particular attention is given to properly pad all pressure points and secure the patient to the table. Using biplanar fluoroscopy, we perform either the bullseye or triangulation technique for percutaneous access. The bullseye technique is described in Chapter 12 in this volume and here we will detail our supracostal approach using the triangulation technique (see Video 18.1).

### Triangulation technique

For upper calyceal access, we generally prefer a puncture site within the 11th and 12th intercostal space, just lateral to the erector spinae muscles. A supra-11th rib puncture is avoided when possible. Following identification of the targeted upper pole calyx under fluoroscopy, the triangulation technique is started with an 18G diamond-tipped access needle puncture in the inferior border of the 11th rib at the skin (Figure 18.4). The needle is angled acutely so that it enters at the center of the intercostal space, thus avoiding the intercostal nerve and vessels of the 11th rib. Biplanar fluoroscopy is performed using the C-arm in two positions, anteroposterior and

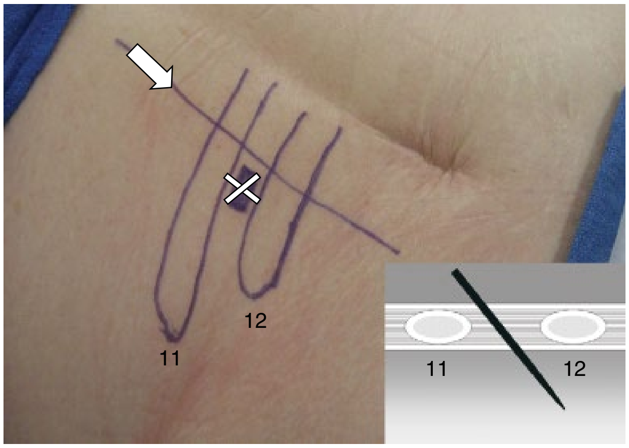

Figure 18.4 Initial puncture for a supra-12th rib approach is lateral to the erector spinae muscles (arrow) at the inferior border of the 11th rib angled towards the middle of the intercostal space (X).

oblique. The anteroposterior view is along the plane parallel to the line of puncture. When the C-arm is in the anteroposterior position, adjustments to the needle position are made in the mediolateral (left–right) direction (Figure 18.5). The oblique view is obtained by rotating the C-arm through 30°. When the C-arm is positioned obliquely, adjustments to the needle position are made in the cranial–caudal (up–down) orientation with care not to drift into the mediolateral position (Figure 18.6). Ventilation is suspended in full expiration as the access needle is advanced towards the desired calyx. The C-arm is maintained in the oblique position in order to gauge the depth of puncture. After initial advancement, the C-arm is rotated back to the AP view to confirm the mediolateral orientation before continuing needle movement in the oblique view. Simultaneous retrograde instillation of contrast via the open-ended catheter allows for collecting system opacification and identification.

After entry into the renal calyx, aspiration of fluid is performed to confirm the needle position in the collecting system. A 0.035 inch hydrophilic nitinol core glidewire is advanced through the access needle and

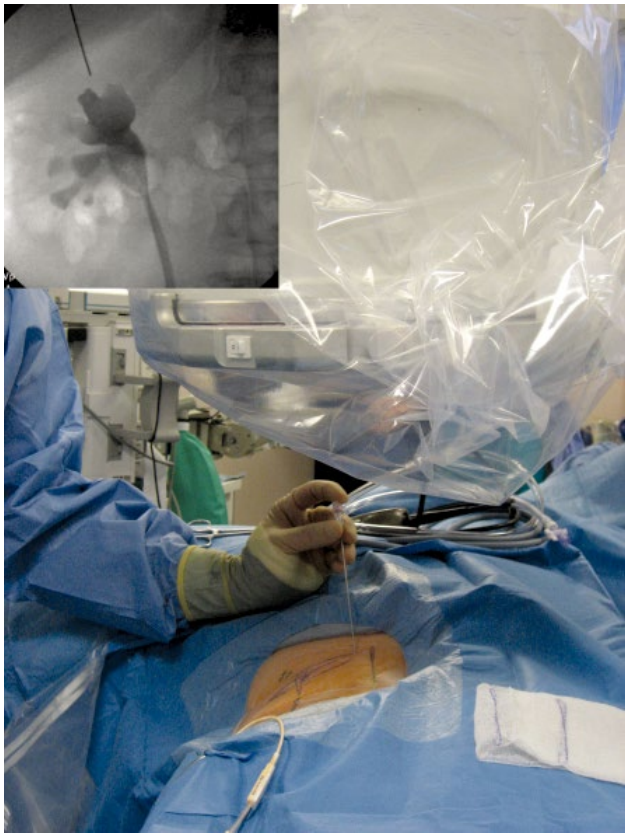

Figure 18.5 Using the triangulation technique for supracostal percutaneous renal access, adjustments to the needle position are made in the mediolateral (left–right) direction when the C-arm is in the anteroposterior position (along the plane parallel to the line of puncture).

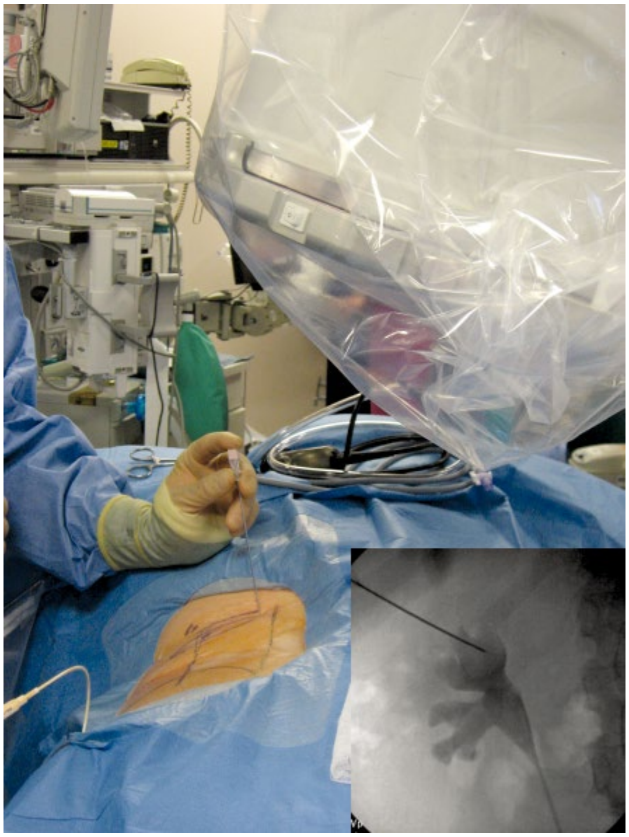

Figure 18.6 Using the triangulation technique for percutaneous renal access, adjustments to the needle position are made in the cranial–caudal (up–down) direction when the C-arm is in the oblique position (rotating the C-arm 30°).

manipulated down the ureter if possible. If entry to the ureter is prohibited, the wire is coiled in the renal pelvis or in the calyx that is accessible and furthest away from the calyx of puncture. An 8 Fr fascial dilator and subsequently a 5 Fr Cobra-tipped angiographic catheter are sequentially passed over the glidewire in order to facilitate wire positioning in the ureter. The glidewire is next exchanged for an Amplatz super-stiff wire. A second standard guidewire is placed as a safety wire into the ureter and secured to the drape following placement of an 8/10 Fr coaxial dilator over the super-stiff wire. A NephroMax balloon is advanced over the super-stiff wire until the radiopaque marker is noted just inside the collecting system. Following balloon inflation to 14–20 atm, the 30 Fr Amplatz sheath is advanced over the balloon into the collecting system and standard stone treatment is performed. Some patients, such as those with complete staghorn calculi, may require additional access into a different calyx following initial percutaneous tract placement in the upper calyx. In this situation, the Amplatz sheath is left in the upper pole while working through the second access tract in order to prevent excessive extravasation from the upper pole calyx into the pleural cavity.

At the conclusion of the procedure, fluoroscopy is performed over the ipsilateral chest and lung fields to exclude the presence of hydrothorax. In the operating room, a pigtail catheter is inserted into the chest under fluoroscopic guidance in patients noted to have significant hydrothorax or pleural effusion. Patients who are symptomatic or for whom there is concern for a hydrothorax in the postoperative period are followed with an upright chest X-ray in the recovery room and monitoring of clinical respiratory vital signs. In the postoperative period, patients with symptomatic fluid collections are managed by tube thoracostomy. On the first postoperative day, a stone-protocol computed tomography (CT) scan, which includes the lung bases, is performed in all patients to evaluate for residual stones.

### Alternative technique

To avoid supracostal puncture, some authors have advocated a renal displacement technique. The initial placement of a sheath, dilator, or externalized through-and-through wire is performed via an interpolar or lower pole renal access in order to allow for torque of the kidney downward. This can be held by an assistant while upper calyx puncture is performed via a subcostal route [12–14]. Additionally, simultaneous fluoroscopy with retrograde flexible ureteroscopy via a ureteral access sheath has been described for endoscopically guided percutaneous access [15]. This modification may aid in rapid and precise percutaneous puncture into the desired upper pole calyx [16].

## Outcomes

Reported stone-free rates following supracostal access PCNL are comparable to infracostal approaches and range between 68 and 90% [17–24] (Table 18.2). The lack of strict criteria defining stone-free status with utilization of multiple imaging modalities may account for some of the variation in reported outcomes. Additional percutaneous access was required up to one-third of the time; this is not surprising given that complete staghorn calculi are one indication for upper pole access. Similarly, ancillary procedures, including second-look PCNL, ureteroscopy and shock-wave lithotripsy, were performed in 3–46% of cases.

## Operative complications

Overall complication rates following supracostal access during PCNL range from 10 to 26% (Table 18.3) [2, 9, 17–24]. Significant hemorrhage requiring blood transfusion or bacteremia and sepsis can occur following any

**Table 18.2** Operative parameters following supracostal renal access/PCNL.

| Study | *N* | Additional access (%) | Overall stone-free rate (%) | Ancillary procedures[a] |
|---|---|---|---|---|
| Golijanin et al. (1998) [17] | 115 | 23 (20) | 78 (67.8) | 53 (46) |
| Kekre et al. (2001) [18] | 102 | Not specified | 81 (79.5) | Not specified |
| Gupta et al. (2002) [19] | 63 | 15 (23.8) | 57 (90) | 13 (20.6) |
| Lojanapiwat and Prasopsuk (2006) [20] | 170 | 0 (0) | 140 (82.4) | 6 (3.5) |
| Shah et al. (2006) [21] | 144 | 22 (15.3) | 127 (88.2) | 5 (3.5) |
| Sukumar et al. (2008) [22] | 110 | 9 (8.2) | 95 (86.4) | 15 (13.6) |
| Shaban et al. (2008) [23] | 30 | 11 (36.7) | 24 (88.9) | 3 (11.1) |
| Lang et al. (2009) [24] | 103 | Not specified | 91 (88) | Not specified |

[a] Includes shock-wave lithotripsy, second-look PCNL, and ureteroscopy.

**Table 18.3** Supracostal complications associated with renal access/PCNL.

| Study | *N* | Supra-12th (%)<br>Supra-11th (%) | Overall number of complications (%) | Sepsis/ bacteremia (%) | Thoracic (%)<br>Pneumothorax<br>Hemo/hydrothorax<br>Renopleural fistula<br>Needed treatment | Other organ injury (%) | Significant blood loss/ required blood transfusion (%) |
|---|---|---|---|---|---|---|---|
| Golijanin et al. (1998) [17] | 115 | 115 (100) | 30 (26.1) | 0 (0) | 4 (3.8)<br>0 (0)<br>4 (3.5)<br>0 (0)<br>4 (3.5) | 0 (0) | 20 (19.2) |
| Munver et al. (2001) [2] | 98 | 72 (73.5)<br>26 (26.5) | 16 (16.3) | 1 (1) | 7 (7.1)<br>1 (1)<br>4 (4.1)<br>2 (2)<br>6 (6.1) | 0 (0) | 4 (4.1) |
| Kekre et al. (2001) [18] | 102 | 102 (100) | 10 (9.8) | 0 (0) | 10 (9.8)<br>1 (1)<br>9 (8.8)<br>0 (0)<br>9 (8.8) | 0 (0) | 0 (0) |
| Gupta et al. (2002) [19] | 62 | 62 (98.4)<br>1 (1.6) | 14 (22.2) | 7 (11) | 7 (11)<br>0 (0)<br>7 (11)<br>0 (0)<br>4 (6.3) | 0 (0) | 6 (9.5) |
| Yadav et al. (2006) [9] | 332 | 328 (98.8)<br>4 (1.2) | 74 (22.2) | 53 (16) | 11 (3.3)<br>0 (0)<br>11 (3.3)<br>0 (0)<br>7 (2.1) | 0 (0) | 6 (1.8) |
| Lojanapiwat and Prasopsuk (2006) [20] | 170 | 170 (100) | 31 (18.2) | 1 (0.6) | 26 (15.3)<br>0 (0)<br>26 (15.3)<br>0 (0)<br>9 (5) | 0 (0) | 4 (2.4) |
| Shah et al. (2006) [21] | 144 | 110 (76)<br>35 (24) | 19 (13.2) | 6 (4.1) | 5 (3.5)<br>0 (0)<br>5 (3.5)<br>0 (0)<br>1 (0.7) | 0 (0) | 7 (4.9) |
| Sukumar et al. (2008) [22] | 110 | 110 (100) | 13 (11.8) | 2 (1.8) | 10 (9.1)<br>0 (0)<br>10 (9.1)<br>0 (0)<br>10 (9.1) | 0 (0) | 2 (1.8) |
| Shaban et al. (2008) [23] | 30 | 24 (80)<br>6 (20) | 4 (13.3) | 1 (3.3) | 2 (6.6)<br>0 (0)<br>1 (3.3)<br>1 (3.3)<br>2 (6.6) | 0 (0) | 1 (3.3) |
| Lang et al. (2009) [24] | 103 | Not specified | 11 (10.7) | 0 (0) | 1 (1.0)<br>0 (0)<br>1 (1)<br>0 (0)<br>Not specified | 0 (0) | 7 (6.8) |

PCNL procedure. Specific complications in relation to supracostal approaches are described in more detail below. See also Chapters 33–35.

## Pulmonary complications

Intrathoracic complications have been reported in approximately 1–15.3% of cases [2, 9, 17–24]. Supra-11th rib access, in particular, is associated with increased occurrence of pulmonary injuries. In one series, six of 26 (23.1%) supra-11th PCNLs resulted in intrathoracic complications as compared to one of 72 (1.4%) supra-12th rib accesses [2]. Hydrothorax is the most common pleural injury noted secondary to collection of irrigation fluid in the pleural space. In an analysis of isolated upper pole access from the Clinical Research Office of the Endourological Society (CROES) Global study, intercostal access above the 11th rib was associated with a 5.6-times higher rate of hydrothorax than those above the 12th rib [25]. In addition to minimizing access above the 11th rib, the occurrence can be decreased with the judicious use and positioning of the Amplatz sheath to avoid leakage into the pleural space and maintenance of a low-pressure system as well as adequate renal drainage postoperatively [19]. A delayed hydrothorax may occur secondary to urine leakage through the PCNL tract to the pleura, often secondary to the formation of a renopleural fistula. Prolonged fluid accumulation in the setting of a urinary tract infection can manifest as an empyema. A hemothorax may occur following injury to the intercostal vessels during initial needle puncture. The occurrence of an isolated pneumothorax, however, is uncommon [26].

The diagnosis of pulmonary injuries can be made intraoperatively and/or postoperatively. At the conclusion of the PCNL, prone fluoroscopy of the ipsilateral lung fields should be performed in all cases involving supracostal access. A distinct fluid demarcation laterally along the chest wall from the lung or an obscured costophrenic angle warrants further evaluation or intervention if ventilation is difficult. An upright chest X-ray or CT scan can be used to confirm the fluid density at the lung base in less defined cases with high suspicion during the postoperative setting. While under anesthesia, concerning fluid collections may be aspirated during hyperventilation or treated with tube thoracostomy [27]. In the postoperative setting, a period of observation may be warranted with small fluid collections, but aspiration or tube thoracostomy connected to underwater drainage should be utilized in symptomatic patients. An evaluation by a thoracic surgeon for potential thoracotomy or video-assisted thoracoscopic surgery (VATS) may be required for non-improving or infected pulmonary complications. In patients with ureteral stents that show delayed presentation, the effusion may be secondary to stent-related reflux and additionally treated with anticholinergics and maximal bladder decompression. Patients without ureteral stents may have delayed effusions secondary to transient obstruction from small calculi or blood clots, and require ureteral stent and Foley catheter placement [26].

## Other organ injury

Although less common than pulmonary complications, injuries to adjacent organs, including the liver, spleen, and intestines, may occur rarely during upper calyceal access. A retrorenal left colon, occurring in 10% of patients in the prone position, may prohibit access to the 10th or 11th intercostal space with increased risk associated with medial punctures [28]. Additionally, a supra-11th access could puncture the liver in 14% and spleen in 33% of patients, particularly during inspiration [7]. In hemodynamically stable patients, liver injuries can often be managed conservatively with tube drainage and serial monitoring [29]. Moreover, transhepatic PCNL has been reported to be safe if necessary [30]. Splenic injuries, however, are associated with increased bleeding and may require immediate exploration and splenectomy [31]. Preoperative CT imaging to determine the relationship of adjacent structures, as well as evaluation under fluoroscopy in multiple planes intraoperatively prior to needle placement are important methods to minimize injury to other organs [32]. When possible, preoperative imaging should be obtained in the same orientation as the planned surgical position. On planning CT imaging, evaluation of the kidney, particularly to the upper pole calyx, in relation to adjacent organs may differ between the prone and supine positions [33]. In patients at increased risk for adjacent organ injury on preoperative CT, intraoperative ultrasound in place of or augmenting fluoroscopic guidance may additionally be used to gain the optimal and safe access [34].

## Postoperative pain

While not typically quantified in most studies, supracostal access during PCNL results in increased discomfort as compared to subcostal approaches secondary to traversing of the diaphragm [21]. During needle placement, medial puncture through the paraspinal muscles is associated with increased pain and should be limited if possible [3]. Nephrostomy access should be directed to the middle of the intercostal space. While access at the inferior border of the 11th rib should be avoided to minimize injury to the intercostal nerve and vessels, needle puncture and sheath manipulation along the superior border of the 12th rib may result in increased periosteal irritation and pain [35]. Several recommendations have been made to decrease pain following upper pole access. Intercostal nerve block has been advocated as a method to minimize supracostal tube discomfort [36]. Instead of placing a supracostal tube, a lower pole nephrostomy tube may be placed at the conclusion of the procedure via a second nondilated subcostal puncture and allowing the supracostal puncture site to close [37]. Additionally, downsizing to a small-bore percutaneous catheter at the conclusion of the procedure is associated with reduced postoperative symptoms as compared to large percutaneous catheters [38]. Tubeless supracostal PCNL has been reported with decreased need for postoperative analgesia [19, 39, 40]. Tubeless PCNL should be performed only in cases in which complete stone extraction is a near certainty. Candidates for tubeless approaches should meet strict criteria, including no collecting system perforation or significant bleeding [40]. Tubeless procedures should also be avoided in patients with concerns for magnesium ammonium phosphate stones to minimize any potential spread of infection to the chest.

## Conclusions

Supracostal percutaneous access to the upper pole of the kidney during PCNL is a useful technique when optimal visualization is required for the upper calyx, UPJ, and proximal ureter. Supra-12th rib puncture should be approached lateral to the erector spinae muscles towards the superior portion of the rib during maximal expiration. Supracostal access above the 11th rib should be avoided when possible. Intraoperative fluoroscopy of the lung fields should be performed at the conclusion of the procedure, and a strong suspicion for pulmonary injuries should be maintained in the postoperative period. Patients should be counselled appropriately regarding the potential risks and complications when upper calyceal access is anticipated, particularly with regards to intrathoracic complications. However, with attention given to anatomic considerations, supracostal access to the upper pole can be obtained safely and efficiently to contribute to successful percutaneous renal surgery.

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# 19

# Percutaneous Nephrolithotomy Access Without Image Guidance

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## Introduction

In 1955, Goodwin described the percutaneous placement of a needle nephrostomy for hydronephrosis, opening the door to percutaneous renal access [1]. The rapid dissemination of image-guided techniques in urology and interventional radiology has contributed to the innovation of percutaneous renal procedures. Simple drainage has evolved into percutaneous treatments for stone disease, upper tract and renal cancers, and urinary diversion/drainage, among others. The advancement of endourologic techniques has led urology into the minimally invasive era. This rapid innovation has forced urologists to become proficient in percutaneous renal procedures, offering optimal treatment for the expanding number of pathologies amenable to percutaneous treatment.

## Indications

Percutaneous access has been described using various imaging modalities, including ultrasound and fluoroscopy [2–6]. Fortunately, there are few instances in which access must be achieved blindly. Urologists have largely been dependent upon interventional radiology colleagues for percutaneous drainage, but it is becoming an essential skill as it is the procedure of choice for renal access in the acute setting. The inability to obtain retrograde access or opacify the collecting system in a retrograde fashion may be due to previous cystectomy and urinary diversion, locally invasive prostate cancer, benign prostatic hyperplasia, urinary tract fistulas, alternate primary cancers obstructing the ureters, pelvic lipomatosis, and retroperitoneal fibrosis [7]. Renal insufficiency may preclude the use of intravenous pyelography. On rare occasions, access to various imaging modalities may be unavailable, or proficiency with image-guided percutaneous nephrostomy placement may be lacking.

## Anatomy (see also Chapter 6)

The retroperitoneal location of the kidney allows for relatively safe percutaneous access via a posterior approach. Nephrostomy placement without image guidance is completed utilizing anatomic landmarks, assuming normal renal anatomy. A thorough understanding of renal anatomy and relations is essential to avoid complications and gain access to the collecting system [8].

The kidney is a mobile organ and its position can vary depending on patient position and phase of respiration. With respiratory excursion, the kidneys descend on average 4–5 cm, reaching as far as the iliac crest. Generally, the right kidney lies 1–2 cm lower than the left due to its position below the liver. The pleural reflection is posterior to the upper third of both kidneys and needle placement above the 12th rib places patients at additional risk for pneumothorax. The renal hila are directed ventromedially and are approximately 5 cm lateral from the margin for the spinous process of the L1 vertebra. The right kidney is intimately associated with the liver anteriorly and laterally, the colon anteriorly, and the duodenum and vena cava anteriorly and medially. The left kidney is intimately associated with the spleen laterally, colon anteriorly, and tail of the pancreas and aorta anteriorly and medially. Careful needle placement is crucial for safe nephrostomy placement and to avoid visceral organ injury.

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## Bony and muscular relations

The average size of each kidney is approximately 11 cm in length, 6 cm in width, and 3 cm in thickness. They lie between the 12th thoracic (T12) and 3rd lumbar (L3) vertebrae. The 11th and 12th ribs are superficial to the upper pole of the kidneys. The intercostal neurovascular bundle courses inferiorly to the corresponding rib, and should be avoided if possible (Figure 19.1).

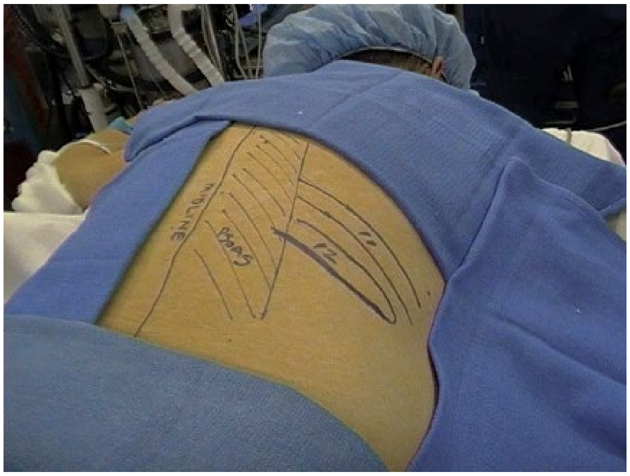

**Figure 19.1** Muscular and bony relations relevant to percutaneous renal access.

The kidneys lie in an oblique plane abutting the psoas which directs its longitudinal axis 30° from the midline, and renders the lower poles more anterior (further from the skin surface) in the prone position. The lumbar notch has been described as a depression that can be palpated, allowing for safe placement of needle puncture [9]. The superior margin consists of the latissimus dorsi and 12th rib, is medially bounded by the sacrospinalis and quadratus lumborum muscles, and laterally by the transversus abdominus and external oblique muscles (Figure 19.2).

## Vascular considerations

The renal artery arises from the aorta at the L1 level, dividing into anterior and posterior branches. The anterior branch divides into three to four segmental arterial branches which supply the anterior and polar regions. The posterior branch gives rise to one posterior segmental renal branch that supplies the posterior surface of the kidney, excluding the polar regions. The segmental arteries give rise to a variable number of interlobar arteries that divide and become the arcuate branches, which subsequently become the interlobular arteries. The interlobular arteries course peripherally in the cortex to supply the afferent arterioles of the glomeruli. Broedel's line represents a watershed zone between the distribution of the anterior and posterior divisions of the renal artery [10]. It allows for percutaneous access through a

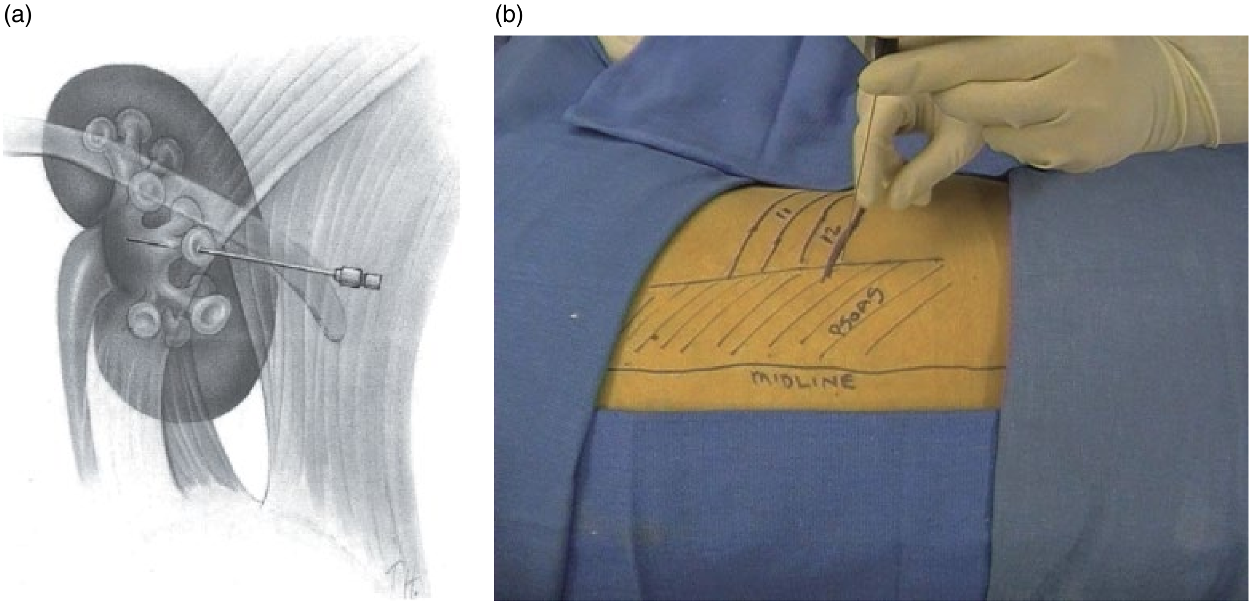

**Figure 19.2** (a) Lumbar notch. The superior margin consists of the latissimus dorsi and 12th rib, is medially bounded by the sacrospinalis and quadratus lumborum muscles, and laterally by the transversus abdominus and external oblique muscles. (b) Needle puncture through lumbar notch in anatomic model.

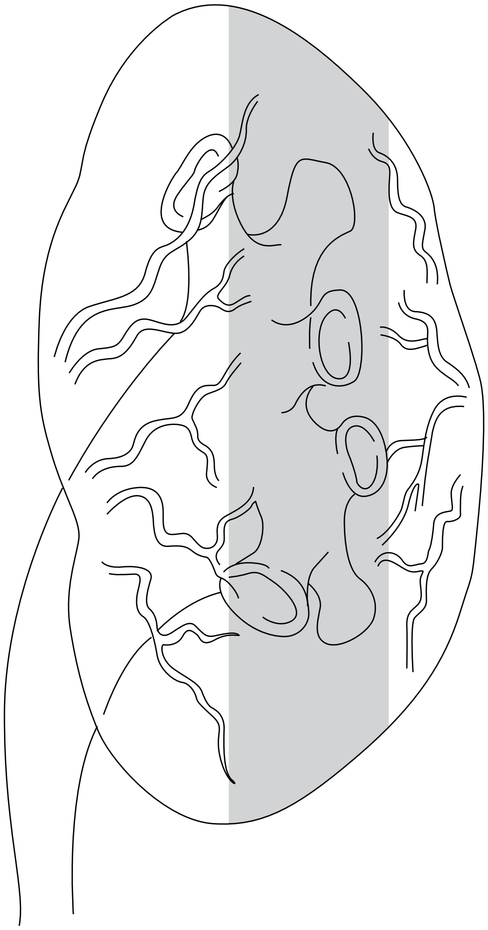

Figure 19.3 Broedel's avascular zone (shaded).

relatively avascular plane that avoids major arterial branches, potentially avoiding excessive bleeding, pseudoaneurysm formation, and development of arteriovenous malformation (Figure 19.3).

### Calyceal anatomy

Calyceal architecture exhibits a considerable degree of variability. Calyces can be divided into superior, midzone (anterior and posterior), and inferior. Two types of calyceal configurations have been reported, the Broedel and Hodson types [10, 11]. The Broedel configuration describes anterior calyces as being angled medially and posterior calyces more peripherally. The Hodson configuration is in direct opposition with the anterior calyces angled laterally, and the posterior calyces more medially. Kaye and Reinke studied calyceal distribution on computed tomography (CT) imaging and determined that the Broedel type is more commonly seen on the right, and the Hodson type on the left [12].

In clinical practice, emergent nephrostomy decompression without image guidance can most easily be done using a posterolateral approach to access a posterior or lower pole calyx.

## Technique

Prior to proceeding, the patient should be educated on the inherent risks of percutaneous nephrostomy. The lack of image guidance places the patient at slightly greater probability of experiencing an adverse event, as multiple passes may be required to obtain initial access. Preprocedural laboratory values are reviewed, including a coagulation profile, platelet count, and urinalysis. Preoperative broad-spectrum antibiotics are given, and narrowed according to sensitivity profiles when clinically appropriate. General anesthesia is not required in most cases, as use of a local anesthetic and sedation is usually sufficient. The patient is positioned prone with all pressure points padded. The ipsilateral flank is prepped widely, and draped with adequate exposure to facilitate choosing the site of skin puncture.

Initial skin puncture is guided by anatomic landmarks, as discussed previously. The lumbar notch can be palpated, and is an anatomic window that provides the path of least resistance when determining the ideal tract for collecting system access. The 12th rib is identified, and needle entry should be below this point to minimize the risk of pneumothorax and intercostal nerve irritation. After selection of the puncture site, the skin and subcutaneous tissues are infiltrated with local anesthetic.

An 18G sheathed access needle provides stability, can be torqued easily, and does not require exchange to place a suitable working wire. An obstructed, dilated system provides a larger target area to obtain access and can be achieved safely with the convenience of a larger needle. Alternatively, a 22G spinal needle may be used with a 0.018-inch wire for initial entry. A smaller-gauge needle can diminish the risk of clinically significant hemorrhage associated with renal puncture, as well the risk of visceral organ injury [13]. The needle is positioned at the lumbar notch, oriented slightly cephalad, and angled approximately 30° in relation to the vertical axis. The needle is advanced to a depth of 4–5 cm and aspiration can confirm entrance to the collecting system. If initially unsuccessful, negative pressure is applied to the needle while being withdrawn as it may then be slowly pulled back into the collecting system. The needle can be repositioned at the same puncture site and slight modification of angle and depth will allow access to the pelvicalyceal system. Once access is confirmed with aspiration of urine, a hydrophilic atraumatic tipped guidewire is passed gently into the system, to ensure no resistance is encountered. If the initial indication for blind nephrostomy was the inability to opacify the collecting system, an antegrade pyelogram can be performed to retarget an alternate calyx if deemed necessary. In the case of obstruction causing infection, the primary goal is drainage, and which calyx is accessed becomes less relevant. The remaining steps mirror those of the standard percutaneous access. A skin incision is made, and tract dilation is performed 2–4 Fr greater than the size of the desired nephrostomy tube. The nephrostomy tube is passed over the guidewire and deployed along the percutaneous tract in the collecting system.

## Results

The blind percutaneous technique should be reserved for emergent cases in which retrograde access cannot be obtained, opacification of the collecting system is not feasible, or imaging is unavailable. Chien and Bellman reported a 98% success rate in a retrospective review of 40 blind percutaneous renal access procedures, equivalent to that of image-guided access [7]. A single procedure required ultrasound guidance to obtain successful access. No adverse events or complications were reported in their series. The majority (75%) of initial collecting system entries were at the renal pelvis with 17.5% being achieved within the kidney itself, and the remaining being obtained in the upper/lower pole. A comparison of retrograde stent placement versus nephrostomy tube insertion for obstructing calculi with evidence of clinical infection revealed no significant differences in time to clinical improvement or length of stay, although those undergoing percutaneous nephrostomy had increased perceived back pain [14].

## Complications

Percutaneous renal access without image guidance theoretically places patients at increased risk of morbidity. Bleeding complications arise when segmental or interlobar branches are injured and the incidence of severe bleeding ranges from 0 to 2.6% in published series [15]. These can be reduced by ensuring that preoperative coagulation abnormalities are addressed, that 22G spinal needle placement is towards Broedel's avascular plane when possible, and that the number of punctures is minimized [16]. Emergent decompression is largely completed for an obstructed, potentially infected urinary tract. The incidence of septic complications ranges from 1 to 21%, and decreasing manipulation and broad-spectrum antibiotics preoperatively can reduce these events [17, 18]. The risk of pleural transgression increases with intercostal punctures, the rates of pneumothorax and effusion reaching up to 4 and 8%, respectively [19–21]. If intercostal puncture is absolutely necessary, a postoperative chest radiograph should be completed, especially when access is obtained blindly. Bowel perforation is fortunately a rare complication, reported in fewer than 1% of cases, and can be treated conservatively in the majority of cases [22–24]. Visceral organ injury is also rare, yet patients must be informed of this potential complication [25].

## Conclusions

Blind percutaneous renal access can be performed safely, with minimal morbidity when all preoperative factors are addressed. In the appropriate setting, knowledge of this technique can provide urologists with an essential skill set to expedite management and improve patient care.

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# 20

# Percutaneous Nephrolithotomy Access: Robotic

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## Introduction

Since the latter part of the twentieth century, robotic technology has been applied to a number of industrial and manufacturing processes. Due in great part to potential advantages of motion finesse associated with robotic manipulation, recent years have witnessed an increased interest in the introduction of robotics to the healthcare system. Robots were first introduced to the surgical field in the 1980s, and at that time were focused primarily on neurosurgical and orthopedic applications [1]. As interest in robotics expanded into other medical specialties, urologic applications were soon identified. Since that time, robotics has rapidly assumed an integral role in the urologic armamentarium.

The first reported urologic application of robotic technology was described by Davies et al. in 1989, who designed a robot (PROBOT) to perform transurethral resection of the prostate [2–4]. Since that time, a number of targeted research projects have been undertaken to identify and develop applications for robotics within the urologic specialty. In many cases, robot-assisted surgical approaches have become commonly accepted; robot-assisted laparoscopic radical prostatectomy and partial nephrectomy may be the best examples of this.

The suitability of robotics for urologic surgical applications derives from the properties inherent to robotic technology, namely that these devices are versatile, mechanically capable, and programmable. Tasks that are particularly suited to robotic technology are those that require accuracy, reproducibility, fine motor movements, as well as motion that is difficult to perform by hand due to constrained access, such as for laparoscopy, and ergonomic limitations, such as for magnetic resonance imaging (MRI)-guided interventions. To that end, robotic technology can improve on conventional techniques in, for example, securing percutaneous access to the renal collecting system. In this chapter we review the genesis and present applications of robotic systems designed to facilitate percutaneous renal access.

## Goals of robotic percutaneous renal access

Urology has been one of the surgical disciplines at the forefront of the application of robotic technology, and the kidney is rapidly becoming a target organ for this technology. Robot-assisted laparoscopic renal surgery, although only recently described, is becoming a standard surgical approach for renal malignancy and reconstruction. Image-guided percutaneous surgery is likely to be the next generation of renal surgery to benefit from robotic technology [5]. Percutaneous renal surgery encompasses a wide diversity of procedures: nephrostomy tube placement, percutaneous nephrolithotomy (PCNL), percutaneous treatment of transitional cell carcinoma, renal biopsy, renal cyst or abscess drainage, radiofrequency ablation of renal tumors, and percutaneous renal tumor cryoablation. These many procedures are all potential clinical applications for a robot designed to gain renal access percutaneously.

There are a number of practical advantages to robotic assistance for percutaneous renal therapies. For the urologist, one of the most significant challenges of a percutaneous procedure is applying the three-dimensional (3D)

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renal anatomy to a two-dimensional image representation. In many cases, this anatomic transposition may be confusing. Reliably and safely attaining an optimal point of renal access can require extensive training and experience. Certain clinical situations, such as entry into a nondilated renal collecting system or anatomical variation (e.g. duplex system, malrotation, horseshoe kidney), can be challenging, even for the experienced clinician. There is associated risk of injury to adjacent structures with percutaneous renal access and complex cases may increase this risk. An additional complexity for the urologist, which is not encountered in the orthopedic and neurosurgical fields, is the mobility of the kidney within the retroperitoneum, including its continuous movement with respirations. At many institutions, urologists lack the requisite experience in placing percutaneous access, and such procedures are performed by the interventional radiologist. A lack of participation by the urologist in obtaining percutaneous access for PCNL, for example, may result in the patient undergoing more than one procedure if the access and nephrolithotomy portions of the procedure are performed at times and locations remote from one another. The urologist may also have insights into the manner in which stone removal should be performed, and a lack of such input may result in suboptimal access location. This may translate to longer operative and fluoroscopic times, and subsequently greater risk for complications and higher radiation exposure. Additionally, there are certain complex clinical scenarios where multiple access sites may be necessary, thus requiring further procedures.

Unlike humans, robots are digital devices that are controlled in 3D space. With proper image registration and navigation algorithms, these can be used to address many of the challenges associated with renal access: improved spatial accuracy, programmable, mechanical, and flexible capabilities, and once designed they can be reproducibly used by a surgical novice. With novel technology that allows constant impedance measurements and rotating needle drivers, many of the above-mentioned challenges, such as renal mobility, could possibly be overcome.

The ultimate goals in applying robotic technology to percutaneous access are to increase the ease and decrease the technical challenges of this task, while improving accuracy, efficiency, and reproducibility. Robotic technology holds the potential to provide greater precision than the human hand can, with improved puncture accuracy. Robotic assistance for percutaneous access may ultimately improve surgical performance and decrease complication rates, radiation exposure to patient and providers, and operative times [6].

## Development and evolution of robotic percutaneous renal access systems

Robotic percutaneous renal access systems were first proposed by Potamianos et al., who performed pioneering work in the creation of a passive robot to facilitate needle placement for percutaneous surgery [7–9]. The system was mounted on an operating room table, required fluoroscopic imaging to guide placement, and had five degrees of freedom (DOF). System performance experiments reported at that time described a 1.5 mm targeting accuracy.

In 1996 our urology engineering program, URobotics, was initiated at Johns Hopkins Medicine [10]. This program is dedicated to the development of new technology and gathers both clinical and technical personnel working in close communication to achieve the goal of robotic image-guided surgery. Many of the robotic systems that have been developed over the last 15 years were developed through this program; these systems are discussed below.

### Modified LARS

A prototype system using a modified Laparoscopic Assistant Robotic System (LARS) was introduced in 1997 by Cadeddu et al. [9]. LARS was a modified laparoscopic assistant active robotic system which maintained seven DOF. Each robotic joint was moved by an electric motor, so the access procedure was totally automated. Biplanar fluoroscopic imaging was used to guide the access procedure. The authors described that *in vitro* accuracy was 0.43 mm, and *ex vivo* success with the first attempt was 83%. The authors noted that problems arose with tissue and needle deflection. No comparison to nonrobotic human placement was done with this device, but rather this was a proof-of-concept experiment. This study, despite its limitations, demonstrated that robotic percutaneous access was feasible, although the need for multiple improvements and modifications, such as advanced software, increased DOF, and improved needle design and feedback mechanisms, were identified.

### PAKY

The next generation of robotic systems that was developed for renal indications was termed PAKY (which stood for percutaneous access to the kidney), and also is a product of the URobotics program at Johns Hopkins. PAKY consists of a passive mechanical arm with active translational motion providing needle insertion in a compact and radiolucent module. The device is mounted on an operating room table and can be fitted with a standard trocar needle. An active translational mechanism is used for needle advancement, and fluoroscopy is used to align and monitor needle placement. *In vitro* experiments using PAKY were carried out in 1998 with porcine kidneys and *in vivo* studies were completed in nine human patients [11]. Accuracy was 100% in both *in vitro* and *in vivo* attempts. The mean targeted calyx was 14.7 mm in diameter, and the mean time required to gain access was 8.2 minutes. No complications occurred in any of the trials. These *in vivo* studies demonstrated the robotic system to be steady, safe, and effective, thus serving as a springboard and providing the groundwork for further development of a complete robotic system.

### PAKY-RCM

In 2002 the second-generation PAKY robot, PAKY-RCM (percutaneous access to the kidney with the remote center of motion device), was also introduced by the URobotics program. This is a robot with three active DOF that can remotely align the needle along a selected trajectory pathway under fluoroscopic guidance, minimizing radiation to the surgeon's hands. PAKY is the needle driver and the RCM device is an active robotic arm attached to PAKY that allows the tip of the needle to pivot about a fixed point on the skin. There is a joystick control located on the control box used to advance the needle. Clinical comparison was done using PAKY-RCM versus manual needle placement [12]. There were 23 patients per group and variables measured were number of access attempts, time to successful access, estimated blood loss, and complications. In the robotic group, 87% (20 of 23) of attempts were successful in gaining access. Three patients were converted to manual techniques for various reasons including mechanical failure, and these were successful but took longer than 30 minutes, illustrating the complexity of the access. All manual access attempts were successful. Only single access was needed for all patients, and no major complications occurred in either group. Time to access was not significantly different between the groups ($P = 0.06$), with a mean of 10.4 minutes required for robotic access versus 15.1 minutes needed for manual access. These investigators again demonstrated the robotic access to be both feasible and safe, with acceptable success rates.

### Electrical impedance needle sensor

Entry into the renal collecting system is the requisite endpoint of percutaneous renal access. However, in many cases the urologist has little objective information to confirm this outcome; radiographic imaging can be uncertain and aspiration of urine can be unreliable. To address this clinical problem, the URobotics program designed a "Smart Needle" system, which consists of an access needle fitted with a sensor on the exposed stylet tip that continuously measures electrical impedance (Figure 20.1) [13]. When the collecting system is entered, resistivity drops precipitously. This system was invented to provide objective feedback to the surgeon that access into the renal collecting system has been successfully gained; malpositioning of the needle should be reduced with this device. A series of experiments in which image-guided access to porcine kidneys was performed revealed a significant reduction in resistivity when the needle entered the collecting system in 11 of 16 attempts. The promise of the Smart Needle system rests in its ability to optimize renal access, potentially reducing needle-related complications which may occur during this procedure. This needle, which can provide objective feedback to the surgeon gaining access, may reduce the number of access attempts, increase puncture accuracy, and decrease procedure duration and radiation exposure. The Smart Needle can be used in combination with any of the previously described robotic systems. It should be noted that the Smart Needle was evaluated only in dilated collecting systems and it is unclear if impedance will drop so precipitously in a nondistended system. In addition, urine with altered chemical makeup, such as grossly bloody or purulent urine, may not demonstrate such an objective reduction in resistivity. Further studies are required to better define these potential limitations.

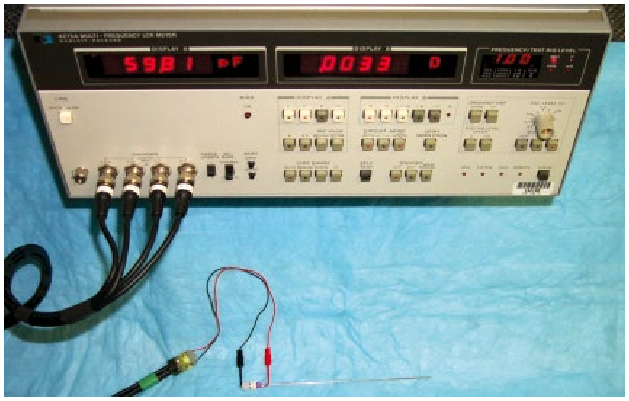

**Figure 20.1** Electrical impedance system for the "Smart Needle."

### AcuBot robot

Needle-based therapies such as thermal ablation and cryoablation are increasingly being utilized for the treatment of renal tumors. Due to the image-guided nature of these procedures, there is interest in the design of computer-assisted navigational systems to increase

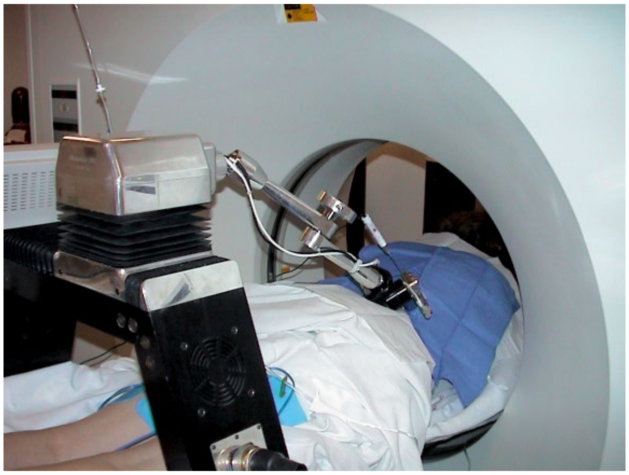

**Figure 20.2** Clinical demonstration of the AcuBot robot.

treatment accuracy. AcuBot is a novel, completely automated, robotic system with six DOF capable of needle placement based on imaging data (Figure 20.2). It has the advantage of changing skin locations for entry and has force sensors. Studies have been conducted in phantom models with computed tomography (CT)-guided imaging to assess and compare accuracy between robotic and manual placement by experienced surgeons and radiologists [14]. Accuracy was 1.2 mm for AcuBot needle placement versus 5.8 mm in manual placement ($P < 0.0001$). The mean time from target acquisition to needle placement was 37 seconds for the AcuBot and 108 seconds for the surgeon ($P = 0.001$). This robotic system has the potential to increase accuracy and decrease operative time and radiation exposure, thus decreasing complications and improving clinical outcome. Further studies in animals and clinical experiments are needed to better characterize this promising technology.

## Revolving needle driver

Most image-guided robots position and orient a needle guide so that the needle is manually placed through the guide [15]. There are advantages in manually inserting the needle through a guide, such as keeping the physician in direct control of the needle, instrument simplicity, and perhaps facilitating regulatory approvals for clinical trials and use. However, this compromise also mediates the full potential benefits of robotic image guidance [16, 17]. The Johns Hopkins URobotics group has recently developed a two-DOF needle driver that, in addition to automated insertion, can spin the needle and perform a set of experiments to assess the influence of needle spinning on the accuracy of needle insertion (see Video 20.1) [18]. Figure 20.3 shows the revolving needle driver device supported by the AcuBot robot. Experiments revealed that spinning is useful for improved targeting and could reduce errors by as much as 70%. Another group at the University of Pittsburgh also focused on the needle driver design for percutaneous kidney access assistance, developing a needle steering system via duty-cycled rotation, although this was only tested *in vitro* [19].

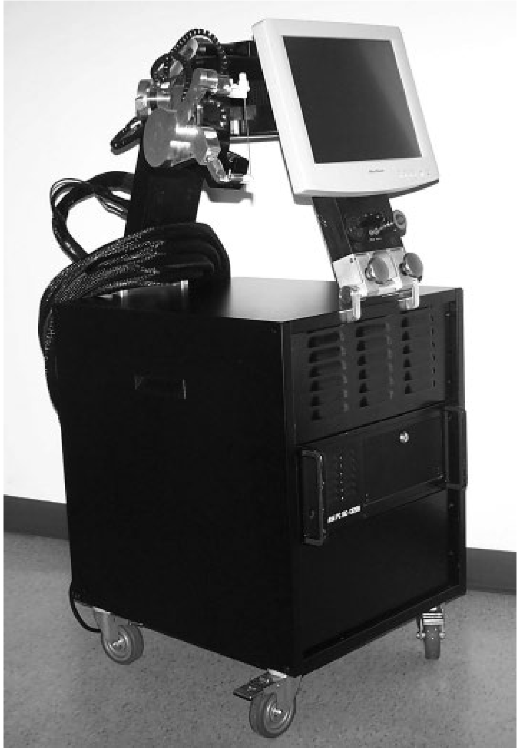

**Figure 20.3** The AcuBot robot with revolving needle driver.

## Mechanical gantry system

While many of these robotic systems are promising, they are also quite expensive. A group from South Africa developed a mechanical gantry system to assist with renal access during PCNL that is more cost-effective [20]. It is also portable and lightweight. It consists of a needle alignment device and a mechanical gantry with six DOF that attaches directly to the operating table. Two images are taken with the C-arm in anteroposterior and oblique positions and subsequently uploaded to a computer software program. The urologist selects the desired access on the screen and the software calculates the needle trajectory. Values are provided for the surgeon to manually adjust the gantry on the table and the needle is then able to be advanced via the needle guide. The system was tested in a phantom model and also porcine kidneys and was accurate and precise.

### Telerobotics and telementoring

Telemedicine has emerged as a promising new field, and provides the ability to disseminate surgical knowledge, particularly complex techniques, to novice surgeons. Both AESOP (a robot for remote manipulation of an endoscopic camera) and PAKY (percutaneous access of the kidney) have been used to study the utility and feasibility of telesurgery and international mentoring [21, 22]. Among the procedures completed were renal biopsy and percutaneous access to perform nephrolithotripsy or place a nephrostomy tube, which was successfully achieved with PAKY [23].

Telesurgery has been the subject of a randomized controlled trial, which compared human versus robotic and telerobotic access to the kidney. Using a validated kidney model, the authors found that in over 304 access procedures, humans were faster than the robot (35 vs. 57 seconds). The robot, however, was more accurate with 88% success of access gained on the first attempt versus 79% success by humans ($P = 0.046$) [24].

## The future

Although much robotic percutaneous access remains investigational, several systems have been tested and applied to clinical situations with human patients. Several of these systems, as described above, have demonstrated great promise in improving safety, accuracy, and clinical outcomes, while decreasing operative times and complication rates. If these goals are achieved, robotic systems have the potential to be both cost-effective as well as medically desirable. Importantly, in the present medical climate, the cost-effectiveness of these systems must be considered, an area of research that remains to be done. However, as time passes and technology continues to be refined, it is anticipated that robots will play ever increasing roles in precise and accurate techniques such as those required for percutaneous access. Additionally, navigation systems for percutaneous renal access, such as iPad-assisted puncture, laser-guided puncture on Dyna-CT, electromagnetic tracking for puncture, and optimal tracking for ultrasound-guided access, continue to develop and may serve to enhance the robotic technology further.

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## 21

# Dilation of the Nephrostomy Tract

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## Introduction

In the past, dilation of the percutaneous nephrolithotomy (PCNL) tract was thought to be essential to extract stones under radiological control [1] or to disintegrate and extract them endoscopically [2]. Today, however, the uses of PCNL tract dilation is decreasing and the options vary between no dilation and one-shot dilation, which is a kind of penetration. No dilation is needed with the microperc PCNL technique performed through a 16 gauge needle sheath [3]. Even a large tract access can be established by "one-shot" without any dilation [4].

All dilation or penetration techniques can be applied safely and with comparable good success and low complication rates when the conditions are ideal and when the surgeon is familiar with the technique and experienced. The classical dilation techniques using serial dilators or balloons [5–7] may continue to exist for a certain time and certain indications parallel to the increasingly popular miniaturized and one-shot PCNL techniques.

## Dilators

The essential difference between balloon dilators and fascial, Amplatz, or Alken dilators and one-shot instruments used in a serial fashion or for one-shot dilation is that the latter all apply forward forces during their advancement while balloon dilation does not.

### Fascial dilators

Fascial dilators made of plastic have a cone-shaped tip and come in different lengths and sizes. Primarily designed for vascular procedures as catheter introducer sets they are available with thin-walled simple sheaths or peel-away sheaths. They are disposable. A reusable metallic 9 Fr dilator and 11 Fr sheath are part of the Alken dilators [8]. For PCNL, fascial dilators are used for preliminary dilation steps before application of the larger dilator systems or together with simple sheaths or peel-away sheaths in a one-shot dilation technique for miniaturized PCNL [9, 10].

### Amplatz dilators

The Amplatz system [6] consists of 12 plastic dilators with conical tips and sheaths of different length and sizes up to 36 Fr. A long 8 Fr dilator fits over a guidewire for a preliminary dilation and to stabilize the guidewire to prevent kinking. The Amplatz system requires repetitive in-and-out movements of the increasing size dilators. As a disposable system it is designed for one-time use only.

### Alken dilators

The Alken dilators [11, 12] were the first purpose-built PCNL instruments and were designed for one-session (pincture–dilation–nephroscopy–stone removal–nephrostomy) PCNL. The system consists of a conical metallic 9 Fr dilator and an 11 Fr metallic sheath which are used for preliminary dilation, introduction of a safety guidewire and atraumatic placement of the 8 Fr hollow guide rod [8]. The eight successive metal dilators up to 30 Fr are advanced over the guide rod, one over the other, up to the required size. The dilators are flat at the dilation end point. Finally a 24 or 26 Fr continuous-flow nephroscope sheath or any Amplatz sheath is advanced over the dilators.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

In difficult situations with no passage of the guidewire or the guide rod into the renal pelvis, an 18 Fr nephroscope could be introduced after the third dilation step to inspect the calyx for a safe dilation route into the renal pelvis.

The rigid metallic guide rod (Alken guide) is currently frequently used for one-shot dilations [4, 13–21].

### Balloon dilators

Balloon dilators [7] come with pressure devices to inflate the balloon up to the required diameter of 20 to 30 Fr and sheaths up to 36 Fr and of different length. Preliminary tract dilation with fascial dilators is frequently done. The advantages of balloon dilation are that it is a one-step process, speed (with consequently reduced fluoroscopy time), and the exclusively radial forces during dilation. Balloon dilation is the most expensive technique available.

## Dilation in miniaturized percutaneous nephrolithotomy

The miniaturized PCNL technique was first used in 1997 for the treatment of a child [9]. The tract was dilated to 16 Fr, established with a 15 Fr angiocatheter introducer set with a peel-away sheath, and stones were extracted with a pediatric cystoscope.

Jackman et al. were the first to apply the technique in a series of children and adults [10]; they called it “mini-perc” [22]. They used an 8/10 Fr guidewire introducer set and an 11/13 Fr ureteroscopy sheath set which was cut to the desired working length to introduce ureteroscopes or pediatric cystoscopes. Stones were disintegrated with laser or ultrasonic probes.

Lahme et al. [23] developed the first purposely designed instrument for miniaturized PCNL, called the mini PCNL (MPCNL). They used a single-step dilation with a 14 Fr plastic dilator, 15 Fr and 18 Fr metal sheaths and a 12 Fr nephroscope; the set was designed as a continuous-flow system with outflow via the sheath.

The microperc technique has been designed to allow one-step instrumental access without the need for dilation by puncture only using a 4.85 Fr needle to puncture the collecting system and a 16 gauge needle sheath with an attached three-way connector for irrigation, passage of a telescope, and a laser fiber [3]. Other miniaturized techniques frequently initially use fascial dilators. A recent meta-analysis comparing miniaturized PCNL with standard PCNL showed that dilation was best done with fascial dilators of 13–18 Fr [24]. One study [25] used the minimally invasive PCNL one-shot technique described by Nagele et al. [26] with a metallic one-shot 16 Fr dilator/18 Fr sheath.

Depending on the type of miniaturized instruments, various dilation procedures are used. In a large series on children, serial fascial dilators and 14–16 Fr peel-away sheaths were used [27].

Zeng et al. reduced the fluoroscopy access time by using scaled fascial dilators and sheaths of 18 Fr [28]. With their >10 000 Chinese minimal invasive percutaneous nephrolithotomies Zeng et al. dilated the main tract to 18– 20 Fr and secondary tracts to 14–18 Fr [29]. Bhattu et al. used miniaturized systems from different instrument makers and dilated in single-step or sequential fashion to sheath sizes of 18, 19.5, and 20 Fr [30]. In super-mini percutaneous nephrolithotomy (SMP), tracts are dilated to between 10 and 14 Fr with fascial dilators [31]. Datta et al. dilated with fascial dilators to 7 Fr and 12 Fr and introduced the 13 Fr ultra mini percutaneous nephrolithotomy (UMP) outer sheath [32]. Karakan et al. did a one-shot dilation to 14 Fr using a modified UMP technique [33].

There are various different competing miniaturized PCNL instruments on the market. With all techniques the dilation is less important than what is offered for instrumentation, irrigation, and/or suction within the sheaths and the nephroscopes used.

The small tract of a miniaturized PCNL will forgive a bad puncture much more than a large dilated tract because the trauma is limited size-wise and so puncture-driven complications, such as bleeding or extravasation, will be less frequent and less severe. Complications include (i) vascular lesions of intra- or extraparenchymal vessels, (ii) collecting system lesions by a nontranspapillary access, (iii) rupture of the collecting system in the case of a mismatch between dilation size and collecting system, and (iv) frontal forward perforations.

## One-shot dilation

Establishment of a large tract by “one-shot” access was first used by Frattini in 1998. After puncture of the collecting system and guidewire placement “a single 25 F or 30 F Amplatz dilator was pulled in on the Alken guide or on the 8 F first polyurethane dilator of the Amplatz set. This single passage allowed the insertion of the 34 F working sheath. … Each procedure was performed by a surgeon with great experience in the field of endourology” [4].

Successfully applied for large tract diameters, the one-shot technique can of course also be applied independent of size in all miniaturized PCNL procedures. Previous open surgery on the same kidney had no influence on the good success rate of one-shot dilation [34]. In children, one-shot dilation compared favorably with the Alken technique [17].

A one-shot principle for all sizes is made available by the minimally invasive PCNL (MIP) instruments of Karl

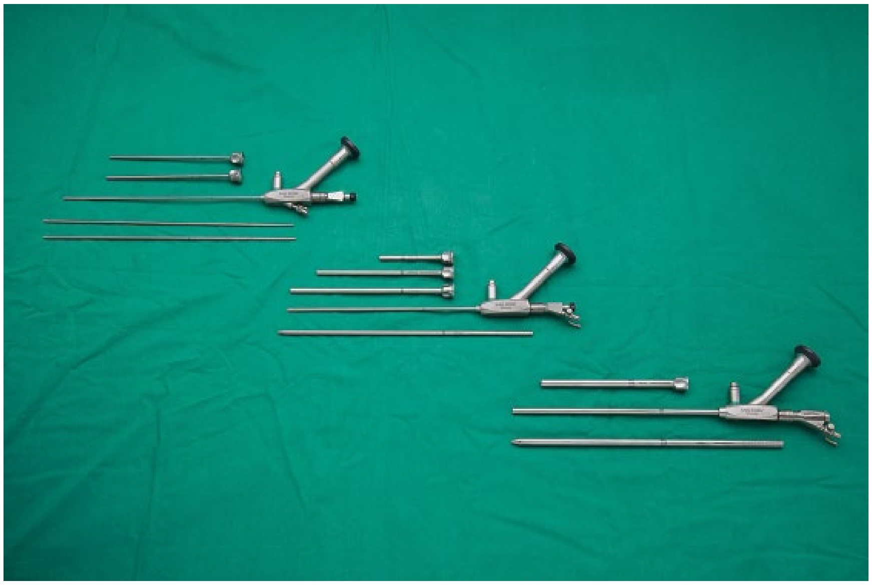

**Figure 21.1** Minimally invasive percutaneous nephrolithotomy dilators, sheaths, and nephroscopes. *Source*: Karl Storz Endoscopy-America, Inc., 2017. Reproduced with permission of Karl Storz GmbH.

Storz, which come in seven dilators sizes between 8,5 and 26 Fr with matching operating sheaths between 8.5 and 26 Fr (Figure 21.1) [35, 36].

The data in Table 21.1 show that access time and access fluoroscopy time are approximately halved with one-shot procedures.

Two recent meta-analysis comparing the different dilation techniques both principally recommended that one-shot dilation should be offered to most PCNL patients [44, 45]. As frequently stated in surgical literature, one additional remark was: "Nonetheless, a large number of multicenter randomized controlled trials of high quality are still required to explore the differences among OSD [one-shot dilation], MTD [metallic telescoping dilation], BD [balloon dilation], and AD [Amplatz dilation]" [44].

Li et al. concluded "Urologists could first choose one-shot dilation for tract creation in PCNL. Even if failure occurs, it is easy to shift from the one-shot to the standard dilation technique" [45]. I agree, but at the same time in a few cases there might be a procedural step when this strategy leads to irreversible catastrophes because the resistance of the tissue is misinterpreted as invitation to double the forward pushing forces – just as with the old techniques. Many of these problems happen but are unpublished.

## Tract dilation: ideal and special situations

Once the access is established by the puncture, the surgeon is aware of the primary quality of the access: probably good = transpapillary; probably bad = every other route. For the following steps the experienced surgeon will rarely have to change or is audaciously using the less than perfect tract; the unexperienced surgeon has the option to change but will frequently choose not to because he or she does not want to give up the access that has been established. These options, the realized or neglected need to do an alternate/better puncture to improve access quality is rarely described or even discussed in relevant publications. Bleeding during PCNL signals a bad puncture or a traumatic intrarenal instrumentation. The contribution of dilation to blood loss is mainly only secondary to widening the needle tract and increasing the trauma of the wrong puncture. Thus comparing transfusion or extravasation rates of different dilation techniques only transfers other details of the whole procedure to the dilation step. This also explains some of the reported variety seen in the literature [46, 47] (Table 21.1). The Clinical Research Office of the Endourological Society (CROES) publications on dilation did not differentiate between Amplatz and Alken dilators and had to do extensive subgroup analysis to try to differentiate between causal and casual relations [46, 47].

The first PCNL step after puncture is the positioning of a guidewire for the subsequent dilation. This is usually possible independent of the access quality. The passage of the guidewire gives first information on the tract quality: it varies between down the ureter "through and through" to outside the urethral meatus and just to the stone. These are first messages on access safety and access perfection.

The puncture is straight but within the collecting system, anatomy and stone shape may require a curved tract. Preliminary dilation with small-diameter fascial dilators will inform the surgeon through any resistance

**Table 21.1** Overview of published dilation procedures, tract sizes, transfusion rates, fluoroscopy, and access times.

| Author, year, RCT | Dilation technique, tract size (Fr) | | | | Dilation technique, transfusion rate (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | One-shot | Alken | Amplatz | Balloon | One-shot | Alken | Amplatz | Balloon | Fluoroscopy time | Access time |
| Frattini [4] 2001 | 34 | | | | 0 | | | | Guidewire to sheath 20 ± 3 s | n.a. |
| | | 34 | | | | 4 | | | 60 ± 7 s | n.a. |
| | | | | 34 | | | | 12 | 35 ± 7 s | n.a. |
| Safak [37] 2003 | | | 32 | | | | 15.6 | | n.a. | Tract formation time 16.3 ± 2.4 min |
| | | | | 32 | | | | 13.7 | n.a. | 11.2 ± 3.0 min |
| Ziaee [21] 2007 | Without previous open surgery 30 | | | | 5.6 | | | | Before insertion of access needle to nephroscopy 0.60 ± 0.68 min | Access by needle to nephroscopy 5.93 ± 4.94 min |
| | With previous open surgery 30 | | | | 10.9 | | | | 0.65 ± 0.75 min | 6.24 ± 3.63 min |
| Gönen [38] 2008 | | | 34 | | | | 21.3 | | n.a. | n.a. |
| | | | | 34 | | | | 18.6 | n.a. | n.a. |
| Amjadi [39] 2008 Previous open surgery, RCT | 28 | | | | 5.9 | | | | Guidewire to Amplatz sheath 27 ± 15 s | n.a. |
| | | 28 | | | | 5.9 | | | 81 ± 53 s | n.a. |
| Wezel [40] 2009 | | 26 | | | | 2 | | | n.a. | n.a. |
| | | | | 30 | | | | 8 | n.a. | n.a. |
| Falahatkar [41] 2009 RCT | 30 | | | | 3 | | | | Insertion of needle to Amplatz sheath 22 ± 4 s | Puncture by needle to Amplatz sheath 6 ± 2 min |
| | | 30 | | | | 4 | | | 65 ± 12 s | 7 ± 2 min |
| Aminsharifi [13] 2011 RCT | 30 | | | | 0 | | | | Before insertion of access needle to nephroscopy 0.77 ± 0.41 min | From getting access by needle to nephroscopy 5.72 ± 1.75 min |
| | | 30 | | | | 0 | | | 1.12 ± 0.68 min | 10.47 ± 2.97 min |
| Ozok [42] 2012 | | 30 | | | | 11.6 | | | n.a. | Tract formation time 5.42 ± 3.07 min |
| | | | 30Fr | | | | 13.4 | | n.a. | 6.56 ± 3.04 min |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Amirhassani [14] 2014<br>RCT | 28–30 | | | | 2 | | | | “X-ray exposure time” 41.2 ± 17 s | n.a. |
| | | 28–30 | | | | 2 | | | 48.4 ± 15 s | n.a. |
| El Harrech [16] 2014 | 30 | | | | 1.25 | | | | Access needle to Amplatz sheath: 25 ± 17 s<br>Total fluoroscopy time 142 ± 54 s | Needle puncture to nephroscopy 2.1 min (range 0.7–6.2) |
| Hosseini [17] 2014 | Children 24–26 | | | | 0 | | | | Not defined<br>22.0 ± 5.6 s | Not defined<br>5.9 ± 1.5 min |
| | | Children 24–26 | | | | 0 | | | 70.0 ± 8.9 s | 7.3 ± 1.2 min |
| Ren [43] 2014<br>Staghorn stones, ultrasound control only | | | 24 | | | | 27.9 | | n.a. | 15.1 ± 3.6 min |
| | | | | 24 | | | | 13.2 | n.a. | 10.0 ± 3.3 min |
| Nour [19] 2014<br>RCT | 30 | | | | 4 | | | | Total fluoroscopy time<br>10.5 ± 4.7 min | n.a. |
| | | 30 | | | | 4 | | | 11.8 ± 0.42 min | n.a. |
| Süelözgen [34] 2016 | One-shot 25–30 previous surgery | | | | 4.8 | | | | Total fluoroscopy time 230 ± 294 s | n.a. |
| | One-shot 25–30 no previous surgery | | | | 1.2 | | | | 194 ± 44 s | n.a. |

RCT, randomized controlled trial.

felt about tract curves that do not become apparent in the anteroposterior fluoroscopy projection.

The tract diameter is negligible outside the kidney, but becomes important within the parenchyma depending on the structures traversed. Within the collecting system it should match the space offered by the collecting system and available between stone and collecting system. The smaller the tract size, the more it will forgive a bad access or unfavorable intrarenal conditions.

### Ideal situation

In the ideal situation all dilation techniques are equally effective and safe: the puncture is transpapillary; its direction exactly matches the long axis of the access calyx; the tract leads through a wide calyx straight into a capacious renal pelvis; the tip of whatever dilator used is well within the renal pelvis; and the collecting system is a significant part of the tract, adding safety space for movements. Only the parenchyma is dilated in an avascular area.

### Less than ideal situations

Less than ideal is a small access calyx or a diverticulum with a caught guidewire because of an angulation between puncture path tract and calyceal axis, or because of a stone blocking the calyceal neck. The risk of losing the tract is increased. Dilators with cone-shaped ends, such as balloons and Amplatz dilators, may create a problem when their straight part is not within the collecting system. With this kind of "short" dilation, advancing the sheath may catch and cut tissue between sheath and dilator. Visual advancement with help of the scope is equally traumatic. Boston Scientific has realized this problem and reacted by producing short-shoulder balloons to allow for dilation within a small space.

The tips of all Alken dilators are in one line when completely advanced, and this design proved to be advantageous in these tricky cases compared to balloon dilators, with access failure rates of 0% and 38%, respectively [48]. Another option is preliminary dilation with a 9/11 Fr dilator/sheath and percutaneous inspection with a rigid ureteroscope to find a proper route for the guidewire or a space between stone and calyceal wall for further dilation [49–51]. A visual dilator, such as an optical trocar in laparoscopy, could be advantageous in these situations [52].

Narrow calyceal necks with nonpliable walls or – even worse – an almost nonexistent simple or bifid renal pelvis are bad candidates for any form of dilation to a standard size as a disproportional diameter of the dilator will cause tissue disruption, extravasation, and subsequent scarring. In these cases the diameter of the different sections of the collecting system dictate the tract size or even the type of procedure. A small-diameter access with flexible ureteroscopy or miniaturized PCNL may be preferable to standard PCNL.

A completely stone-filled calyx is the impossible situation. The needle tip is felt touching the stone but neither dye nor a guidewire enters the calyx. "No PCNL can be performed" [53]. Dilation with flat-tipped telescope metallic dilators directly on that area, while strictly maintaining direction and position, has been done successfully. The nephroscope sheath is introduced and the thin tissue layer is removed with ultrasound lithotrity until the stone becomes visible and access is gained into the stone and the collecting system [54].

## Dilation procedure

Dilation is usually controlled by fluoroscopy but success with sonographic control has been described since 2008 [55]. If the surgeon is familiar with sonography, puncture and dilation with all techniques and even one-shot can successfully be done under pure ultrasound control [18] with few failures (2.8%), even in obese patients [18]. The technique was successfully applied in children to establish a 30 Fr tract in one shot [20]. Preliminary endoscopy through a 16 Fr plastic sheath with a ureteroscope helped to find the right way in the largest series done under ultrasound control [49].

All forward-advancing movements with any dilator or sheath should principally be done with one hand, in a twisting bidirectional rotation with approximately 70–80% of the force turning the dilator and 20–30% pushing it forward. This is surprisingly easier than a predominant forward movement. The force should primarily come from the fingers and the wrist. To prevent forward perforation the pushing hand should always be ready to stop the forward movement immediately; the other hand controls the guidewire or guide rod. Frequent short imaging controls with fluoroscopy or sonography are advisable.

It is only in case of strong tissue resistance outside the kidney that both hands may be used to advance the dilator; again both hands should be able stop the advancing movements within fractions of a second. To prevent a sudden jerky forward movement and perforation the surgeon's arms should be bent at the elbows and drawn to the surgeon's flank. The force does not come from the surgeon's body leant against the dilators but from the arms. If the resistance within the kidney is due to a narrow, scarred collecting system, the dilation process should be abandoned and a different technique of stone removal used. The telescopic dilators may catch tiny pieces of tissue material hindering the twisting movement. Pulling out the last two dilators, cleaning and reintroducing them may help. If using a guide rod (Alken guide) for telescoping or one-shot dilation, its tip should be in a position with as much safety space ahead to the pelvic wall as possible, and this position should be repeatedly adjusted if necessary.

## Complications, renal trauma, and renal function

Any discrepancy between forward pushing forces and the rigidity of the guidewire carries the risk of permanent guidewire kinking or passive guidewire retraction. This can jeopardize the access and make a new puncture necessary. Reinforced guidewires, such as the Lunderquist wire or the Alken guide, should therefore be used during dilation.

Alken dilators require precision and a firm and stable grip on the guide rod to prevent inadvertent advancement and forward perforation with the rod or dilators. The Amplatz system requires repetitive in-and-out movements of the increasing size dilators; bleeding from the tract can happen in between the steps. Tissue resistance to the dilation may lead to repeated buckling of the dilators and uncontrolled tract displacements. Having Amplatz dilators in the deep freeze ready for use has been described as a solution.

Guidewire kinking and losing access with balloon dilation are rare compared to serial dilation techniques. Failures to dilate the tract, especially after previous renal surgery, of up to 17% have been described in earlier series, with scarred tissue not being sufficiently expanded [56], but failure was negligible in a more recent series [57].

A cone-shaped end of any dilator leaves space between sheath and dilator. If during sheath advancement the dilator tip is partially or totally outside the collecting system, so-called short dilation, the sheath will catch, cut, and traumatize any tissue around the dilator tip.

Forward perforation of the collecting system is not a problem with balloon dilation itself and only seldom happens during the subsquent advancement of the sheath; forward perforation with rigid instruments should rarely be a problem by imaging control of the process and a judicious use of whatever dilation technique.

Tangential disruption of tract structures such as the collecting system or the invisible blood vessels is more difficult to control because it is not easy to determine if the structure to be dilated is extensible enough to accept the desired tract diameter and direction. With one-shot dilation this problem may be aggravated as neither the slowly expanding balloon nor the increasing resistance during serial dilation signals a problem to the surgeon. The latter problem is reduced with diminishing tract sizes such as in miniaturized PCNL.

Dilation to 24 Fr did not change serum creatinine or glomerular filtration rate (GFR) significantly in uncomplicated cases, and DMSA SPECT scans showed minimal functional losses below 1.8%. Only cases with complications had more significant changes of creatinine, GFR, and DMSA scans up to 2.7% [58]. This is not very different from recent studies on 30 Fr tracts with split renal function assessed by MAG3 renography. Functional losses were insignificant with one tract and only 2.28% with multiple tracts [59]. Balloon Alken or Amplatz dilation showed no different effects on renal function [60].

Tract dilation to different sizes has minimal measurable permanent effects on renal function. Traxer et al. saw no statistical difference in scar formation six weeks after dilation to 30 Fr or to 11 Fr in animal experiments with fractional losses of parenchyma of 0.63% and 0.91%, respectively [61].

The renal trauma caused by balloon and one-shot dilation may be comparable in its acuteness and if identical tract diameters are reached within one step. The brittle renal parenchyma reacts differently in the different dilation techniques to 30 Fr. In animal experiments serial dilation caused small round defects of 6–12 mm diameter, while ballooning caused 2–3 cm rupture-like parenchymal fragmentation. Nevertheless, final scar formation was similar in these and other experimental studies [62]. A recent clinical study comparing the effects of one-shot and serial dilation on scar formation and renal function showed a small but significant reduction of DMSA uptake and new scar formation or scar progression in nearly 50% of the patients with one-stage dilation compared to only 11% after serial dilation [13]. It may be that one-shot dilation has different consequences.

## Alternative devices and techniques

Alternative dilation devices and techniques have been described, such as the visual dilator [52], single-step balloon/sheath combinations [63–65], tract vaporization [66], a coaxial telescopic dilator set attached to the puncture needle [67], and a small Amplatz set for use in children [68].

The above list is incomplete but then most ideas did not make it to the market. To be generally accepted devices must be applicable in both easy and difficult cases, easy to use, safe, and not expensive. At present, one-shot dilation seems to be the winner on these grounds and with respect to cost (e.g. US$50 in Morocco) [16].

The goal of continuously advancing and technically sophisticated puncture techniques is to render successful access independent of the endourologist's experience. When these techniques are perfected in the near future, publications on combined one-step/one-shot access are to be expected. They could then be classified as penetration.

See accompanying Videos 21.1 and 21.2.

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# Part 5 Stone Removal

## 22

## Rigid and Flexible Nephroscopy

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### Introduction

The first reported nephroscopy was performed when Rupel and Brown inserted a rigid cystoscope through a nephrostomy tract to remove stones during open renal surgery in 1941. Fifteen years later, Goodwin obtained the first percutaneous renal access when contrast was injected into the collecting system while attempting to perform a renal arteriogram.

Since that time, the techniques and technology associated with the percutaneous route for intrarenal surgery has grown tremendously [1]. Percutaneous nephrolithotomy (PCNL), first described in the 1980s [2], is now the gold standard for the removal of staghorn renal calculi due to its minimally invasive nature and high stone-free rates [3]. With advances in instrumentation, use of percutaneous access has also expanded to treating renal diseases such as symptomatic renal cysts, stenotic infundibula, excluded calyces, and upper tract transitional cell carcinoma.

Rigid nephroscopes, with their offset lens and straight working channels permitting rigid instrumention, are the most commonly used instruments to clear stones from the collecting system during PCNL because of their durability and efficiency; however, there are times when, due to anatomic constraints, this instrument cannot perform all of the functions needed to render a patient stone free.

This chapter discusses recent advances in rigid nephroscopy and flexible nephroscopy through percutaneous access and covers equipment and techniques that can maximize efficiency and minimize morbidity for various percutaneous renal procedures.

### Indications for nephroscopy

#### Diagnostic indications

With advances in endoscope technology, scope design (including digital imaging), and the use of access sheaths, the diagnostic accuracy of retrograde ureterorenoscopy for upper tract urothelial carcinoma is now 76–98%. Rigid and flexible nephroscopy as purely diagnostic procedures are therefore not routinely performed [4–6]. However, in certain patient populations, for example patients who have had cystectomy and urinary diversion who no longer have readily obtainable reterograde access, the percutaneous route may be the only option for access to the pelvicalyceal system.

#### Therapeutic indications

With the combination of rigid and flexible nephroscopy techniques, percutaneous nephroscopy can be used to treat the following:

- Stone disease: treatment of large or complex/staghorn calculi.
- Obstructed calyces, infundibular stenosis, and calyceal diverticula: access obtained in a “direct” manner in which the percutaneous access is directed at the obstructed area or an “indirect” approach where the obstructed area is accessed via another puncture site.
- Ureteropelvic junction (UPJ) obstruction: antegrade endopyelotomy and/or endopyeloplasty with a balloon cutting device, holmium:YAG laser incision, hook knife, Sachse urethrotome, or endoscopic shears [7].
- Upper tract transitional cell carcinoma (TCC): ablation of tumors with lasers or resection with a cautery system.

*Smith’s Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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This chapter focuses on rigid and flexible nephroscopy for stone disease. Chapters 28, 30, and 31 provide further detail on using antegrade access for calyceal diverticulae, UPJ obstruction, and upper tract TCC, respectively.

### Indications for flexible nephroscopy

The chief indication for flexible nephroscopy is access to calyces with stones or tumors that cannot be reached with the rigid nephroscope.

Achieving stone-free status with a single procedure is an important consideration for both the patient and the provider. From a patient perspective, a second procedure can be very costly in terms of time away from work or quality of life. For the urologist, performing a secondary procedure during the 90-day global period can be unappealing. It is common, however, for a surgeon to encounter a case where a patient cannot be rendered stone free using a single access and a rigid nephroscope. As such, the flexible nephroscopy is an important adjunct to rigid nephroscopy for complete stone clearance.

Flexible nephroscopy has been growing in popularity recently as surgeons have shown its use can avoid the need for an additional access. Williams and Leveillee showed that a combination of flexible and rigid nephroscopy can be successfully used to render patients stone free, even in the face of complex stone disease [8].

Flexible nephroscopy can also be used through a percutaneous access to treat obstructed calyces or a calyceal diverticulum when a rigid nephroscope cannot reach the infundibulum due to its acute angle or tightness (Figure 22.1) [9]. This indirect approach to an obstructed calyx or calyceal diverticulum is becoming more commonly utilized as opposed to a direct approach, wherein the obstructed calyx itself is percutaneously punctured, a tract established, and the stenosis treated directly. The advantage of the indirect approach is that it obviates the need for a separate nephrostomy tract with its attendant morbidity.

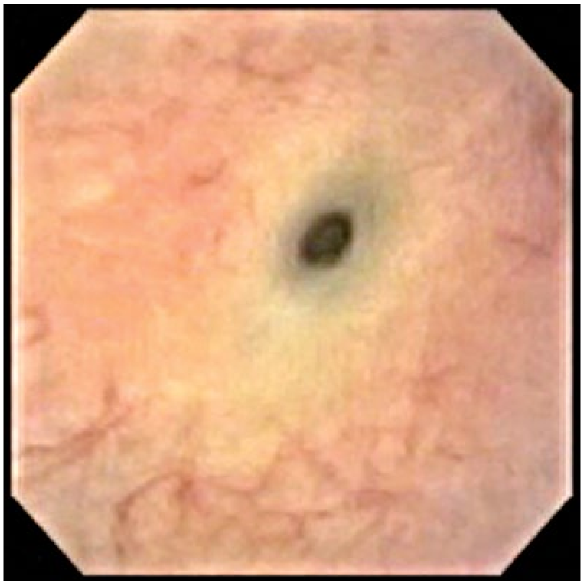

**Figure 22.1** A stenotic infundibulum.

Occasionally, a conventional flexible cystoscope may be too large or too cumbersome to be maneuvered into a calyx. In such instances, use of a flexible ureteroscope to access difficult-to-reach calyces increases the chances of rendering a patient stone free. These are generally 7 or 8 Fr and tend to have better deflection than the flexible cystoscope. Problems are encountered with fiber-optic flexible ureteroscopes because their long length renders them not ergonomically suited for use in the kidney, their relatively flimsy nature makes them torque unstable, and their slender profile and tight distal radius of deflection make them difficult to maneuver in hydronephrotic collecting systems. Use of antegrade ureteroscopy with a flexible ureterosocpe can prove valuable for stone fragments that are located in the distal ureter, since this area usually cannot be directly accessed with a flexible cystoscope because of its distance from the percutaneous site and because of the diameter of the ureter.

The need for flexible nephroscopy during PCNL depends largely on the location of the stone and of the access. Most urologists prefer to obtain access below the 12th rib in order to reduce the risk of pleural injury. In those cases, the rigid nephroscope is usually introduced into the lower pole. The renal pelvis can usually be reached with this access, but reaching upper and mid pole calyces without placing substantial torque on the renal parenchyma is difficult, especially in obese patients or in patients with low-lying kidneys due to hindrance from the iliac crest. It can also be challenging to reach other lower pole calyces from this position and almost impossible to evaluate the proximal ureter with a rigid nephroscope (Figure 22.2). Alternatively, if access is into the upper pole, it can also be difficult to reach the lower pole calyces, especially in patients with narrow intercostal spaces or nonmobile (fixed) kidneys.

## Recent advances in scope technology

Since this volume's last edition, the armamentarium of digital flexible ureteroscopes has expanded. Although the Invisio digital DUR-D flexible ureteroscope (ACMI, Southborough, MA, USA) is no longer available, the Flex-X$^c$ (Karl Storz, Tuttlingen, Germany) and the URF-V (Olympus, Tokyo, Japan) are commonly used. Each scope offers a reasonably narrow tip (8.5 Fr) and 270° deflection in both directions. Additionally, the

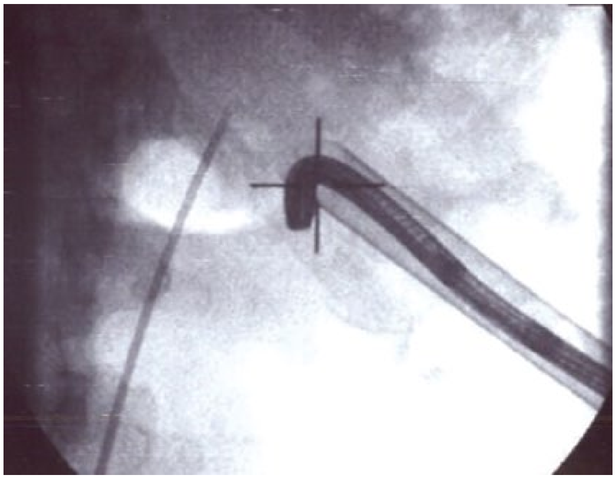

Figure 22.2 Reaching a lower pole calyx with the flexible nephroscope.

URF-V offers narrow band imaging and the Flex-X$^c$ offers Storz professional image enhancement system (SPIES)™ technology (Karl Storz, Tuttlingen, Germany), which can improve detection of upper tract urothelial tumors [10]. Richard Wolf (Vernon Hills, IL, USA) offers the Boa Vision and Cobra Vision digital ureteroscopes, which have similar functionality as the URF-V and Flex-X$^c$.

Recently, the LithoVue™ flexible ureteroscope (Boston Scientific, Marlborough, MA, USA) has been introduced as a new-generation single-use instrument. Dragos et al. demonstrated similar performance in terms of maneuverability, angle deflection, and ability to access calyces during retrograde renoscopy [11]. As an alternative to reusable ureteroscopes, its proposed advantages include high-quality images with each use (as there would be no damage to a new scope) and financial savings on servicing and cleaning costs. Overall, the improved torque stability of digital ureteroscopes in comparison to fiber-optic ureteroscopes allows for improved manuerverability through tight infundibula or hydronephrotic systems.

Similarly, improvements in image-processing technology have yielded benefits for the endoscopic surgeon. The SPIES™ provides a high-definition image with real-time image enhancements useful for nephroscopy [12]. The SPIES CLARA™ feature automatically brightens darkened areas, which eliminates the need for either increasing the light intensity or bringing the scope closer to a darker area. These improvements eliminate the need for maneuvers that may cause glare or result in loss of perspective of the surgical field.

Digital cystoscopes offer similar improvements in visualization compared with their fiber-optic counterparts. However, in contradistinction to digital ureteroscopes, the increased rigidity and girth of these scopes and their more limited deflection can limit their maneuverability and their ability to reach all calyces within the collecting system. As such, oftentimes a fiber-optic cystoscope can be of greater utility for flexible nephroscopy.

Since the publication of the last edition, few changes in rigid nephroscopy and in technology for rigid nephroscopes for standard PCNL have been described. Innovations in scopes for smaller caliber PCNL (i.e. mini-, ultra-mini, and micro-PCNL) are described in Chapter 24.

## Importance of access site (see Video 22.1)

The initial percutaneous access to the kidney influences which calyces can be reached. If a patient has a single stone in an interpolar calyx, it makes sense to access that calyx directly. If there are multiple stones or staghorn calculi, access is usually first obtained in the upper or lower pole, making interpolar access difficult to achieve with a rigid scope. Also, since a rigid scope entering posteriorly faces the anterior calyces, it is more difficult to go from a posterior calyx to another posterior calyx. Some general guidelines for various access sites are given below.

### Posterior upper pole access

If posterior upper pole access is obtained, generally the other more anteriorly located upper pole calyces can be reached with the rigid nephroscope, especially if there is a moderate degree of hydronephrosis. If there is no significant hydronephrosis, or if the access site is close to the infundibulum instead of the peripheral end of the calyx, then it most likely will not be possible to visualize or enter the other upper pole calyces and flexible nephroscopy is necessary. From the upper pole, the rigid nephroscope can be used to enter the anterior lower pole calyces, but entry to the posterior lower pole calyces is challenging (Figure 22.3). Unless there is significant hydronephrosis, the rigid nephroscope cannot enter the interpolar calyces and flexible nephroscopy must be used.

### Interpolar access

As previously mentioned, if posterior interpolar access is obtained, usually the rigid scope cannot access anything other than the renal pelvis and ureter. This access should only be chosen if stones are located in a solitary interpolar calyx and/or the renal pelvis or proximal ureter.

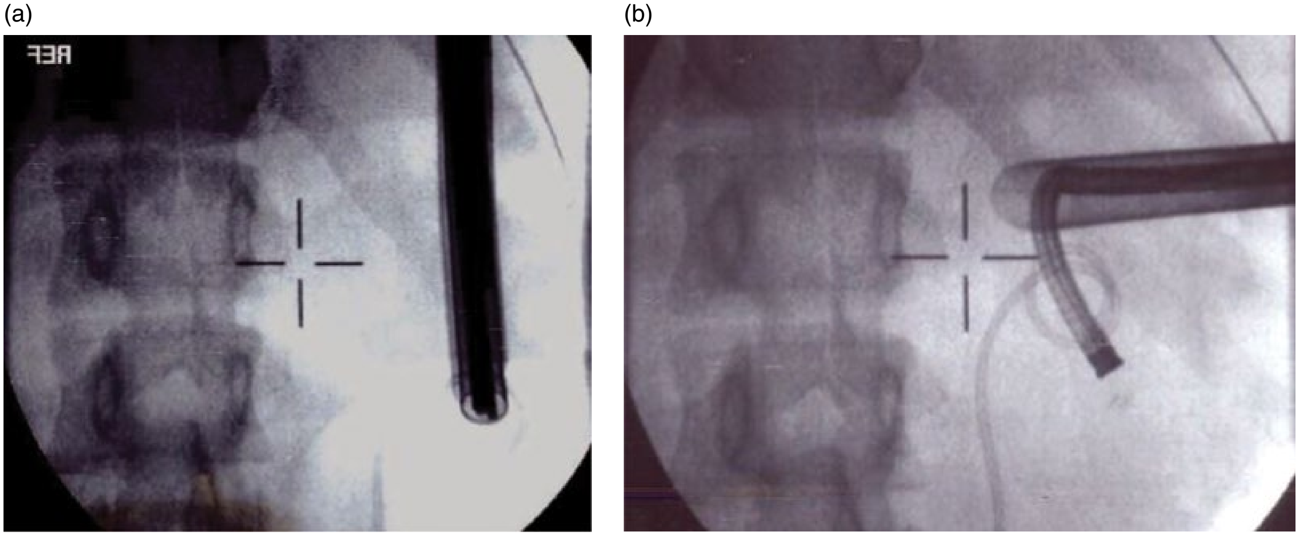

Figure 22.3 (a) Reaching a lower pole calyx with a rigid scope. (b) Reaching a lower pole calyx with a flexible nephroscope.

## Posterior lower pole access

With a posterior lower pole approach, often the other more anteriorly located lower pole calyces can be entered if the access site chosen is more *medial* than usual. To achieve this, instead of rotating the C-arm through the usual 30° toward the surgeon, it is rotated only 20°. This slightly more medial approach, in our experience, does not risk vascular injury and yet provides excellent ability to reach all lower pole calyces. It is particularly useful for partial staghorn calculi that have no upper or mid pole components. From the lower pole, unless there is severe hydronephrosis, the upper and mid pole calyces cannot be reached at all and flexible nephroscopy is necessary to clear them of residual stones (Figure 22.4).

Likewise, the ureter cannot be accessed with rigid scopes or instruments, and flexible scopes are needed. Use of the Accordion™ device (Percsys, Palo Alto, CA, USA), a 15 mm coaxial film-based occlusion device, permits lower pole access for complex stones without fear of stones migrating down the ureter that will then require flexible ureteroscopy at the end of the procedure (Figure 22.5) [13]. Use of this device can ultimately help save time and cost of percutaneous stone procedures.

## Intercostal access

The degree of maneuverability also depends on whether triangulation was used to obtain upper pole access or if an intercostal approach was chosen. Intercostal access will usually allow more maneuverability with less torque on the renal parenchyma, provided that the intercostal space is wide enough. On occasion, the space between ribs is very narrow and the sheath is sandwiched so tightly that maneuverability is significantly hampered.

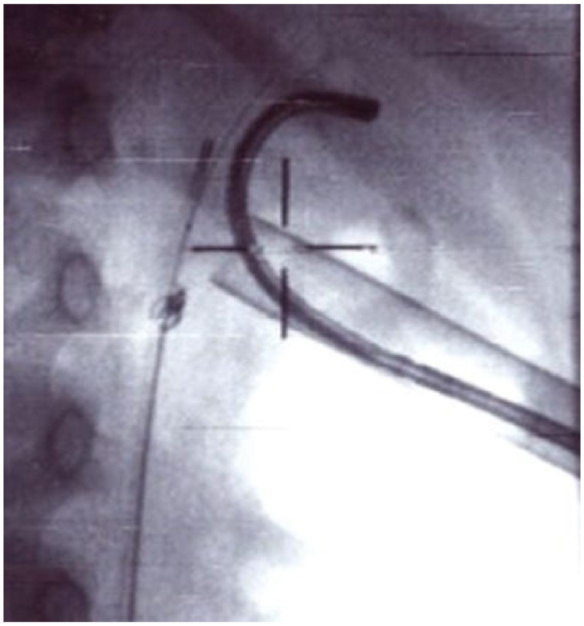

Figure 22.4 Reaching upper calyces with a flexible nephroscope through a lower pole access.

## Preventing ureteral stone migration and obtaining safe percutaneous access

During PCNL the coaxial Accordion™ device can serve several purposes. It is usually placed in the collecting system over a guidewire at the beginning of the case and deployed at the UPJ. Since the lumen of the device accommodates a 0.038-inch guidewire, it is ideal for performing urine sample collection as well as retrograde pyelography. Once it is deployed at the UPJ, it is very effective in preventing stone migration down the ureter, obviating the need for ureteroscopy at the end of PCNL.

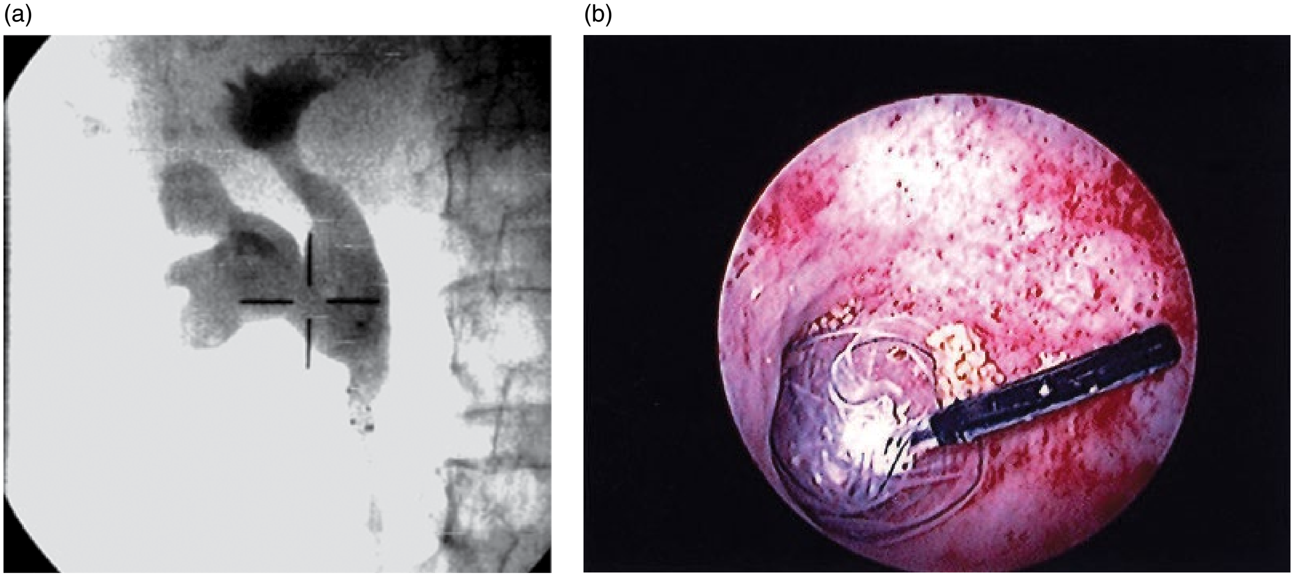

**Figure 22.5** (a) Fluoroscopic image of the Accordion device deployed at the ureteropelvic junction. (b) Accordion device preventing antegrade stone migration.

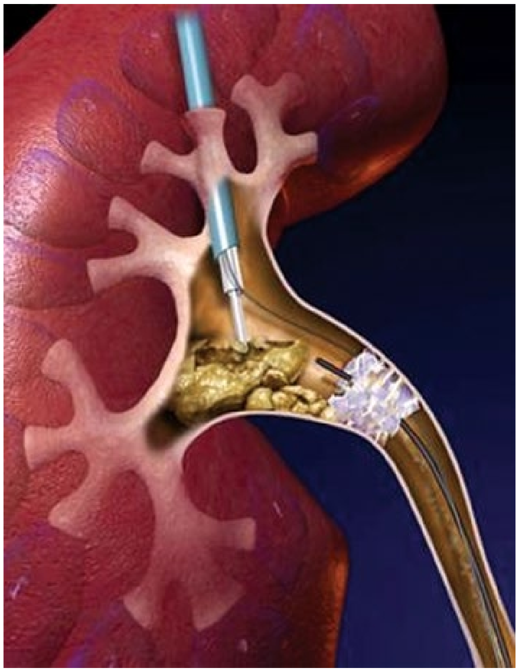

**Figure 22.6** Accordion device deployed at the ureteropelvic junction.

Intercostal renal access during PCNL and other percutaneous renal procedures are associated with an increased incidence of pneumothorax, hydrothorax, or hemothorax postoperatively. The Accordion device can be used to prevent upward migration of the kidney in situations when intercostal access initially appears unavoidable, allowing establishment of a more favorable subcostal renal access (Figures 22.6 and 22.7). Deployment of a coaxial film-based occlusion device at the UPJ can be used to gently hold the kidney in its lower position during ventilation, and in this position percutaneous needle placement can be obtained without the need to go above the ribs. This method provides an effective way to obtain more favorable percutaneous access, limiting the risk of complications associated with intercostal renal access. Visual endoscopic inspection of the UPJ has confirmed the atraumatic nature of this maneuver.

## Stone fragmentation and retrieval

### Rigid nephroscope

The step-by-step processes of obtaining access, dilating the nephrostomy tract, and placing an access sheath are described in detail earlier in this volume. After these steps are completed, the rigid nephroscope is inserted.

Depending upon the nature of the stone burden, retrieval may involve simply grasping the stone fragments and removing them through the sheath. Alternatively, if the stones are too large to pass through the sheath, fragmentation may be required. A variety of lithotripsy devices are used for stone fragmentation during PCNL and are discussed in Chapter 26. In our experience, the combination of selective fragmentation with the StoneBreaker™ Pneumatic Lithotripter (Cook Medical, Spencer, IL, USA) and retrieval with a two-prong atraumatic forceps allows for efficient stone removal with minimal trauma to the urothelium. In addition, use of a

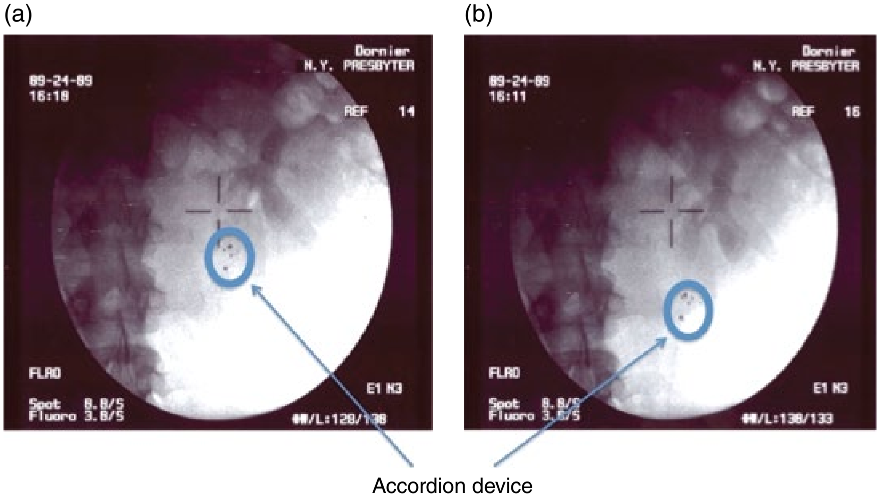

**Figure 22.7** Accordion device preventing upward migration of the kidney to facilitate subcostal upper pole access.

ureteropelvic junction occlusion device, such as the Accordion, is helpful in preventing ureteral migration of stones during this process.

## Flexible nephroscope

Once the affected calyx is reached with the flexible nephroscope or ureteroscope, the size of the stone(s) to be removed must be gauged relative to the width of the infundibulum. If it is likely that the stones can be pulled through the infundibulum intact, a basket or grasper can be used. The NGage® basket (Cook Medical) is particularly useful for efficiently grasping a stone (Figure 22.8). The advantage of this device is that it has an open end and can "cup" a stone that is attached to a papilla or is impacted against the wall. In addition, if the stone is too large to pull through the infundibulum, it can be easily released.

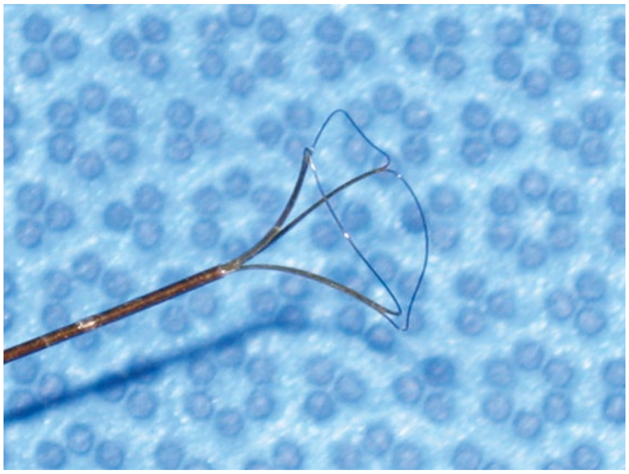

**Figure 22.8** NGage basket.

Baskets are useful for free-floating stones. A basket must be chosen that is sturdy enough to remove the fragments but small enough to allow the scope to deflect. For flexible nephroscopes with their large working channels, 2.4 or 3 Fr nitinol baskets should be used because they are sturdier than smaller profile baskets and can grab larger fragments. For flexible ureteroscopes, 2 Fr or smaller baskets are preferred because they permit better irrigation.

If the stones to be removed are too large, the holmium:YAG laser can be used for lithotripsy. It is important to balance the size of the fiber with the deflection of the scope; a larger fiber will make it more difficult to deflect but will disintegrate the stone faster because of the larger fiber surface area in contact with the stone. Most endourologists generally use a 360 μm fiber through the flexible nephroscope, but a 200 μm fiber through a flexible ureteroscope as it easily fits through all flexible ureteroscopes without significantly affecting deflection or irrigation. The settings to be used depend on the effect desired and the nature of the stone. If the intention is to create miniscule particles that will be left behind for spontaneous passage or flushed out of the calyx and then suctioned (uric acid, phosphate, and struvite compositions are most amenable to this), then low power (i.e. 0.5 J) at a faster frequency (i.e. 10–40 Hz) should be used, and the periphery of the stone should be ablated gradually until the center is reached. The remaining central piece can be retrieved with a grasper or basket. If the stone is very durile (e.g. a calcium oxalate monohydrate or cystine stone), then it should be carved into a few large pieces using high power (1.0 J) and lower frequency (3–5 Hz). The resultant pieces should be removed in piecemeal fashion.

Tiny fragments that are too small to basket are often broken off by the laser. One technique to eliminate these is to irrigate with a 10 ml syringe through the working channel of the flexible scope to flush these fragments out of the calyx. If they are small enough, they can even be aspirated with the syringe. The most effective technique also includes changing the position of the patient to maximize the drainage of these fragments. For example, if the patient is in the prone position and the fragments being flushed are in an anterior calyx, the patient can be rotated to the opposite side so the fragments fall into the renal pelvis. One can also use Trendelenburg and reverse Trendelenburg as necessary to allow stones to enter the renal pelvis. In our experience, fragment migration into the ureter is mitigated by using the Accordion device described above. From the renal pelvis, the fragments can be easily retrieved by the rigid nephroscope using atraumatic peanut forceps with minimal to no irrigation, keeping the patient tilted away from the surgeon to keep the fragments from falling back into the anterior and lateral calyces.

On occasion the Perc NCircle® device (Cook Medical) can be invaluable for retrieving stones from otherwise inaccessible calyces via the rigid scope (Figure 22.9). This unique device is a 5 mm coaxial semirigid instrument with a tipless, large nitinol basket on the distal aspect. Deployment of the basket into a calyx is usually possible as long as the infundibular neck of a calyx can be directly visualized, even if the neck is too small or too peripheral to allow direct access with the scope. Using a combination of direct vision or fluoroscopy, stones can be readily insinuated into the basket and retrieved by pulling them out through the infundibulum. If the neck is too tight to allow stone removal, it is a relatively simple task to open the basket and disengage the stone.

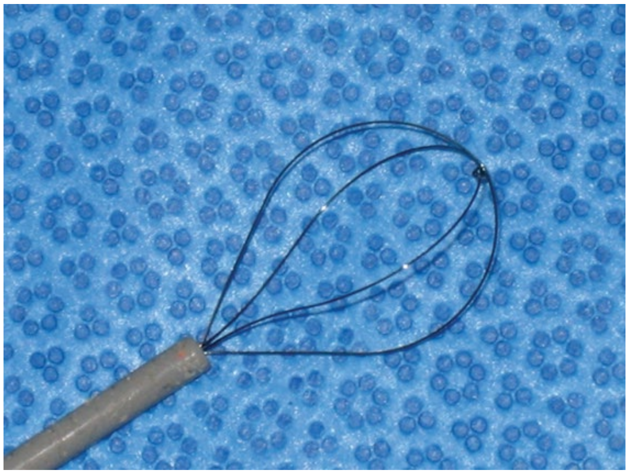

**Figure 22.9** Perc NCircle device.

## Tips and tricks

### Rigid nephroscopy

Although it is preferable that the nephrostomy tract enters directly into the calyx of interest, at times this may not be possible (i.e. calyceal diverticulum or calyx densely filled with stone). In situations where the dilated tract is short of the collecting system, the balloon dilator can be reinserted deeper and re-dilated. Alternatively, if it is known that the tract is directly adjacent to a calyx full of stone, the rigid nephroscope and the atraumatic peanut forceps can be used to carefully probe the surrounding tissue for hard stone. Upon identifying the stone, the mucosa can be gently opened with the forceps and the access sheath advanced to allow direct access to the stone. If, while probing, it is challenging to identify the collecting system, diluted methylene blue can be injected through the retrograde ureteral catheter. This can distend the collecting system with a blue hue and also make entry into a calyx very obvious as there will be a rush of blue fluid that can be followed to the collecting system.

In our experience, we have found that dilation to and use of a 24 Fr access sheath has allowed for several benefits while maintaining the same high stone-free rate associated with standard PCNL. Lipsky et al. reported a significant decrease in blood loss, shortened operative time with decreased hospital length of stay [14]. Additionally, the smaller access diameter results in higher velocity flow through the sheath, which facilitates greater expulsion of stone fragments and can help decrease operating time. This "modified PCNL" has been our technique of choice over the last 5 years due to the aforementioned benefits.

### Flexible nephroscopy

Minimizing the use of contrast with the flexible nephroscope is important as contrast extravasation would render fluoroscopic visualization of residual stones very difficult. In our experience, contrast is used only at the very beginning of the procedure to outline calyceal anatomy and to help guide access, then again at the very end after the nephrostomy tube has been placed.

Visualization is often adequate with a rigid scope because of high volume irrigation, but once the flexible scope is employed, visualization can significantly deteriorate in the presence of bleeding. This is partly due to the optics, but even more to the reduced irrigation with a flexible scope and the inadequate distention of the collecting system. Raising the level of the irrigation fluid or use of pressure bag irrigation can significantly enhance visualization by clearing the field of blood and by distending the collecting system. In addition, advancing the sheath over a particularly troublesome site of bleeding can be of utility to help limit bleeding into the field.

One important technique is the use of fluoroscopy to help guide placement of the flexible nephroscope. If direct visualization is not sufficient to visualize an intended calyx (either because of angulation, a severely hydronephrotic collecting system, or bleeding), brief continuous fluoroscopy can be used to gently maneuver the scope toward a stone in a peripheral calyx. This is generally a very safe maneuver because the blunt end of a flexible nephroscope is wide and atraumatic. Also, since the scope is flexible, perforation is unlikely.

If the opening to a calyx can be visualized with a rigid scope, but it is difficult to find with a flexible scope because of bleeding or incomplete distention of the collecting system, a guidewire can be placed into the intended calyx via the rigid scope. The best wire to use for this purpose is a short, heavy-duty J wire (Cook Medical). The short J wire with the "J" hooked distal tip is atraumatic and therefore is less likely to perforate the calyx or to be dislodged while transitioning from the rigid scope to a flexible one. The flexible scope is not placed over the wire, as this almost always dislodges the wire from the calyx; instead, the flexible scope is advanced alongside the wire and follows it to the calyx of interest. In this manner, the working port of the flexible scope is free for the placement of instruments. In addition, the calyx can be entered again and again without the wire having to be replaced.

On occasion, a stone can be visualized with the flexible nephroscope, but upon passage of an instrument (such as a basket) through the working sheath, deflection is limited to prevent access to the stone. In this case, with fluoroscopic guidance one can target the stone with the access needle in a direction that dislodges it to a more accessible position. This technique can help achieve a stone-free procedure while avoiding the need for an additional access tract.

Another tip mentioned earlier is placing a flexible ureteroscope through the rigid nephroscope. This is particularly useful when the infundibulum to the targeted calyx is narrow and will not accommodate a flexible nephroscope. The smaller girth of the flexible ureteroscope means it can enter almost all calyces, but maneuvering these scopes in the collecting system can be challenging because of poor irrigation through their small working channels, their excessive length, their tight radius of curvature, and their lack of torque stability. By visualizing the infundibulum with a rigid scope, the flexible ureteroscope can be guided into the calyx by a second surgeon through the working port of the rigid scope, which the first surgeon holds steady. Once the calyx is entered, the camera can be switched to the flexible scope. Alternatively, two video towers can be employed so that simultaneous views from the rigid and flexible scopes can be obtained.

Finally, as all visualized stone pieces are cleared, it is customary to evaluate the kidney with fluoroscopy to assess for residual radiopaque fragments [15]. At times, it can be challenging to differentiate a possible stone fragment from overlying structures. In this scenario, it is useful to move the kidney by gently maneuvering the access sheath inferiorly or superiorly; radiopacities that move with the kidney suggest residual stone.

## Conclusions

Advances in flexible nephroscopy and instruments available for percutaneous renal procedures have made it possible to perform surgery more efficiently and safely. Many of the instruments and techniques discussed increase access to difficult calyces during percutaneous renal procedures and reduce the need for additional percutaneous access. It is hoped that the techniques outlined in this chapter will help urologists to expand their indications for flexible nephroscopy, increase their comfort level with new scopes and accessories, and attempt the techniques before adding another access during a difficult percutaneous renal procedure.

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# 23

# Percutaneous Antegrade Ureteroscopy

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## Introduction

The optimal treatment for large proximal ureteral stones remains controversial. Treatment for ureteral stones includes shock-wave lithotripsy (SWL), semirigid/flexible ureteroscopy (URS), percutaneous antegrade URS, open and laparoscopic surgery. Each modality has its advantages and disadvantages. SWL is noninvasive, can be utilized as an outpatient procedure and is associated with low morbidity. However, it has a limited role in managing large, impacted upper ureteral stones, due to its low success rate and high retreatment rate [1]. Retrograde URS is recommended as first-line treatment for ureteral stones >10 mm [2]. However, treatment of proximal stones is associated with higher intraoperative complication and retreatment rates compared to distal stones [3]. On some occasions, proximal ureteral stones are unlikely to be accessible with URS due to tortuosity and angulation of the ureter or other anatomic abnormalities (Figure 23.1a,b). Moreover, flexible URS requires specific instrumentation and expertise and is costly. Percutaneous antegrade URS is an effective alternative when SWL and/or retrograde URS are not indicated or have failed [4–6]. In rare cases, patients with large or complex stones and/or coexisting anatomic abnormatilites may better be suitable for open or laparoscopic surgery [7, 8]. In this chapter, we describe perioperative considerations, surgical technique, and clinical outcomes of antegrade percutaneous URS.

## Indications

The antegrade approach may be most useful for patients in whom retrograde access is difficult or challenging (Figure 23.2a,b). Prior access failure, large and obstructing ureteral stone burden, concomitant ureteral and renal stone, pediatric patients, prior bladder or ureteral surgery, large median lobe of the prostate, transplanted kidneys, prior urinary diversion with ileal conduit, heterotopic, or orthotopic diversion are scenarios for which antegrade access may provide higher success rates and prove more efficient.

## Contraindications

Uncorrectable bleeding diathesis, ipsilateral kidney tumor, pregnancy, and untreated urinary tract infection are contraindications to percutaneous renal surgery. All attempts should be made to ensure sterile urine and correct bleeding diathesis prior to the procedure.

## Preoperative assessment

Proper preoperative imaging includes computed tomography (CT) for comprehensive evaluation of stone size, position, composition, degree of hydronephrosis, and surrounding anatomy. Evaluation of the CT characteristics allows selection of the preferred calyx for access. Presence of severe renal atrophy should prompt a functional imaging study to determine differential renal function. If stone size is large and renal function is poor, the option of simple nephrectomy or therapeutic nephrostomy can be entertained. A comprehensive discussion including risks, benefits, and alternatives should be undertaken and informed consent obtained.

Preoperative laboratory evaluation should include baseline renal function, serum electrolytes, blood count, platelets, and coagulation factors. Blood type and screen for crossmatch should also be obtained. Antiplatelet agents should be discontinued at least 5 days prior to the

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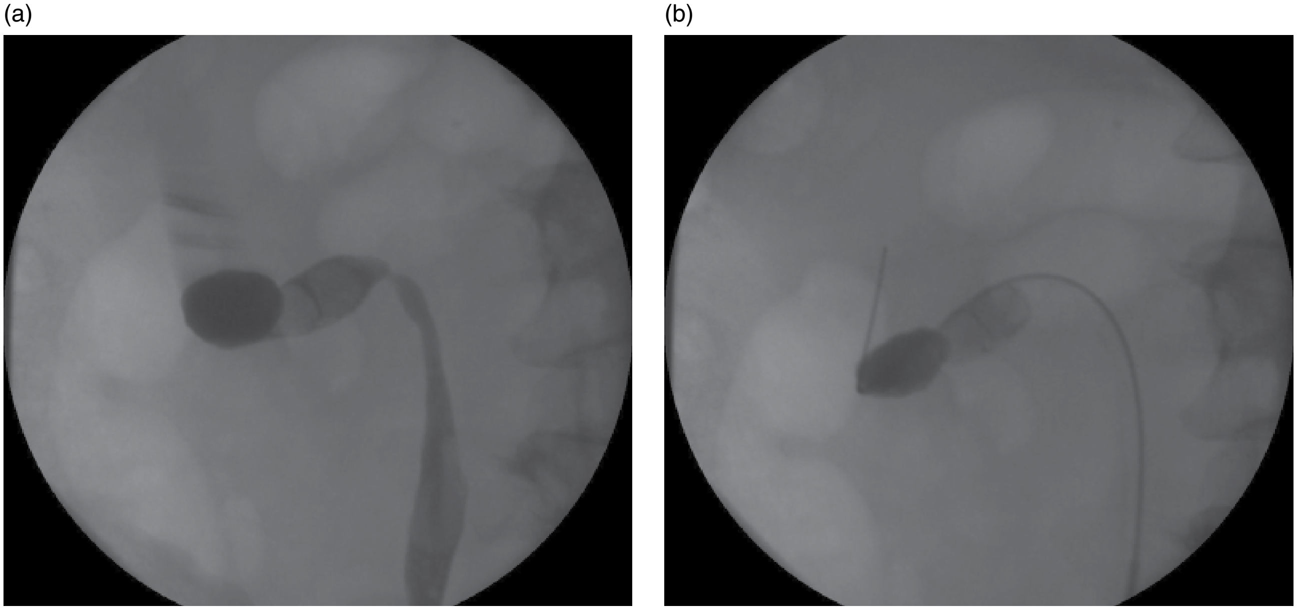

**Figure 23.1** (a) Retrograde pyelogram shows filling defects (due to stones) as well as tortuosity and angulation of the proximal ureter. (b) The guidewire demonstrates the acute angulation of the ureter due to impacted proximal ureteral stones.

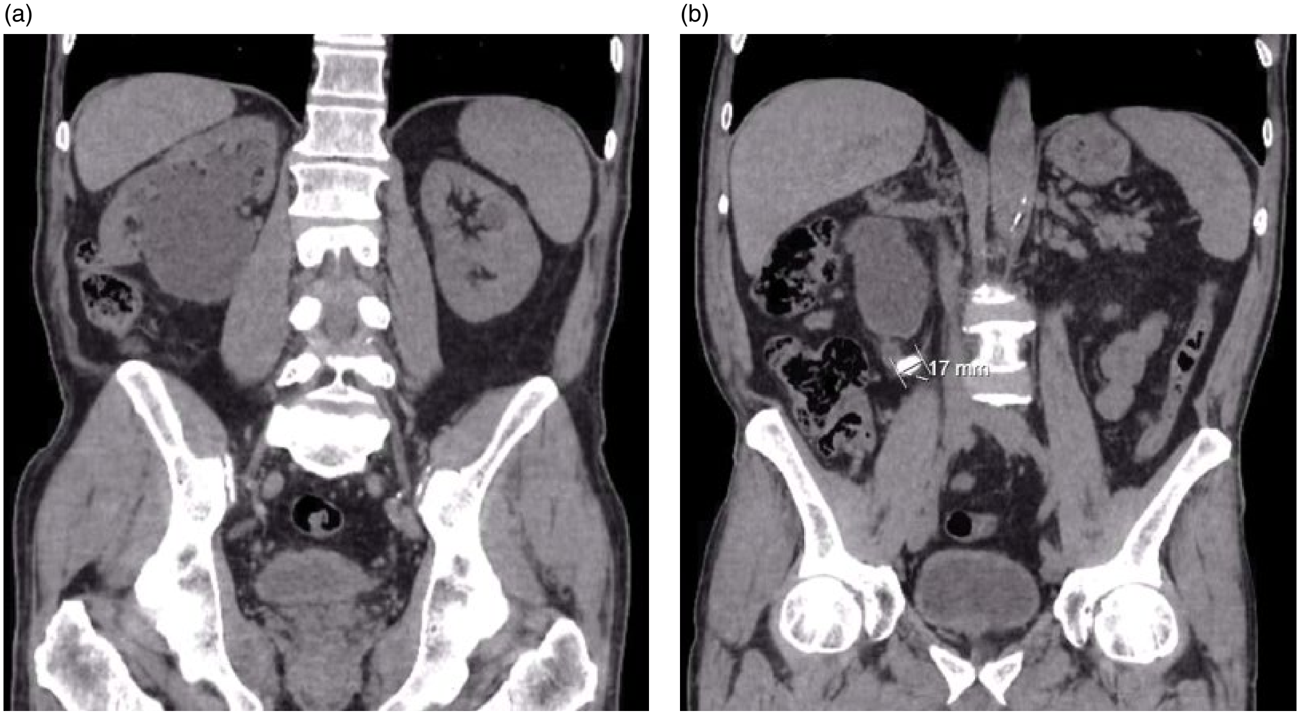

**Figure 23.2** (a) CT scan image (coronal section) shows a 17 mm proximal ureteral stone causing obstruction. (b) CT scan image (coronal section) shows marked hydronephrosis due to the proximal ureteral stone.

procedure and heparin or low molecular weight heparin can be substituted preoperatively for warfarin. A urine culture should be obtained preoperatively and, if positive, sensitivity-specific antibiotics should be administered. Repeat urine culture should ensure sterile urine. If sterile urine can not be achieved by antibiotics, preoperative percutaneous nephrostomy should be considered. Once sterile urine is present, prophylactic antimicrobial coverage should be administered prior to anesthesia and continued perioperatively.

## Percutaneous antegrade ureteroscopy technique (proximal ureteral stones)

Instrumentation required for the procedure is listed in Table 23.1.

Following induction of general anesthesia, a 22 Fr rigid cystoscope is inserted transurethrally and used to place 6 Fr open-ended ureteral catheter to the ipsilateral renal collecting system in the lithotomy position. If the stone does not allow passage of the ureteral catheter into the renal pelvis, the catheter is placed a few milimeters below the impacted stone. Position is confirmed using fluoroscopy. A retrograde pyelogram using the catheter delineates collecting system anatomy. Special considerations regarding inappropriate retrograde pyelogram in the presence of impacted stone or other situations are discussed below. Foley catheter is inserted, the ureteral catheter is then fixed to the Foley in order to prevent catheter dislodgement.

**Table 23.1** Instrumentation required for antegrade percutaneous ureteroscopy.

| Instrument/disposable | Quantity |
|---|---|
| 15.5 Fr flexible cystoscope | 1 |
| 7.5 Fr flexible ureteroscope | 1 |
| 24 Fr rigid nephroscope | 1 |
| 0.038-inch PTFE-nitinol guidewire with hydrophilic tip | 2 |
| Amplatz super-stiff guidewire | 1 |
| Cystoscopic camera | 1 |
| Light cord | 1 |
| Pressure bag/saline irrigation | 1 |
| Video tower | 1 |
| Nitinol stone basket | 1 |
| Holmium:YAG laser | Optional |
| 272 micron holmium laser fiber | Optional |
| 10 Fr dual lumen ureteral catheter | 1 |
| 18 gauge percutaneous access needle | 1 |
| 8/10 coaxial dilator | 1 |
| C-arm fluoroscope | 1 |
| 30 Fr Amplatz serial dilators/nephroscopic sheath | 1 |
| 11/13 ureteral access sheath | Optional |
| Ultrasonic lithotripter | 1 |
| Pneumatic lithotripter | 1 |
| Nephroscopic grasping forceps | 2 |
| 26 cm 6 Fr double-J ureteral stent | 1 |
| 8 Fr nephrostomy tube | Optional |
| Surgical lubricant | 1 |
| Radiologic contrast material | 1 |
| Small containers for saline and for radiographic contrast material | 2 |
| 10 ml syringes | 2 |

The patient is then turned prone. Under fluoroscopic guidance, a disposable 18 gauge access needle is advanced percutaneously into the calyx of choice. Access is achieved through the middle calyx or the upper calyx in order to have direct access to the renal pelvis and the ureter; the upper calyx provides more direct access but more risk of thoracic complications. The aim is to get a short, straight percutaneous tract to the upper ureter and the calculus. Our technique for access involves targeting the preferred site in the anteroposterior plane as well as the oblique plane. Needle placement is confirmed and a 0.038-inch PTFE-nitinol guidewire with hydrophilic tip is advanced into the calyx. At this point, the skin is incised sharply around the cutaneous entry point and the access needle is removed. Clear urine efflux confirms correct entry. After percutaneous renal access is obtained, the next important step is proper dilation and establishment of a nephrostomy tract. An 8 Fr/10 Fr coaxial dilator is passed over the percutaneous wire to the proximal ureter and used to place an Amplatz super-stiff guidewire as a second wire. The access tract is dilated along the guidewire using a series of Amplatz dilators up to 30 Fr (20 Fr if a mini-percutaneous nephrolithotomy (mini PCNL) technique is elected). The choice of use of standard nephroscope versus mini-nephroscope is at the discretion of the surgeon. Once the tract is dilated to 30 Fr (20 Fr for mini PCNL), the accompanying sheath can be gently advanced over the dilator using fluoroscopic control to confirm proper positioning within the collecting system. A 24 Fr (17 Fr for mini PCNL) rigid nephroscope is then advanced into the collecting system and the stones are treated with a combination of pneumatic and/or ultrasonic lithotripsy as well as intact fragment removal (Figure 23.3). Care is taken not to fragment the stones into very small pieces, as this will make stone extraction difficult. If the proximal ureteral stone is visible but not accessible with a rigid nephroscope, a 8 Fr semirigid ureteroscope or a 15.5 Fr flexible cystonephroscope is used. On some occasions, a 7.5 Fr flexible URS can be used during or following nephroscopy in order to aid in lithotripsy as well as to ensure stone-free status where distal ureteral access is difficult. Following PCNL a 0.038-inch guidewire may be placed in an antegrade manner through the nephroscope and down the ureter. The access sheath is removed, the distal portion of the wire is curled in the bladder, and a 26 cm double-J ureteral stent is advanced through the nephroscope and positioned appropriately. Depending

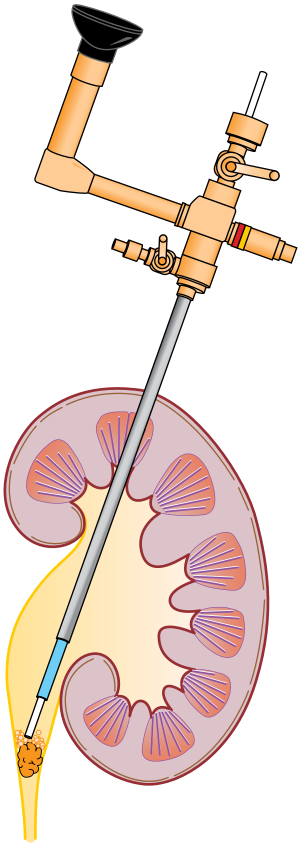

**Figure 23.3** Diagrammatic representation of percutaneous antegrade ureteroscopy. The rigid nephroscope is directed towards the proximal ureter and the stone for pneumatic lithotripsy. Note that percutaneous tract to the upper ureter and the stone is in a straight line.

upon the ease of the procedure as well as the confidence in a stone-free status, the placement of a nephrostomy tube can be elected.

A mini PCNL procedure rather than standard PCNL can be elected to perform an antegrade percutaneous URS in order to decrease the morbidity of the procedure. The principles are the same as standard antegrade URS. Mini PCNL is performed with a miniature nephroscope (i.e. 17 Fr nephroscope) via a smaller percutaneous tract (<20 Fr).

## Percutaneous antegrade flexible ureteroscopy technique (distal ureteral stones)

Percutaneous access is performed under fluoroscopic guidance in the prone position. The upper calyx is preferred for more distal ureteral pathology. If a nephrostomy is already in place, a guidewire is placed to the collecting system under fluoroscopic guidance. A second guidewire (safety wire) is introduced with the use of a double-lumen catheter into the ureter. Tract dilation is peformed up to 14 Fr with Amplatz dilators. A 11–13 Fr ureteral access sheath is inserted, under fluoroscopy, into the ureter over the guidewire. A 7.5 Fr flexible ureteroscope is inserted under endoscopic vision. The stone is visualized in the distal ureter and fragmented with holmium:yttrium–aluminum–garnet (YAG) laser under endoscopic vision. An access sheath provides low pressure in the collecting system and easy re-entry of the flexible ureteroscope. A nitinol basket is used to extract any significant fragments. A 6 Fr double-J stent is placed in an antegrade fashion and/or a 8 Fr nephrostomy tube is left in place.

## Special considerations

One of the challenges when using the antegrade approach is to perform retrograde pyelogram for impacted ureteral stones and in difficult ureteral access scenarios (i.e. prior urinary diversion). If a ureteral catheter cannot be advanced from the distal ureter or impacted stone, there are several options to opacify the collecting system for further percutaneous renal access. One option is to use an ultrasound for initial access (requires expertise). Percutaneous renal access allows for antegrade injection of contrast material to help delineate anatomy and points of obstruction. The second option is to administer the contrast by intravenous route. CT-guided access preoperatively is necessary in select cases. Lastly, the large impacted stone can initially be treated ureteroscopically to open a little window between the stone and the ureter and a guidewire is passed to the renal pelvis. A 4 Fr ureteral catheter is then placed over the guidewire into the collecting system.

## Postoperative care

Routine blood tests, including hemoglobin, are obtained postoperatively and a chest X-ray is performed in cases with supracostal access. After performing the antegrade technique, our preference is to leave the Foley catheter for one day and the double-J stent for approximately two weeks and then to remove the stent using flexible cystoscopy in the outpatient clinic. In complicated cases, we also leave a 8 Fr nephrostomy tube and remove it on postoperative days 2–3 after confirmation of normal nephrostogram. Patients are followed in an outpatient setting with a noncontrast CT at one month post operation in order to assess for residual stones.

## Percutaneous antegrade ureteroscopy outcomes

There have been several published reports since the first description of percutaneous antegrade URS by Gumpinger et al. [9]. In this initial report, 22 patients were managed by percutaneous antegrade URS technique with a stone-free rate of 100% after one session. Several other centers demonstrated the efficacy and safety of this technique [10, 11]. In these series, percutaneous antegrade URS was performed for large stones (>15 mm) that were densely impacted and located between the ureteropelvic junction and the lower border of the fourth lumbar vertebra. Most patients (>90%) were stone-free in a single session through a single tract without any major complications.

Location of the ureteral orifices, access to the ureter, and subsequent retrograde ureteroscopy are challenging in patients after any form of urinary diversion. However, these patients are at risk of developing urinary stones due to various anatomical and metabolic causes. El-Nahas et al. have elegantly demonstrated that percutaneous treatment of large upper tract stones after urinary diversion offered an effective treatment with minimal morbidity in 24 patients [6]. The challenges of retrograde ureteral access in patients with prior urinary diversion makes antegrade percutaneous URS an ideal management strategy in this patient cohort, as demonstrated in our video (see Video 23.1).

Table 23.2 summarizes the prospective and retrospective comparative series [12–21]. Most of these series have been published by high-volume Chinese centers. They demonstrate excellent rates of stone clearance in one session with acceptable morbidity. Antegrade access to the ureter, though minimally invasive, has the potential risks of hemorrhage, sepsis, pneumothorax, and other complications associated with percutaneous surgery.

Comparison of outcomes from pure antegrade and retrograde URS were evaluated in seven series [12, 13, 15–17, 20, 21]. Notably, semirigid URS was utilized in most patients. These studies demonstrated low morbidity with infrequent minor complications and no major complications in patients treated with antegrade URS. A criticism of antegrade URS compared to retrograde URS includes its more invasive nature. Its use can be justified because of the higher stone-free rates in a single session.

**Table 23.2** Comparative outcomes for minimally invasive surgical management of proximal ureteral stones.

| Author [ref] | Year | Study | Study type | No. of patients | Success rate (%) | Complication rate (%) |
|---|---|---|---|---|---|---|
| Maheshwari et al. [12] | 1999 | URS vs. PCNL | Retrospective | 43 | URS 55%<br>PCNL 100% | URS 0%<br>PCNL 0% |
| Juan et al. [13] | 2008 | URS vs. PCNL | Retrospective | 53 | URS 58%<br>PCNL | N/A |
| Basiri et al. [14] | 2008 | URS vs. PCNL vs. Lap | Prospective | 150 | URS 76%<br>PCNL 86%<br>Lap 90% | N/A |
| Sun et al. [15] | 2008 | URS vs. mini PCNL | Prospective | 91 | URS 86.4%<br>Mini PCNL 100% | URS 2.3%<br>Mini PCNL 2.3% |
| Li et al. [16] | 2013 | URS vs. PCNL | Prospective | 174 | URS 75.8%<br>PCNL 96.4% | URS 32.5%<br>PCNL 33.8% |
| Gu et al. [17] | 2013 | URS vs. mini PCNL | Prospective | 59 | URS 89.7%<br>Mini PCNL 100% | N/A |
| Zhu et al. [18] | 2014 | URS vs. PCNL vs. Lap | Retrospective | 73 | URS 77.3%<br>PCNL 100%<br>Lap 90.5% | N/A |
| Topaloglu et al. [19] | 2014 | PCNL vs. Lap | Retrospective | 58 | PCNL 100%<br>Lap 100% | N/A |
| Bozkurt et al. [20] | 2015 | URS vs. PCNL | Retrospective | 86 | PCNL 97.8%<br>URS 82.9% | PCNL 22%<br>URS 17% |
| Hu et al. [21] | 2016 | fURS vs. mini PCNL in elderly | Retrospective | 179 | Mini PCNL 90.9 %<br>fURS 79.0% | Mini PCNL 25%<br>fURS 13.8% |

N/A, not available; URS, ureteroscopy; PCNL, percutaneous nephrolithotomy; fURS, flexible ureteroscopy; mini PCNL, mini-percutaneous nephrolithotomy; Lap, laparoscopy.

However, it may be possible to achieve better outcomes with use of current-era flexible ureteroscopy and lithotripsy, albeit at higher cost.

Although antegrade URS techniques are generally standardized, Chinese centers mainly use mini PCNL, whereas other centers prefer standard PCNL instrumentation. In a recent meta-analysis comparing PCNL with flexible URS, standard PCNL was associated with higher stone-free rates at the expense of higher complication rates, whereas flexible URS provided higher stone-free rates than mini PCNL [22].

Hu et al. have recently compared the effectiveness and safety of mini-percutaneous antegrade URS to the retrograde flexible URS in 179 elderly patients with medium-sized renal and ureteral stones [21]. No significant differences were found in terms of complications, but a statistical trend in favor of URS was observed. The overall stone-free rate was higher with mini PCNL for multiple stones, but similar for solitary stones.

Retrograde, antegrade, and laparoscopic approaches were compared for management of proximal ureteral stones in two series (Table 23.2) [14, 18]. When taking into account both efficacy and safety, the antegrade approach provided more advantages compared to the other two techniques. Importantly, an additional benefit includes the availability of PCNL instrumentation and technique in most urology units.

## Conclusions

The antegrade technique for ureteroscopy can provide several advantages over an exclusively retrograde approach, especially in cases in which retrograde access is challenging. Its invasive nature and undefined degrees of benefit limit our ability to recommend an antegrade approach routinely for all proximal ureteral stones. Careful patient selection and preparation, as well as familiarity with instruments and techniques, help to increase the efficacy and decrease the morbidity associated with antegrade ureteroscopy.

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# 24

# Small-caliber Percutaneous Nephrolithotomy: Mini, UMP, and Micro-Perc

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## Introduction and instrumentation including miniaturization

The story of percutaneous nephrolithotomy (PCNL) began in 1941 when Rupel and Brown of Indianapolis, removed a stone through a previously established surgical nephrostomy track [1]. Fernstrom and Johannson first reported the establishment of a percutaneous track with the specific intention of removing a stone [2]. Thereafter advances in endoscopes, imaging equipment, and stone disintegration devices allowed urologists to refine these percutaneous techniques through the late 1970s and early 1980s into well-established methods for removal of upper urinary tract calculi. The development of minimally invasive surgical techniques for the treatment of patients suffering from urinary lithiasis has been greatly dependent on technologic advances in the fields of fiber-optics, radiographic imaging, and intracorporeal lithotripsy (mainly novel and highly efficient laser emitters). These advancements have accelerated the evolution of modern techniques of calculus removal, including mini PCNL, ultra-mini PCNL (UMP), and micro-perc.

In general, the percutaneous treatment of kidney stones might be considered to be relatively invasive, in particular considering substantial perioperative morbidity such as bleeding and infection rates [3]. An extended analysis can be found in a publication on PCNL initiated by the Clinical Research Office of the Endourological Society (CROES) [4].

With regard to the perioperative morbidity of PCNL, a phenomenon related to the size of Amplatz sheath has been observed: the most feared complication of bleeding increases directly depending on larger volume of the access tract [4]. In order to improve perioperative safety of percutaneous stone treatment several clinical studies have been conducted and modifications made.

The history of percutaneous access to renal pelvis is long and fascinating. Three decades ago when Alken laid down the steps of renal dilation the endoscopic companies made instruments that helped us view the pelvicalyceal system and bring out the stones [5]. Surgeons in the United States subsequently used a track size of almost 38–40 Fr, mainly because the disintegration devices were not well developed and large pieces of stones had to be removed intact through a large Amplatz sheath [6]. It was soon observed that 38–40 Fr dilation was just too large and therefore Kurt Amplatz and Arthur Smith settled on an Amplatz size of 30 Fr for standard PCNL. Thereafter many scientific articles stated that if we could reduce the track size the bleeding would be less, the parenchymal damage would be reduced, and the recovery time would be shortened. Sven Lahme in Germany proposed in his paper published in 2002 that a track size of 20 Fr could easily remove renal stones and by reducing the dilation we could reduce bleeding and damage [7]. This was called mini PCNL. Smaller size nephroscopes and sheaths were made by instrument makers and many urologists across the world embraced the concept of mini PCNL [8].

In parallel, Udo Nagele proposed a similar concept called minimally invasive percutaneous nephrolitholapaxy (MIP) [9]. The main focus of this development was on avoiding high-pressure peaks (over 30 $cmH_2O$) during percutaneous _ procedures, which might lead to pyelovenous reflux and fluid overload. Such conditions may be the reason for PCNL-related infectious complications such as sepsis [10].

In 2010, Janak Desai and colleagues in India developed what they called ultra-mini PCNL (UMP). The first articles on UMP were published in 2013 [11, 12]. UMP involves a telescope of 1 mm size and a sheath size of either 11 Fr or 13 Fr. The sheath has a special design that helps to remove the fragments by creating a mini whirlpool effect in the pelvicalyceal system. This moves the stone

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

fragments from a high-pressure zone to the sheath, which is a low-pressure zone (Figures 24.1 and 24.2) [12]. In 2010 Shaft and Bader developed a needle nephroscope called an “all-seeing needle” [14]. It is 4.85 Fr in size and the puncture is performed in a single-step setting. M. Desai added a modification that enabled passing a laser fiber to disintegrate the stone [14]. Since the stone fragments are not removed we have to wait for natural expulsion of these fragments. This technique was called micro PCNL. Thus from conventional PCNL we have now arrived at a stage where mini PCNL, ultra-mini PCNL, and micro-perc can remove most kidney stones.

## Mini PCNL and minimally dilated punctures

The “mini-perc” technique was first developed for use in children. An 11–15 Fr peel-away vascular access sheath was used, instead of the more commonly used 24–30 Fr Amplatz sheaths [15]. The mini-perc technique was adapted to adult patients with stones smaller than 2 cm by use of a 13 Fr ureteroscopy sheath for percutaneous access and a 6.9 Fr rigid ureteroscope. Lithotripsy was achieved with a thin ultrasonic probe or a holmium:YAG laser. The authors reported a stone-free rate of 89% with minimal morbidity. Monga and Oglevie used a 20 Fr nephrostomy sheath, and a 9.8 Fr rigid endoscope and reported similar results in a series of 16 patients with an average stone size of 2.8 cm [16]. Several papers have shown the advantage of minimally dilated punctures and the procedures in that ambit are: mini PCNL, ultra-mini PCNL (UMP), and micro-perc [7, 8, 17].

## Classification of different PCNL systems

Different classifications of particular PCNL systems have been introduced by the manufacturers and developers of this technology. Until now there has been no general unified description system reporting on PCNL.

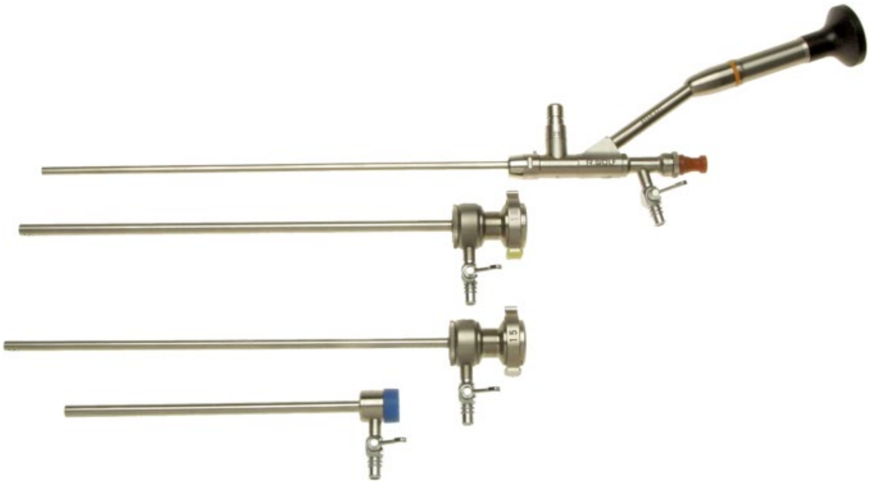

**Figure 24.1** Mini PCNL set according to Lahme. The system consists of a pediatric metallic shaft, 15 Fr adult shaft, 18 Fr adult shaft, and a nephroscope. *Source:* Richard Wolf GmbH, Knittlingen, Germany. Reproduced with permission of Richard Wolf, Germany.

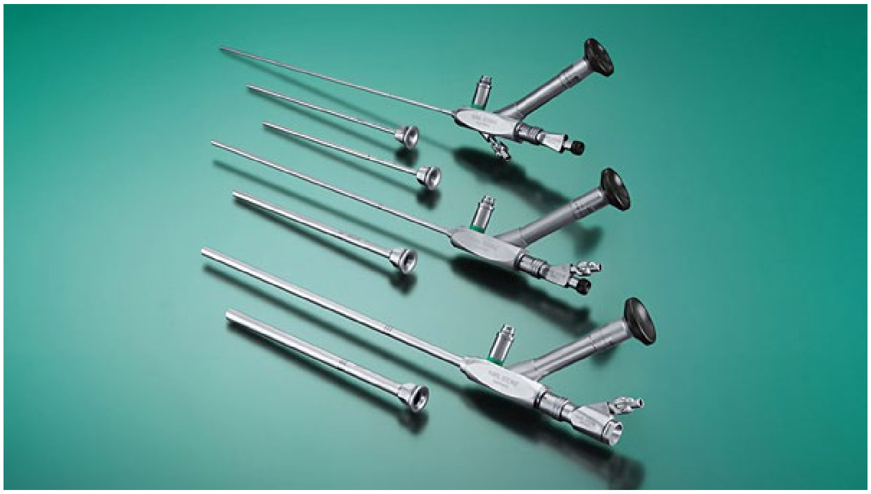

**Figure 24.2** Novel PCNL system including minimally invasive PCNL (MIP) set according to Nagele. *Source:* Karl Storz, Tutlingen, Germany. Reproduced with permission of Karl Storz.

The systems are mainly named according to the outer diameter of the Amplatz shaft. In the last consensus guideline on urolithiasis by the German Association of Urology [18] the following classification was published:

- Standard PCNL: 24–32 Fr
- Mini PCNL: 14–22 Fr
- Ultra-mini PCNL: 11–13 Fr
- Micro PCNL: 4.8–11 Fr.

Other literature sources suggest using the name “mini PCNL” for systems using access sheaths smaller than 20 Fr [19] and “micro PCNL” for tract size 11 Fr or less [20].

Because of the growing number of names and descriptions the proper allocation of a particular technique might still be confusing for urologists. Wright et al. proposed a unified classification for devices used in percutaneous stone treatment (Table 24.1) [21]. As well as sheath size, the approach, fragmentation method, and postoperative drainage of the urinary track should be systematically reported.

## Mini PCNL

Several papers have been published describing the advantages of reducing track size [22], reporting that the amount of bleeding is less, the parenchymal damage is less, and length of hospitalization is reduced (Table 24.2). However, the mini PCNL technique requires longer operative time for fragmentation of relatively small, otherwise extractable stones. It is still under debate whether the track of 18–22 Fr (mini PCNL) does significantly less damage than a track of 28–30 Fr (standard PCNL).

The instruments consist of a thinner nephroscope and instead of the Amplatz sheath, three different sizes of metal sheaths are available. The sheaths are approximately 18 Fr, 21 Fr, and 24 Fr outer diameter. The stone disintegration can be carried out by pneumatic energy or ultrasonic energy and the extraction can be carried out by thinner forceps. If the stone load is less, the fragments can be brought out using fluid dynamics.

**Table 24.2** Transfusion rates in relation to sheath size in percutaneous nephrolithotomy [4].

| Sheath size | No. of patients | Blood transfusion (*n* (%)) |
|---|---|---|
| Small (18 Fr and below) | 271 | 3 (1.1%) |
| Medium (24 Fr and 26 Fr) | 1039 | 50 (4.8%) |
| Large (27 Fr, 28 Fr, and 30 Fr) | 3533 | 208 (5.9%) |
| Largest (32 Fr, 33 Fr, and 34 Fr) | 371 | 45 (12.1%) |

## Ultra-mini PCNL (UMP)

There was an observation that renal parenchyma is resilient enough to withstand a dilation of up to 14–15 Fr. If the dilation is done beyond 15 Fr, the parenchyma may give way to small lateral tears. These tears lead to bleeding and renal damage. The ultra-mini PCNL (UMP) is designed to limit dilation to either 11 or 13 Fr. A set of specially designed instruments include a telescope of 1 mm size that has a resolution of 17 000 pixels; an inner sheath of 6.0 Fr, which has two ports (one for irrigation and the other for a laser fiber); and an outer sheath of 11 or 13 Fr with a side-port that connects to a very thin tube running parallel to its lumen (Figure 24.3).

The stone disintegration is done with a holmium laser of 200 or 365 μm and the aim is to make small fragments of 1.5–2.0 mm. Because the aim is not to turn the stone to dust, the laser setting involves high energy (12 W) and low frequency (8 Hz). The disintegration is slower than in standard PCNL so this technique is limited to removing stones of medium or low bulk (less than 1.8 cm). At the end of disintegration, the stone fragments are removed by creating a mini whirlpool of saline by injecting through the side-port of the outer sheath (see Video 24.1).

Alternatively, a vortex can also be created by injecting saline through the previously placed ureteric catheter. The fluid moves from a high-pressure zone (i.e. pelvis and calyces) to a low-pressure zone (i.e. the lumen of the outer sheath). The saline jet through the small side-tube

**Table 24.1** Proposed terminology for defining percutaneous nephrolithotomy procedures [21].

| Approach | Sheath size (Fr) | Fragmentation method | Drainage |
|---|---|---|---|
| P = Prone | 4.8–34 | Li = Lithotripsy | N = Nephrostomy |
| S = Supine | | U = Ultrasound | S = Stent |
| | | La = Laser | NS = Nephrostomy and stent |
| | | EHL = Electrohydraulic lithotripsy | TT = Totally tubeless |

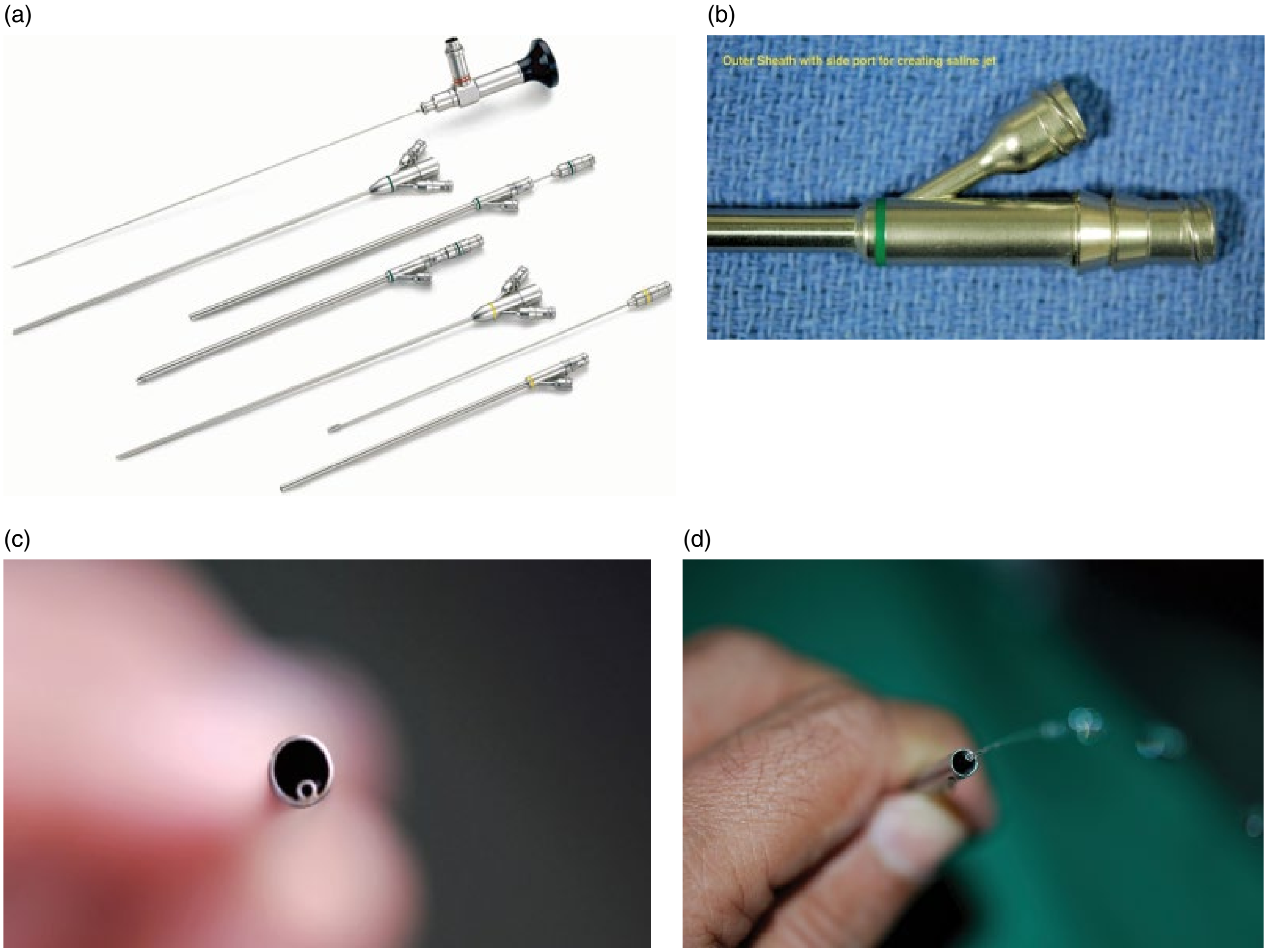

**Figure 24.3** UMP instruments. (a) Full ultra-mini PCNL set consisting of 11 and 13 F shafts and dilatators as well as a miniaturized nephroscope. (b) Outer sheath with a side-port connecting to the waterjet tube inside. (c) View of waterjet tube inside the sheath. (d) Demonstration of the "waterjet" function. Reproduced with permission of Schoelly Fiberoptics GmbH, Denzlingen, Germany & Dr. Janak Desai.

is required to agitate the dormant fragments and bring them into the vortex. Often the fragments will be evacuated automatically by the vortex; however, in certain situations a low suction can be placed on the end of the outer sheath to pull out the fragments. The mini whirlpool effect can be viewed in the small video (see Video 24.2). The endoscopic view is captured by a flexible ureteroscope. When a jet is created by pushing saline through the side-port of the outer sheath, the fragments get trapped in the saline vortex and move towards the main lumen of the outer sheath.

The UMP procedure can be used as a primary procedure for low- and medium-bulk stones or as an adjunct procedure during staghorn calculus removal. A small stone in a different calyx may be removed by UMP (instead of doing a procedure with a larger second track).

The advantages of UMP over retrograde intrarenal surgery (RIRS) are the relative speed of the procedure and the use of minimal disposables. The advantage in terms of stone-free rates needs to be established. UMP and RIRS are compared in Table 24.3 [23]. These data accrue from a few initial users of UMP and need to be verified by the urological community at large.

## Micro-perc

This technique consists of puncture with a needle telescope which is 0.9 mm thick (Figure 24.4). It is a flexible fiber-optic scope that has 10 000 pixel resolution and the needle is 16 gauge thick. The puncture is done with the help of sonography and/or fluroscopy guidance and once the needle enters the system the stone can be visualized directly. With a 200 μm holmium laser fiber the stone is disintegrated and converted into dust/fragments. These fragments are then expected to pass spontaneously. To prevent a rise in intrarenal pressure during the procedure, a 8.0 Fr ureteric catheter is placed at the beginning.

**Table 24.3** Comparison between ultra-mini percutaneous nephrolithotomy and retrograde intrarenal surgery [23].

| | RIRS | UMP |
|---|---|---|
| Total cases | 20 | 32 |
| Operation time (min) | 98 | 46 |
| Hospitalization (h) | 32 | 24 |
| Cost of disposables (euros) | 484 | 80 |
| Complication rate | 8% | 6% |
| Stone-free rate | 80% | 88% |
| Auxiliary procedure | 100% | 1% |
| Fever (percentage of patients) | 20% | 12.5% |

UMP, ultra-mini percutaneous nephrolithotomy; RIRS, retrograde intrarenal surgery.

This large-bore ureteric catheter is expected to drain the kidney and keep the pressures within acceptable limits [24].

Micro-perc is a useful procedure but the main drawbacks are as follows: (i) Puncture with a thicker needle – 16 gauge (1.65 mm) can happen. Each pass leads to relatively more damage than the pass of a 20 (0.9 mm) or 18 gauge (1.27 mm) needle. Although there a telescope positioned within the needle, the telescope starts viewing only when it has reached within the calyx. Prior to that time it sees only red. (ii) Following stone disintegration the procedure relies on nature for stone expulsion. Unlike other PCNL procedures, stone extraction is not possible with this thin apparatus. It can be used judiciously for small stones which are in the calyces or the renal pelvis. Stones trapped in closed calyces cannot be removed by micro-perc because the fragmented stones cannot escape to the pelvis through the extremely narrow infundibulum. Nevertheless, micro-perc can be a good procedure for pediatric patients and also as an adjunct to removal of larger stone bulk in adults, where a small stone is located in the other calyx that cannot be approached by the regular nephroscope.

The advantages of micro-perc as compared to extracorporeal shock-wave lithotripsy (ESWL) need to be established [25, 26].

## General considerations regarding miniaturized PCNL

PCNL is characterized by high stone-free rate in treatment of stones in the upper urinary tract, mainly in the kidney. Substantial perioperative complications such as bleeding and sepsis as well as special patient groups (e.g. children) have stimulated further innovations in this field. The driving force behind miniaturization of PCNL was to make this technique applicable in pediatric patients and to decrease morbidity. For about 15 years size reduced devices have been routinely used in clinical management of urolithiasis. New, highly efficient energy emitters such as lasers have made intracorporeal stone disintegration fast and safe. Better irrigation and knowledge of intrarenal pressure conditions could reduce the complication profile and offer similar clinical outcomes (i.e. stone-free rates) [27]. However, minimally invasive

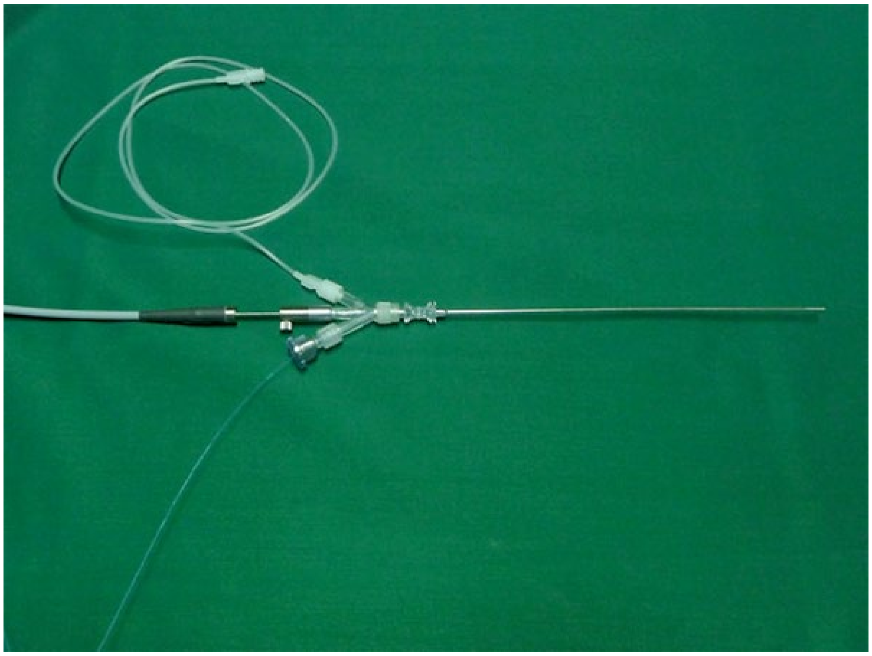

**Figure 24.4** Micro-perc instruments. Telescope within the needle; Connector for irrigation and laser fiber. *Source:* Schoelly Fiberoptics GmbH, Germany (a) and Dr. Janak Desai (b–d). Reproduced with permission of Schoelly Fiberoptics GmbH (a) and Dr. Janak Desai (b–d).

PCNL techiques have to be seen as a further development of the existing standard percutaneous nephrolithotomy procedures.

At least theoretically, miniaturized instruments result in less organ trauma, and thus lower complication rates. On the other hand, manipulation using small devices might be more challenging and associated with longer operating times. Extraction of disintegrated stones might also be more difficult. To address this question high-quality studies are needed. Currently we have scarce and conflicting evidence [28–36].

Zhu et al. published a meta-analysis objectively comparing standard and miniaturized PCNL [37]. Out of 960 studies the authors identified eight trials meeting the inclusion criteria. A data pool was created from three randomized controlled trials (RCTs) (LE: 2b), four prospective case–controls (LE: 3b), and one retrospective case–control study (LE: 3b). The authors assessed the methodological quality as relatively high for all the non-randomized studies and medium for the RCTs [28, 30–36].

### Stone-free rates

The meta-analysis found no difference in stone-free rates between minimally invasive and standard PCNL.

### Hemoglobin decrease and blood transfusion

In the mini PCNL group both hemoglobin decrease and blood transfusion rates were statistically lower than in standard PCNL.

### Operative times and hospital stay

The operating time was shorter in the standard PCNL group. For this analysis data from only seven studies could be evaluated. In contrast, the length of hospitalization was shorter in the mini PCNL group (after data pooling from five trials).

### Postoperative complications

Meta-analysis revealed no differences in terms of fever between the both groups.

### Pain

Using visual analog scale-based data from three studies the postoperative pain perception at day 1 was statistically lower in the mini PCNL group.

### Cost analysis

Two studies analyzed therapy costs, comparing mini PCNL (18 Fr) to RIRS [38] and ultra-mini PCNL (13 Fr) to RIRS [39]. Admittedly, expenses in healthcare might vary widely from country to country and from one healthcare system to another. Schoenthaler et al. [39] analyzed German and British data, whereas Pan et al. [38] investigated the situation in China. Both groups stated that RIRS is significantly more expensive than minimally invasive percutaneous stone treatment. The Chinese study focused on calculi of 2–3 cm, whereas the German–British cohort analyzed medium-size stones (1–2 cm). Looking at clinical outcome, there was no difference in stone-free rates for medium-size fragments. In contrast, mini PCNL was more effective in treatment of the larger 2–3 cm calculi.

## Synopsis

Technically challenging in nature, surgeon experience with PCNL is paramount in developing individualized treatment plans to optimize efficacy with minimal morbidity. A good experience of PCNL is required before taking on minimally invasive modalities such as mini PCNL, MIP, UMP, and micro-perc.

The latest advancements in PCNL technology and clinical introduction of new systems have led to a “revival” of the percutaneous stone treatment. The indication spectrum of PCNL has been tremendously extended and now addresses almost every kidney stone. Despite the continued lack of data from high-quality studies, complication rates seem lower, hospitalization shorter, and stone-free rates comparable to those of conventional, standard systems.

The routine use of the tubeless technique is debatable. Minimally invasive PCNL systems, however, allow lower complications rate if no nephrostomy tube is placed [40, 41].

Bleeding is considered to be one of the most severe complications related to PCNL. The use of miniaturized PCNL systems may help to substantially reduce treatment-associated blood loss. Gazelle et al. [42] demonstrated that larger access sheaths produce more bleeding in an *in vivo* porcine model. Impaired vision and even termination of the procedure might result because of bleeding. Kukreja et al. [43] analyzed various factors potentially related to blood loss. They identified the smaller tracts used in patients with a nondilated pelvicalyceal system or narrow infundibulum, as well as in children younger than 5 years, as one of the factors responsible for lower bleeding rates.

Kidney calculi are conveniently divided into nonstaghorn and staghorn stones, and most controversy is in the area of nonstaghorn stones. For very large stones the treatment of choice is still standard PCNL (with a 28 or 30 Fr dilation). For stones between the sizes of 1.0 and 2.0 cm either UMP or RIRS can be chosen. For stones less than 1.2 cm and where ESWL is not considered a good option, micro-perc can be used.

**Table 24.4** Observational comparison among minimally invasive treatment modalities for kidney stones.

| | Mini PCNL | UMP | RIRS | Micro-perc |
|---|---|---|---|---|
| Cost of equipment | Moderate | Moderate | High | Moderate |
| Learning curve | High | High | Moderate | High |
| Stone-free rate | Good; even for large stones | Good, up to 1.8 cm size stone | Good, up to 1.8 cm size stone | Good, up to 1.0 cm size stone |
| Auxiliary procedure | Almost nil | Almost nil | Stent removal; preprocedure stenting sometimes | Steinstrasse removal sometimes |
| Hospitalization | Two days | One day | One day | One day |

**Table 24.5** Comparison between miniaturized percutaneous nephrolithotomy instruments.

| | Mini PCNL | UMP | Micro-perc |
|---|---|---|---|
| Smallest size of sheath | 17.5 Fr | 11.0 Fr | 4.85 Fr |
| Stone removal | Forceps and fluid dynamics | Creating a fluid vortex | Leave for natural expulsion |
| Telescope size | 3 mm | 1 mm | 0.9 mm |
| Resolution of telescope | 30 000 pixels | 17 000 pixels | 10 000 pixels |

UMP can also be used as an adjunct to standard PCNL; the main bulk can be removed by PCNL and if there is a small stone in an otherwise inaccessible calyx, UMP can be used to remove that stone.

Familiarity with the full spectrum of endourological techniques facilitates a minimally invasive approach to the entire urinary tract.

As the armamentarium of treatment modalities available to the urologist has increased, new controversies regarding the indications for these therapies have developed. Currently, urologists face the challenge of selecting the optimal treatment modality on the basis of the patient's and the stone's characteristics. The choice also depends on the availability of instruments (and thereby experience) in the hospital (Tables 24.4 and 24.5).

Recent technological advances in PCNL might initiate safer and more efficient management of renal stones. A lack of prospective randomized trials comparing treatment modalities coupled with the vast disparity in the access to resources worldwide continues to individualize rather than standardize stone treatment in patients. However, when treating a patient with a renal calculus, the urologist must ask: "Is the patient an appropriate candidate for shock-wave lithotripsy or should other treatment modalities be used?"

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# 25

# Percutaneous Nephrolithotomy: Special Problems with Staghorns

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## Introduction

A "staghorn" calculus is defined as stone within the renal pelvis extending into two or more calyceal systems. A "partial staghorn," as the name suggests, occupies part, but not all, of the collecting system, while a "complete staghorn" occupies essentially the entire collecting system.

Staghorn calculi composition is commonly struvite (magnesium ammonium phosphate) and/or calcium carbonate apatite. These stone compositions are often referred to as "infection stones" due to their strong association with recurrent urinary tract infections caused by urea-splitting bacteria. Cultures of infection stones have shown that bacteria are harbored within the stone material itself, rather than on the surface [1]. This explains why once an infection stone is present, urine infections tend to recur. Calcium phosphate, uric acid, calcium oxalate, and cysteine also commonly form staghorns, particularly in the metabolic patient. Although traditionally it was thought that the majority of staghorns were infection stones, contemporary studies have shown that metabolic stone staghorns are just as, and perhaps even more, common [2]. Preoperative knowledge of stone composition can potentially play an important role in treatment decisions. The holmium:YAG laser, for example, is a very effective lithotrite for fragmenting struvite stones and less effective for calcium oxalate monohydrate (COM) stones. Cysteine, brushite, and COM stones, for example, are also resistant to fragmentation via shock-wave lithotripsy (SWL).

Possible complications of untreated staghorn calculi include urinary tract infections, sepsis, progressive decline in renal function, renal failure, and death. Traditionally, it has been taught that patients with untreated staghorn calculi have a mortality of up to 30%. This was largely based on the landmark Blandly and Singh study in 1976 which reported a mortality rate of 28% at 10 years for 60 patients managed conservatively for staghorn calculi, compared to a 7% mortality rate for those treated surgically [3]. In 1995, Teichman et al. reviewed 177 patients with staghorn calculi followed for a mean of 7.7 years, and found that no patients with complete stone clearance died of kidney-related causes, compared to 67% of patients who refused treatment [4]. As a result, active aggressive management of staghorn calculi has become the standard of care, with percutaneous nephrolithotomy (PCNL) being the mainstay surgical treatment option. With advances in PCNL technique and its more widespread adoption, as well as better urinary drainage and antibiotic treatment, current mortality rates are likely far lower than initially reported, although a large body of literature on the subject matter is lacking. Furthermore, these older studies involved large cohorts of patients with infection stones, whereas more recent studies demonstrate that the majority of patients have metabolic stones, with lower risks of urosepsis [2, 5, 6]. Recently, Deutsch and Subramonian reported on their single-center experience with conservative management of staghorn calculi in 22 patients [7]. In this small series, patients were managed conservatively due to comorbid conditions, poor access/anatomy, or patient choice. Complications included recurrent urinary tract infections (UTIs) in 50%, progressive renal failure in 14%, disease-specific mortality in 9%, and dialysis dependence in 9%. Disease-specific mortality and morbidity were significantly different between the unilateral and bilateral staghorn groups, at 0 versus 40% and 12 versus 20%, respectively. They concluded that candidates for conservative management would ideally have unilateral asymptomatic stones with minimal infection, in addition to specific indications preventing more aggressive therapy.

The American Urological Association (AUA) best practice guidelines on the surgical management of stones

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recommend active treatment of all staghorn stones, if comorbidities do not preclude treatment [5, 6]. Medical therapy and supportive therapy are to be considered only for those not thought to be operative candidates. The 2005 AUA report on the management of staghorn calculi recommends discussion of all treatment options with patients [8]. This includes PCNL, retrograde ureteroscopic approaches (URS), SWL, combined therapies, and open or laparoscopic or robotic surgery, where applicable. PCNL is recommended as the initial modality of choice for treatment of struvite staghorn calculi. This can thereafter be followed by SWL, URS, or repeat PCNL, as required to render patients stone free. In patients not considered candidates for PCNL, clinicians may offer staged ureteroscopy [5, 6]. Unlike adults, the pediatric population has been shown to have great success with SWL in fragmenting even very large stones. In adults, however, SWL and open surgery are not recommended as first-line therapies, with laparoscopic or robotic or open surgery being reserved for situations in which there is expected to be poor success with PCNL and SWL procedures.

The aim of treatment, particularly for struvite calculi, is complete surgical stone removal, as any remaining stone debris may lead to bacterial persistence, recurrent infection, and stone regrowth. Achieving stone-free status also prolongs time to stone recurrence. Stone-free rates for staghorn calculi are widely variable in the literature, but approach 85%, with or without adjunct SWL therapy [9], versus only 51% for SWL monotherapy [10]. Lifshitz et al. reported stone-free rates of 78% with an average of 2.9 procedures [11]. Stone-free rates are lower following PCNL for staghorn calculi, than they are for nonstaghorn stones.

When choosing and planning stone treatment, the urologist must consider stone factors (stone burden, composition, location), renal anatomical factors (obstruction, hydronephrosis, ureteropelvic junction (UPJ) obstruction, calyceal diverticulum, renal ectopia or fusion, lower pole location, reconstructed urinary tracts), and patient and clinical factors (infection, obesity, body habitus, coagulopathy, patient age, hypertension, neurogenic bladder, spina bifida, and renal failure). Current AUA guidelines recommend preoperative workup with computed tomography (CT) of the abdomen and pelvis, urinalysis, urine culture and sensitivity, serum electrolytes, estimated glomerular filtration rate (eGFR), and complete blood count (CBC) [5, 6]. Coagulation parameters are not routinely necessary unless the patient has a history of bleeding diathesis or is on anticoagulant therapy. Further preoperative preparation includes an extended period of antibiotics for actively infected collecting systems and cessation of anticoagulants and antiplatelet agents in preparation for therapeutic procedures. Current AUA guidelines emphasize the importance of obtaining preoperative CT scan in all patients planned for PCNL [5, 6]. In general, a noncontrast CT scan is sufficient, but in patients with anatomic anomalies or UPJ obstruction a triphasic contrast-enhanced CT scan with delayed urographic phase and 3D reconstructions can be very helpful in surgical planning. A differential renal scan can provide clinical useful information, particularly in patients who may have a nonfunctioning kidney with a staghorn stone. They may be better served with nephrectomy (rather than PCNL), particularly for symptomatic or infected stones, and a normal contralateral kidney.

Preoperative assessment of stone complexity is vital, particularly for staghorn calculi. A number of scales have been developed to assess preoperative stone complexity with the aim of predicting postoperative stone-free rates and complications. These scoring systems, such as Guy's stone score [12], S.T.O.N.E. nephrolithometry [13], the CROES nomogram [14], and the Seoul National University Renal Stone Complexity score for PCNL [15], have noted the importance of numerous factors in determining operative success. These include: surgeon case volume, prior stone treatment, presence of staghorn calculi, presence of calyceal diverticula, stone location, stone count, stone size, number of involved calyces, stone density, presence of obstruction, PCNL tract length, anatomical abnormalities, and patient factors (such as spina bifida or spinal injury). These scores, however, are not specific for staghorn calculi. In patients with staghorn calculi, variants of the collecting system anatomy have an important impact on the expected procedural complexity and preoperative, as well as intraoperative, planning. Figure 25.1 illustrates intraoperative images obtained from three patients undergoing PCNL. Figure 25.1a shows a bifid system, which limits the ability to use an upper pole puncture. Figure 25.1b reveals a favorable clinical situation in which the main stone is situated within the renal pelvis, while the calyces are short and dilated. Figure 25.1c shows an unfavorable system with long calyces and relatively narrow infundibula, which will likely require treatment, at least in part, with flexible nephroscopy and laser lithotripsy or multiple punctures to use rigid instruments efficiently and without excessive torque on the renal parenchyma.

Various percutaneous techniques and modifications have been developed with the aim of improving stone-free rates and patient safety. These include variations in patient positioning, number and size of tracts, and instruments for stone removal and fragmentation. In this chapter we review possible difficulties encountered in the treatment of staghorn calculi with PCNL and present our approach, as well as alterative modifications, to treating staghorn calculi via PCNL.

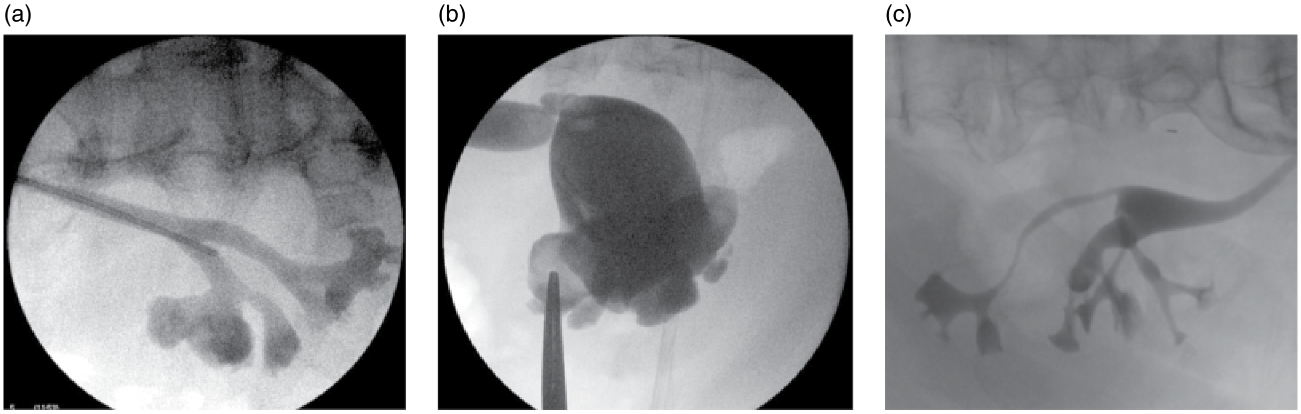

**Figure 25.1** Fluoroscopic images from three patients undergoing PCNL illustrating variation in collecting system anatomy. (a) A bifid system which limits the ability to access the lower pole via an upper pole puncture. (b) A hydronephrotic system with favorable anatomy and short dilated calyces. (c) An unfavorable bifid system with long spidery infundibula.

## Access

Obtaining appropriate access to the pelvicalyceal system is the most challenging and crucial part of PCNL. Technically, access can be obtained by a trained urologist in the operating room or a radiologist preoperatively. Percutaneous renal access, in fact, is not uncommonly performed by interventional radiology preoperatively in the face of obstruction, infection, or complex renal anatomy. Other situations in which radiology-placed access may be quite beneficial include failed retrograde access and inability to opacify the collecting system where fluoroscopic (rather than ultrasound-guided) access is employed, prior urinary diversion which can make retrograde access difficult, or preoperative decompression of an obstructed and/or infected system inadequately drained by stenting. In these cases there should be clear communication between urologist and radiologist to ensure placement of the tract through a posterior calyx ideal for maximizing access to the stone in preparation for PCNL. If the radiologist-placed nephrostomy tube is not ideally placed, it is vital that a new tract be placed intraoperatively, using opacification of the collecting system via the nephrostomy to select and puncture the best calyx (or calyces if multiple tracts are needed).

Urologic surgeon access for PCNL has been shown to be safe and effective. Some studies have reported lower complication rates and improved stone-free rates compared to access obtained by interventional radiology [16]. This can likely be explained by the fact that urologists have intimate knowledge of intrarenal anatomy and angulation of the calyces, the stone complexity, and potential difficulties which can arise during the surgical procedure. Thus, urologists more closely focus on achieving end-on calyceal access through a posterior papilla with a direct access to the stone, as opposed to a potential dangerous tract through the infundibulum or renal pelvis, which, if dilated, can cause significant bleeding and postoperative complications.

Urologist percutaneous access has traditionally been obtained fluoroscopically in the prone position using a bull-seye technique, although various modifications have been developed. Ureteroscopic-assisted puncture, usually in the prone split-leg position, has also recently become more commonplace. Its advantages include the ability to directly visualize a posterior papilla for puncture, as well as decreased fluoroscopy time compared to traditional PCNL [17–19].

Consideration must also be given to the location of the puncture. At our center, we prefer upper pole punctures, when feasible, as this can facilitate single access for staghorn calculi. The upper pole tract tends to be more in line with the axis of the kidney, and allows the efficient treatment of high stone volumes in the upper pole, renal pelvis, and lower calyces with rigid instruments and minimal torque through a single access. The disadvantage, however, of upper pole puncture is that of potential pleural complications. In contrast, although lower pole punctures have a number of advantages including low risk of pleural, liver, and splenic injuries, they involve a longer tract, with a greater skin-to-stone distance, poorer access to the UPJ, and a slightly higher risk of colonic injures. Lower pole punctures are, therefore, more suited for lower pole nonstaghorn stones or lower pole partial staghorns, particularly in bifid collecting systems.

## Patient positioning

Options for patient positioning during PCNL include: prone, prone-flexed, prone split-leg, lateral, lateral-flexed, and supine. The prone position is the standard positioning technique for PCNL. The various modifications to this position change the relative positioning of the kidneys and their surrounding structures, thus altering the incidence of procedural complications.

The prone-flexed position reduces lumbar lordosis and increases working space between the costal margin and iliac crest, which can minimize instrument clashes (Figure 25.2) [20]. In the prone-flexed position, the position of the left kidney is lowered 92% of the time, converting what would have been supra-11th rib punctures in the prone position to supra-12th rib punctures in the prone-flex position 46% of the time, thus minimizing the risk of intrathoracic complications [21]. In addition, the skin-to-kidney distance is shortened (8.4 mm for the right kidney and 13.4 mm for the left kidney) [21]. The kidneys tend to "fall away" from adjacent organs, leading to 11.3° further trajectory to the spleen on the left side and 13.6° further trajectory to the liver on the right side, leading to decreased risk of injury to these organs [21]. Lastly, the prone-flex position sets up an easier trajectory from an upper pole puncture to access the entire collecting system for treatment of staghorn calculi with minimal infundibular torque, as the renal axis is favorably altered in this position. For these reasons, the flexed-prone position is the position most commonly used at our center for PCNL.

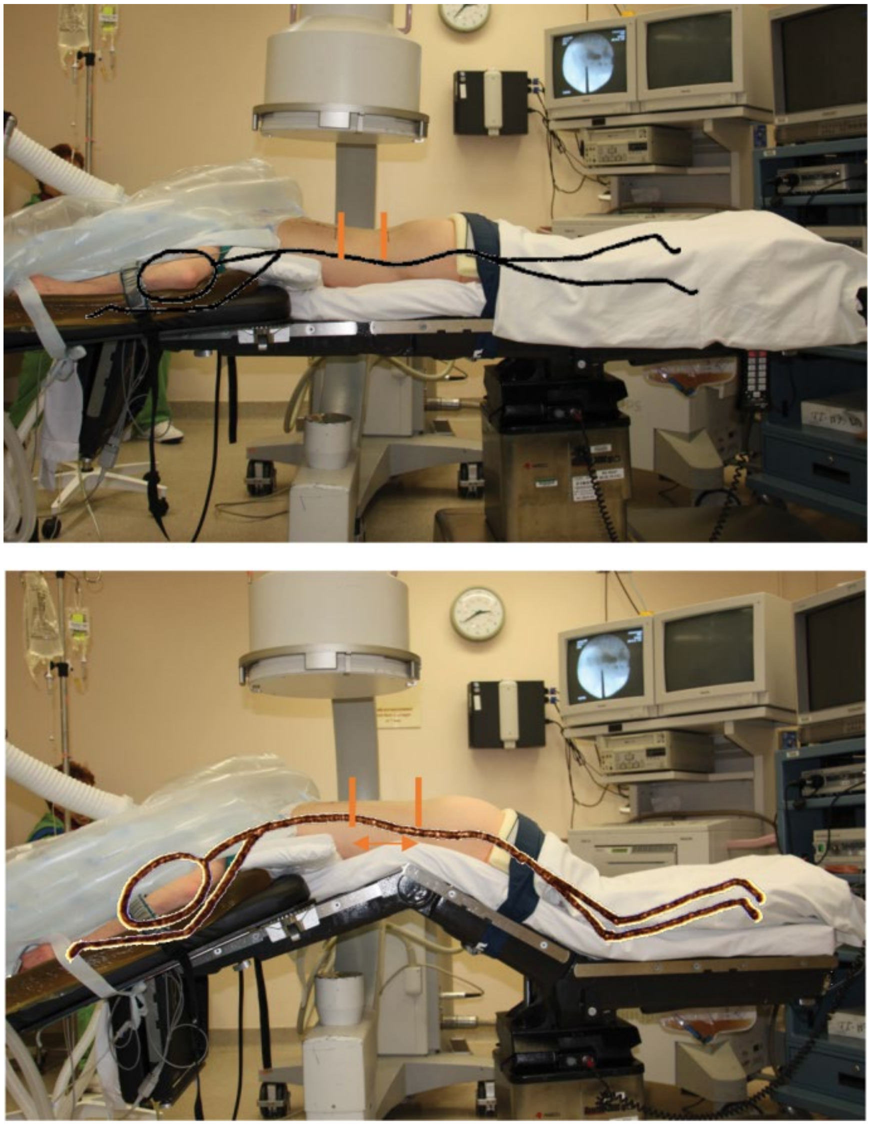

**Figure 25.2** Compared to the prone position, the prone-flexed position for PCNL increases the available flank area for puncture, flattens the back, and decreases instrument clashes with the buttocks. The prone-flex position can thus facilitate the multiple punctures often needed for staghorn calculi. Note the widening of the area between the lines drawn on the flank. *Source:* Ray AA, Chung D, Honey J. Percutaneous nephrolithotomy in the prone and prone-flexed positions: anatomic considerations. *J Endourol* 2009;23(10). Reproduced with permission of Mary Ann Liebert, Inc.

The prone split-leg position is advantageous for performing concomitant retrograde cystoscopy and ureteroscopy without need for repositioning the patient while under anaesthesia. Prone endoscopy, however, has a steep, but easily overcome, learning curve. This positioning also allows for initial attempted treatment via ureteroscopy, in cases where a percutaneous procedure may or may not be necessary and is to be determined based on intraoperative findings.

The lateral and lateral-flexed positions are familiar to urologists as they are often used for open or laparoscopic renal surgery. The most common indications for lateral positioning for PCNL are morbid obesity (due to concerns regarding adequate ventilation in the prone or prone-flexed positions) and skeletal deformities (which mitigate prone positioning). Lateral position has the least effect on cardiac and respiratory function. In addition, the renal pelvis is dependent, providing easier access to mobile stones. The addition of the table flex in the lateral position significantly increases working space and may elevate the lower ribs, reducing the need for supracostal access. In general, the lateral position is more ergonomic for the surgeon, and can be used to perform simultaneous nephroscopy and ureteroscopy. The major disadvantage of this positioning is that fluoroscopic access is technically challenging, as it requires a triangulation technique, rather than the traditional bullseye technique. Ultrasound-guided puncture or radiology-placed access are alternatives. In this position, PCNL can also be successfully performed under spinal anesthetic in patients at high risk for endotracheal intubation.

Supine and modified supine positions (such as the Galdakao-modified supine Valdivia position) are the least common, but are ideal for patient ventilation. They also provide preserved ergonomic access for concurrent retrograde ureteroscopy. In addition, in the supine positioning there is decreased renal mobility, facilitating percutaneous access, particularly to the lower pole. The colon is the furthest away from the kidney in the supine position, and least likely to be injured in this position. This is, however, in part, mitigated by the more lateral placement of the nephrostomy tract which is placed at the anterior axillary line, leading to a longer tract length. Finally, upper pole access is difficult or impossible in the supine position, which limits calyceal selection for the optimal management of more complex staghorn stones.

## Access technique

At our center we begin with the patient in the supine position under general anesthetic with endotracheal intubation. We first perform and save a noncontrast fluoroscopic image to identify the presence and location of the stone(s) before proceeding with flexible cystoscopy and insertion of an open-ended ureteral catheter (5 Fr Flexitip™ ureteral catheter, Cook Medical, Bloomington, IN, USA). The open-ended catheter is advanced toward the renal pelvis, and urine is aspirated to decompress the system. The urine sample is sent for culture and sensitivity. Dye is then injected to obtain a retrograde pyelogram. Anterior–posterior (A-P) and oblique films are taken to identify the three-dimensional calyceal anatomy.

Decompressing hydronephrotic systems, when possible, prevents dilution of the dye and facilitates better opacification, without risk of increased intrarenal pressures and extravasation. Furthermore, should purulent urine be aspirated, the procedure can be stopped at this stage, prior to prone positioning and calyceal puncture. The open-ended catheter is then exchanged over a guidewire (0.035″, 145 cm, fixed-core guidewire, Cook Medical) for a ureteral occlusion balloon catheter (6 Fr, 75 cm, UPJ occlusion balloon catheter set, Cook Medical), which is connected to retrograde flow of contrast. This allows for continuous distention of the collecting system with contrast for eventual fluoroscopic-guided needle puncture. In addition, the balloon catheter prevents migration of stone fragments down the ureter during the procedure and allows for retrograde access later in the case for stent placement. With the retrograde pyelogram performed initially in the supine position, contrast, which is heavier than urine, preferentially enters the posterior calyces, which then appear darker, aiding selection of a posteriorly located calyx for puncture. The targeted posterior calyx is, therefore, initially most easily identified and selected during the supine pyelogram. This is particularly advantageous when there is a hydronephrotic urinary system, which cannot be decompressed prior to dye instillation. In such a system, in the *prone* position, dye will preferentially occupy the anterior calyces, displacing urine in the posterior calyces and making visualization of these calyces difficult fluoroscopically for puncture. In the A-P view, in the *supine* position, posterior calyces are viewed end-on, in line with the infundibulum, and appear dark. As the C-arm is rotated, a posterior calyx will appear to lengthen and move laterally, as the infundibulum comes into view (Figure 25.3) [20].

After placement of the ureteric occlusion balloon and prior to repositioning the patient into the prone-flexed position, a urethral catheter is placed. The catheter balloon is inflated with dye solution and pulled down to the bladder neck, in order to facilitate identification of the bladder neck and placement of a retrograde tethered stent at the end of the procedure. The urethral catheter and ureteral occlusion balloon catheter are secured together.

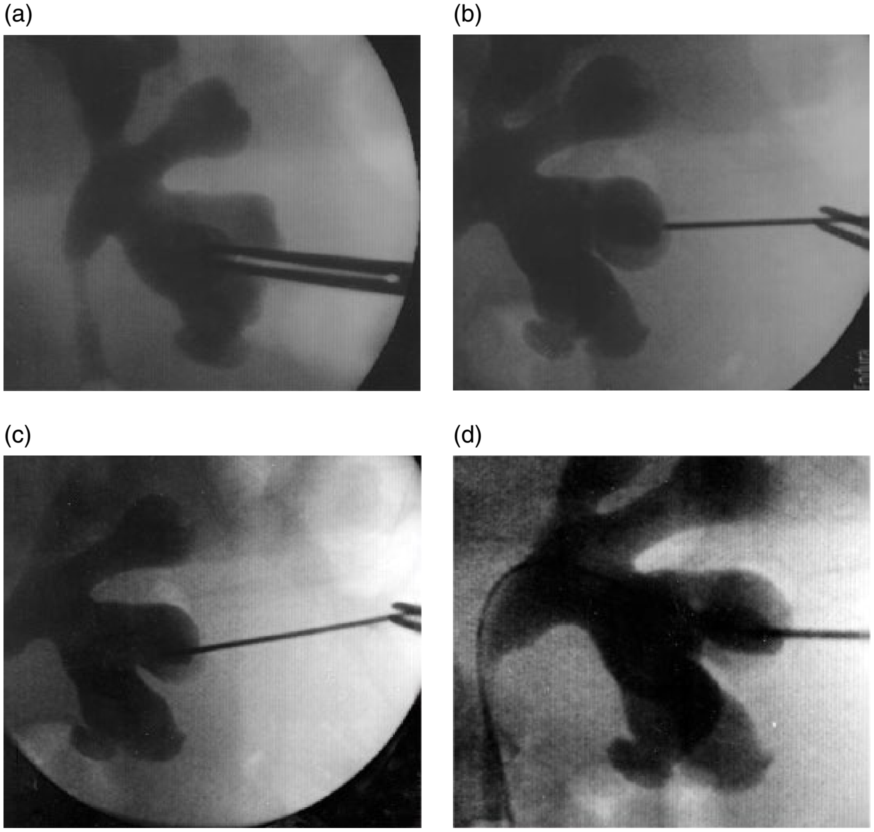

**Figure 25.3** Fluoroscopic images illustrating the bulleye technique of calyceal puncture for a posterior lower pole calyx. (a) "Bullseye" puncture. (b) Needle tip short of calyx. (c) Needle entering calyx. (d) Guidewire down ureter. *Source:* Ray AA, Chung D, Honey J. Percutaneous nephrolithotomy in the prone and prone-flexed positions: anatomic considerations. *J Endourol* 2009;23(10). Reproduced with permission of Mary Ann Liebert, Inc.

The patient is then repositioned in the flexed-prone position. Pressure points are padded, and a bolster is placed under the chest. The C-arm is angled at 0–30° from vertical, and may require further angulation for improved visualization above the 12th rib. An 18 gauge trocar needle (18G, 15cm, trocar needle, Cook Medical) is inserted toward the selected posterior calyx under fluoroscopic guidance, using a bullseye technique. The needle is advanced only during expiration during supracostal punctures to minimize the risk of pulmonary injury. The depth of the puncture is assessed by rotating the C-arm away from the surgeon. The aim is to puncture a posterior-located calyx through the papilla, in line with the infundibulum, thus traversing Brödel's line and minimizing bleeding risk. A "pop" is often felt when entering the collecting system. Once access is believed to be obtained, the inner needle cannula is removed; free flow of contrast confirms successful puncture of the collecting system. Further retrograde dye instillation is then stopped, in order to prevent dye extravasation through the puncture site, which can impair fluoroscopic visualization. An Amplatz extra-stiff guidewire (0.038″, 145cm, Amplatz extra-stiff fixed-core guidewire, Cook Medical) is then inserted through the needle under fluoroscopy. This is ideally aimed down the ureter, beside the occlusion balloon catheter. If this is not possible, an excess amount of wire is curled within the renal pelvis or within a dilated calyx. The skin-to-calyx distance is then measured, the skin incision is enlarged, and the fascia is dilated sequentially to 10Fr using fascial dilators (6Fr, 8Fr, and 10Fr 20cm fascial dilators, Cook Medical). A 10Fr dual-lumen catheter (10Fr, 24cm Flexi-Tip®, dual-lumen ureteral access catheter, Cook Medical) is next advanced over the extra-stiff wire and used to insert a safety guidewire (0.035″, 145cm, fixed-core guidewire, Cook Medical), which is secured to the sterile drape for the remainder of the case. Balloon dilatation of the tract is then performed over the working extra-stiff guidewire (30Fr Ultraxx™ nephrostomy balloon set, Cook Medical) (Figure 25.4). Dilatation of the nephrostomy tract can be performed by balloon dilatation or sequential dilators. Balloon dilation, although more expensive, tends to be faster and less traumatic [22].

## Multiple tracts

Upper pole access has the greatest likelihood of clearing most volume of stone through a single puncture due to the favorable lie of the kidney. Using an upper pole puncture, the upper and renal pelvis stone burden can be cleared with a rigid scope; and most lower calyces can also be accessed with a rigid scope with minimal torque. A flexible nephroscope may then be used to clear the remaining stone burden, unless it is too large. In this

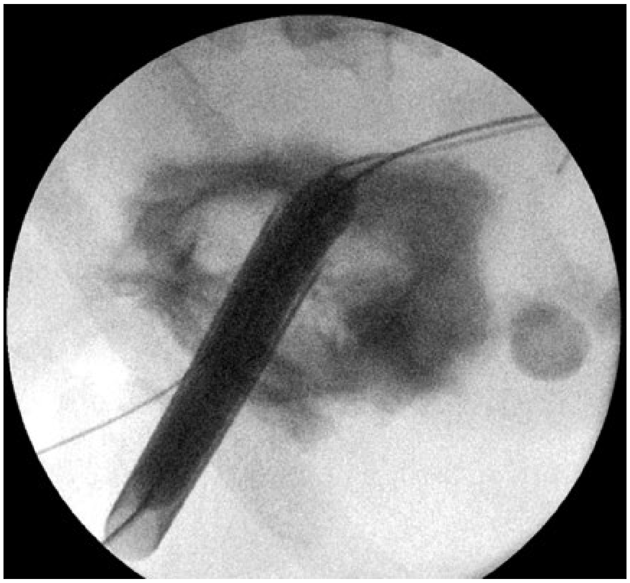

Figure 25.4 Balloon dilatation of the nephrostomy tract with subsequent advancement of the working tract (Ultraxx nephrostomy balloon set, Cook Medical). Dye is placed in the balloon to ensure no "waist" is seen, which would indicate need for further dilation.

case, second wires should be dilated for large mid-calyceal stones or inaccessible large lower calyceal stones.

Although studies have shown that multiple-tract access does not lead to more severe reduction in renal function compared to single tract access, multiple-tract access has been shown to lead to higher complication rates [23]. Nonetheless, as seen in Figure 25.1, collecting system anatomy and stone complexity often dictate a need for placement of further tracts.

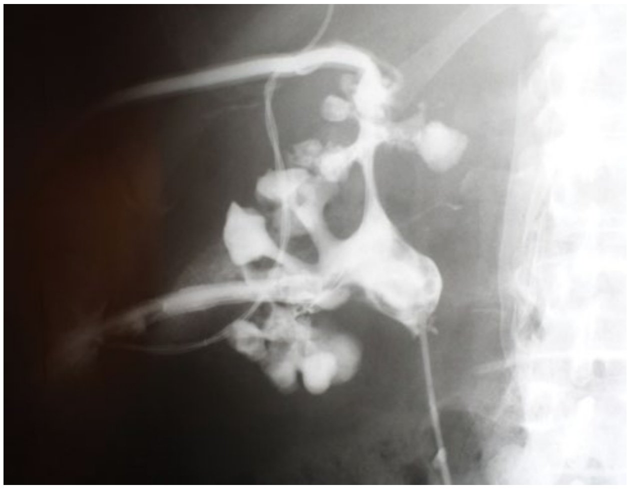

Figure 25.5 Two-tract puncture of the collecting system for treatment of a complex staghorn calculus, with initial dilatation of the upper pole tract, followed by the lower pole tract.

When the need for multiple tracts is anticipated, it is often best to insert multiple wires (such as in an upper, mid, and lower posterior calyx) prior to dilating the first tract when visualization of the collecting system is optimal. Once the wires are in place and secure, the first tract can be dilated (usually the upper tract for staghorn calculi), with dilation of the other tracts performed later in the case as needed (Figure 25.5). The alternative is to obtain multiple radiologist-placed accesses. When working with multiple tracts it is of utmost importance to try to obtain end-on calyceal puncture, as the procedure may be long and bleeding can be problematic. One is also more likely to torque to reach all areas of the kidney; thus careful selection and angulation of the tract is important (Figure 25.6).

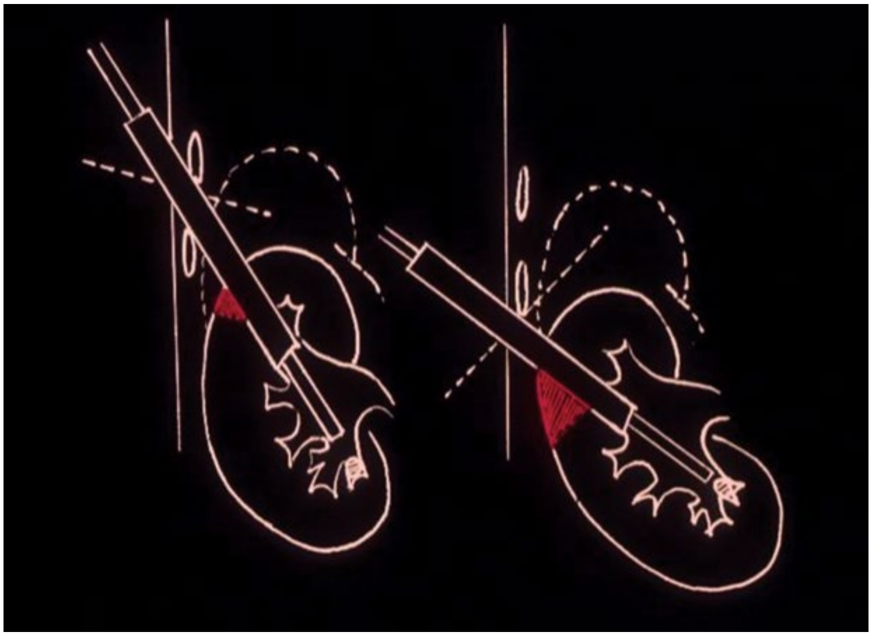

Figure 25.6 Excessive torque on the rigid nephroscope while looking down the axis of kidney can traumatize the renal parenchyma and infundibulum, resulting in bleeding.

## Stone fragmentation and removal

Devices for accessing and treating stone fragments should be used as deemed necessary to ensure complete stone-free status (including clearance of sand) particularly for struvite stones.

Tools for intracorporeal lithotripsy during PCNL include ultrasonic, pneumatic, or ballistic lithotripters, or combinations thereof. The LithoClast™ Master/Select with Vario Handpiece (Boston Scientific, Marlborough, MA, USA), for example, is a combined pneumatic and ultrasonic lithotrite which can be used independently, or in combination, for more efficient and faster stone clearance. Hand-held, standalone, pneumatic lithotripters (such as the Stonebreaker™, Cook Medical) can deliver up to 29 bars of pressure at the tip of the probe, allowing for effective treatment of very hard stones. Lithotripsy through flexible nephroscopes is limited to laser fragmentation, the holmium:YAG laser being the most effective.

Instruments for capturing, repositioning, and removing renal stones via flexible nephroscopy include tip or tipless nitinol baskets (e.g. ACMI Sur-Catch®, Bard Dimension®, Cook NCircle®), four-wire or multiwire baskets. These have no interference, or limited interference, with scope deflection. In addition, tools for removal of larger stone fragments via graspers though rigid nephroscopes include the three-prong grasper (Captura®, Cook Medical) and percutaneous nitinol baskets (Perc NCircle®, Cook Medical).

At our center, we most commonly begin with a trial of ultrasonic lithotripsy through a rigid nephroscope should the stone be easily accessible with minimal torque. Larger stone fragments are removed with a three-prong grasper or percutaneous nitinol basket through the sheath. Stone samples are sent for both stone analysis and culture and sensitivity. If the stone is too hard to fragment via ultrasonic lithotripsy, a hand-held pneumatic lithotripter is employed. Stones inaccessible via rigid nephroscopy are visualized with flexible nephroscopy, basketed, and removed, or repositioned in a calyx with more favorable angulation for treatment via laser lithotripsy.

## Exit strategies

The goals of drainage following PCNL are to ensure adequate urine drainage, minimize bleeding, and provide re-entry access to the collecting system when needed. Options include: nephrostomy tubes (pigtail, cope loop, Foley or Councill or Malecot catheters), re-entry tubes, nephroureterostomy tubes, ureteral catheters, and ureteric stents (tethered or untethered).

Traditional large-caliber tubes (Malecot, Councill, Foley, re-entry tubes) have been standard for post-PCNL drainage for many years. Their benefits include preservation of the tract for second-look procedures, as well as possible improved urinary drainage and hemostasis. However, these tubes can be painful and result in prolonged urinary drainage from the flank post removal. In addition, they require a nephrostogram prior to removal. Alternatively, smaller tubes, such as 10–12 Fr nephrostomy tubes maintain access to the kidney, while reducing patient discomfort. AUA guidelines recommend that in patients undergoing uncomplicated PCNL, who are presumed stone-free, placement of a nephrostomy tube is optional (conditional recommendation, evidence level grade C) [5, 6].

"Tubeless" PCNL has gained popularity over the last decade, and has been shown to be safe and effective [24]. This form of urinary drainage is not completely tubeless, as the name suggests. Rather, urinary drainage is established via a ureteric stent (tethered or untethered) or via a 5 Fr ureteral catheter without a nephrostomy tube. The advantages of "tubeless" (more accurately "nephrostomy-less") PCNL include less pain and internal urinary drainage. The disadvantages include lack of access for second-look procedures, need for cystoscopy for removal of untethered stents, and stent related symptoms. Many studies have documented additional advantages of "tubeless PCNL" including less narcotic use, shorter hospital stay, and faster resumption of postoperative activities [24]. "Tubeless" PCNL should, however, be reserved for uncomplicated procedures with no need for a second look, no major collecting system perforation, and no significant bleeding from the tract upon sheath removal. For patients with complex staghorn stones and particularly with infection stones, the "tubeless" approach is often less advisable and postoperative drainage with either a nephrostomy tube, nephroureterostomy tube, or nephrostomy tube and ureteric stent are preferable.

"Totally tubeless" PCNL has also been described wherein no form of drainage tube is left at the end of the procedure. On some occasions a safety open-ended ureteric catheter is left for 24 hours, then removed prior to the patient's discharge [25]. The advantages again include less pain, no external drainage, and no need for delayed tube removal. There are many disadvantages, however, including: no access preservation, no drainage, and a higher rate of reintervention (such as stent insertion). This exit strategy is best suited for simple PCNL procedures, and not advised for the management of more complex staghorn stones, particularly infected stones.

At our center, we place a tethered ureteric stent retrogradely at the completion of PCNL. The stent is removed in clinic one week post operatively upon completion of postoperative imaging (noncontrast CT scan and/or kidney–ureter–bladder X-ray) to confirm stone-free status. External nephrostomy tube drainage is reserved for significant bleeding, large collecting system perforations, long procedure, and/or multiple tracts, or when a stent cannot be placed.

A compromise to "tubed" and "tubeless" procedures is the placement of a nephroureterostomy tube. Initially, this can be left open, acting as a nephrostomy tube. Twenty-four hours later it can be clamped, acting as a ureteric stent. It can then be removed on an outpatient basis once edema has settled. The advantages of nephroureterostomy tubes include: less pain than large-bore tubes, options of internal and external urinary drainage, maintenance of tract access to kidney, ease of management, and no need for a secondary procedure or nephrostogram for removal. However, the stent component of the tube may still cause irritation. At our center, we prefer to leave a nephorureterostomy tube for complex intraoperative cases, such as those complicated by a small perforation, patients with urinary diversion, or patients at risk for postoperative sepsis (for example spina bifida, struvite stones) since it can provide maximal internal and external urinary drainage.

## Tips and tricks

Performing complex PCNL has a steep learning curve, particularly when obtaining one's own access. Some of the tips and tricks we have found helpful are listed here:

- If contrast is lost from a posterior calyx with the patient in the prone position, a small volume of air can be injected retrogradely via the occlusion balloon catheter, thus obtaining an air nephrogram to aid with calyx localization and puncture.
- If puncturing directly onto stone, it is important to push the needle "into" the stone, increasing the chance that the wire will be advanced into the collecting system rather than outside.
- It is often difficult to advance the working or safety wires down the ureter, particularly for staghorn calculi (although this is usually easiest to achieve from an upper pole puncture). In this case, excess wire should be curled within the renal pelvis or within a dilated calyx.
- In our experience, balloon dilatation of the nephrostomy tract is preferred, should resources allow. However, if metal telescoping dilators are used, additional care must be taken to ensure these are not over-advanced, as significant perforations can occur.
- Repeated use of the nephrostomy balloon for multiple tracts may fail and require a second balloon.
- The working sheath should always be used with the tip just within the collecting system. This tamponades venous bleeding, improves visibility, reduces fluid extravasation, and lessens the chance of hydrothorax with a supracostal approach. Just after placement of the sheath, position can be checked with a zero-degree rigid urethroscope to maximize irrigation flow and forward visualization. If short of the collecting system, further balloon dilatation over the working wire can be performed, and the sheath can be advanced further over the balloon.
- The nephrostomy tract should be placed in line with the axis of the kidney and the path of the infundibulum, where possible. This means that the C-arm should be angled "down" to the upper pole or "up" to the lower pole when puncturing with the bullseye technique (Figure 25.7). It is important to avoid a superiorly angled tract towards the upper pole, with a puncture below the 12th rib. Excessive torque on the rigid nephroscope while looking down the axis of kidney may split the parenchyma or may traumatize the upper pole infundibulum, resulting in bleeding. In this situation, residual stones should be treated with flexible nephroscopy and laser lithotripsy or via placement of a second tract.
- A ureteral access sheath, placed instead of the ureteral occlusion balloon, can be used to retrogradely reposition stones from inaccessible calyces with intraoperative retrograde ureteroscopy.
- For complex cases, the pros and cons of a long single session versus staged procedures must be considered.
- Completion of flexible nephroscopy and fluoroscopy prior to insertion of a stent or nephroureterostomy

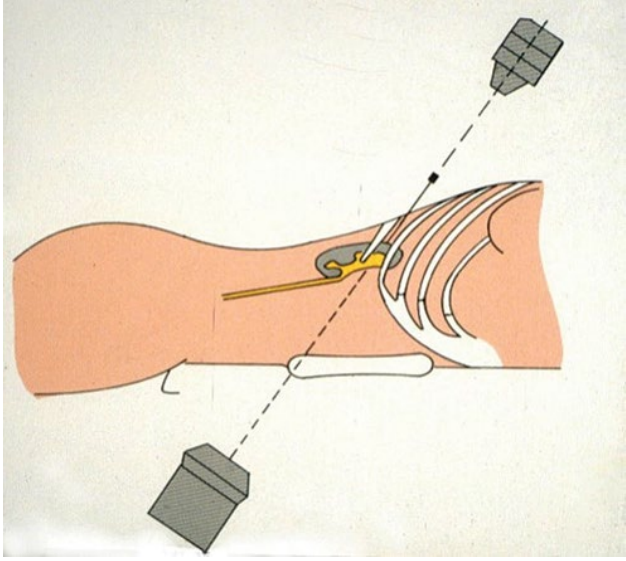

**Figure 25.7** The nephrostomy tract should be placed in line with the axis of the kidney and the path of the infundibulum, where possible. This means that the C-arm should be angled "down" to the upper pole when puncturing with the bullseye technique.

tube is essential for identifying any residual stone fragments. This practice is supported by the AUA guidelines (strong recommendation, evidence level grade B) [5, 6].

- At the end of the procedure, the C-arm can be used to perform fluoroscopy of the chest, ruling our hydrothorax or pneumothorax. If noted, a chest tube (or simple chest drain) can then be placed at the conclusion of the procedure, if deemed necessary.

## Complications

Complications of PCNL are not unique to PCNL for staghorn calculi and include bleeding and need for transfusion, perforation of the collecting system, adjacent organ injury, pleural complications (including hydrothorax, pneumothorax, and hemothorax), sepsis, nerve injury, and loss of nephrostomy drainage.

Transfusion rates have traditionally been reported to be as high as 26% [26]. Although recent series quote these to be much lower, at approximately 1–2% [27, 28]. Medications that may affect platelet function or coagulation must be identified and discontinued for an appropriate period prior to surgery. The most important strategy for minimizing bleeding during PCNL is careful planning and appropriate calyceal selection, with good endoscopic technique to avoid excessive torque on the kidney and large collecting system perforations.

Options for management of excessive bleeding during or immediately post PCNL include aborting the procedure and applying manual pressure on tract site, ensuring adequate drainage and access, temporarily clamping the nephrostomy tube, use of a tamponade balloon, administration of FLOSEAL (Baxter Healthcare, Deerfield, IL, USA) to the nephrostomy tract [29], angioembolization, or cryotherapy to the tract [30]. If the bleed is small and self-limited, a period of observation is reasonable.

Small perforations of the collecting system are not uncommon and usually seal within 48 hours with urinary drainage. Larger perforations of the renal pelvis are usually sustained due to over-advancement of rigid dilators, or the access sheath, or perforation during stone fragmentation. These can be managed with nephrostomy drainage for 7–10 days, and completion of a nephrostogram to document lack of extravasation prior to removal.

Adjacent organ injury to the spleen, liver, colon, and duodenum are extremely rare and can be avoided with patient positioning, correct surgical technique, and careful review of anatomical abnormalities on preoperative imaging. Lumbar nerve damage from too medial an access can also be sustained during PCNL, although this is exceedingly rare.

Intrathoracic complications have been reported at 1–3% [31, 32], and are substantially higher for supra-11th rib punctures. They can be managed conservatively, if small, or may require external tube drainage.

Urosepsis is not an uncommon complication of PCNL, particularly for struvite calculi. Should purulent urine be encountered during endoscopic intervention, the procedure should be aborted, and appropriate drainage and antibiotic therapy should be initiated [5, 6]. To mitigate risks, preoperative urine cultures should be obtained in all patients, and sensitivity-based treatment initiated in those with positive results. Studies have shown that antibiotic prophylaxis in patients undergoing non-extracorporeal shock-wave lithotripsy (ESWL) stone manipulation procedures reduces the risk of postprocedural UTI [32–34]. Periprocedural antibiotics should, therefore, be used in all patients undergoing PCNL. The choice of specific agent should be based, in part, on the local epidemiology of drug resistance in potential uropathogens [33]. Lastly, stone cultures, performed at the time of PCNL, can often better guide the choice of antibiotic post operatively, particularly in symptomatic patients with negative or mixed-growth urine cultures.

## Management of residual calculi

Akman and colleagues demonstrated that >60% of patients with residual stones after PCNL require second intervention [35]. Options for treatment of residual calculi include: SWL, ureteroscopy, repeat PCNL, or observation. Mechanical percussion and inversion is a good nonsurgical option for eliminating lower calyceal fragments, and has been shown to have a substantially higher stone-free rate than observation, with no adverse events [36].

## Conclusions

PCNL for staghorn calculi can be technically challenging, even in the hands of experienced surgeons. Careful preoperative workup and detailed and thoughtful review of preoperative and intraoperative imaging are essential components of successful PCNL. Although numerous innovations to the surgical technique and tools have been introduced, surgeon experience remains of paramount importance, particularly in the performance of complex percutaneous nephrolithotomy.

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# 26

# Percutaneous Nephrolithotomy: Stone Extraction and Lithotripsy

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## Introduction

Intracorporeal lithotripsy involves the fragmentation and extraction of stone fragments during percutaneous nephrolithotomy (PCNL), cystolitholopaxy, and ureteroscopy. The diversity of stone location, size, and composition necessitates the employment of an armamentarium of both nimble and powerful lithotripters.

In complex stone cases, it is reasonable for a surgeon to use a variety of lithotripter devices to effectively clear a patient's stone burden, and therefore it is critical he or she is aware of the strengths and weaknesses of each device. There are four main varieties of lithotripters available for clinical practice: electrohydraulic lithotripsy (EHL), laser lithotripsy, ultrasonic, and pneumatic or ballistic lithotripsy. In this chapter, we discuss the mechanics and surgical technique necessary for the proper use of these instruments and review their specific advantages and disadvantages.

## Electrohydraulic lithotripsy

EHL was the first method designed for intracorporeal use. It was invented at the University of Kiev in 1955 by an engineer named Yutkin [1]. In 1985, EHL was applied to the treatment of ureteral stones after a 5 Fr probe was developed. The modality was deemed safe, as in the initial evaluation of the device there were no long-term complications noted [2]. Later improvements encompassed the development of even finer, even more flexible equipment that could be used in flexible ureteroscopy, first reported in 1988 [3].

### Mechanism of action

The working component of the EHL probe comprises a pair of concentric electrodes maintained at different voltages and separated by an insulating layer. When a current is applied that is strong enough to overcome the insulating gap between the electrodes, an electric spark is created, just like in a spark plug. With the spark procurement, a plasma channel is formed that vaporizes the water around the electrode. The explosive expansion of the plasma creates a hydraulic shock wave that then leads to the formation of a cavitation bubble (Figure 26.1). At a distance of approximately 1 mm from the surface of the stone, the cavitation bubble collapses in a symmetric fashion causing a secondary shock wave that assists in stone fragmentation. A third shock wave develops from the rebound of the cavitation bubble [4, 5].

In intracorporeal use of EHL, in contrast to extracorporeal shock-wave lithotripsy (ESWL), the shock wave is not focused; therefore, the stone must be placed directly in the path of the shock wave that is generated. Concerns over probe safety and the use of the appropriate settings have been closely examined. The original larger probes (9 Fr) have been replaced by probes smaller than 5 Fr. Although the larger ones are more durable, the smaller probes are no less efficient at fragmenting stones and have the additional advantage of flexibility [6].

### Technique

In ureteroscopic procedures, smaller probes measuring 1.6–1.9 Fr are used. Optimally, the probe should be extended at a distance of 2–5 mm from the distal tip of the endoscope. This protects the optics of the scope from damage during probe use. The targeted stone should be clearly visible before it is engaged. The probe is positioned 1 mm from the stone surface to maximize the shock-wave energy transmission to the stone. Energy settings should begin with low voltages between 50 and 60 V and titrated up as needed to fragment the stone. The stone fragments should be small enough to be

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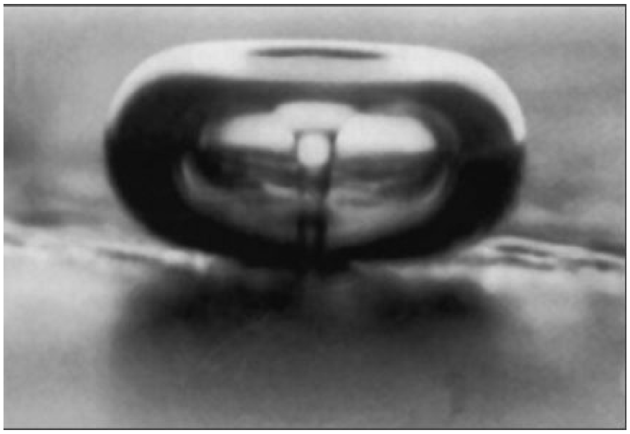

**Figure 26.1** Photograph of liquid microjet produced by an asymmetrically collapsing cavitation bubble. *Source:* Matlaga BR and Lingeman JE. *Campbell Walsh Urology*, 10e, 1382–1386. London: Elsevier, 2012. Reproduced with permission of Elsevier.

retrieved with a grasper or basket device. Pulverization of the fragments to a size less than 2 mm is not recommended, as it can cause unintended damage to the surrounding urothelium [7].

### Advantages and disadvantages

EHL is shown to effectively fragment about 90% of ureteral stones [8]. In a series involving 207 renal and ureteral stones treated with EHL, 90.3% of stones were successfully fragmented and 82.1% of patients were stone free at 20 months follow-up. The characteristics of the stone surface strongly contribute to the efficacy of EHL fragmentation; rough stone surfaces fragment more easily than smooth ones [9]. It has also been suggested that EHL is less efficient in fragmenting uric acid stones compared to calcium oxalate monohydrate varieties [10]. These stone-free rates are in fact inferior to those of other lithotripters. In stones larger than 1.5 cm, Techman [11] reports stone clearance rates of 67% using EHL, a figure significantly higher than that for the holmium:YAG lithotripter.

Like the holmium:YAG laser, EHL is incredibly flexible. The 1.9 Fr probe can be utilized throughout the upper urinary tract with either rigid or flexible ureteroscopy. It has been suggested that the 1.6 Fr EHL probe is even more flexible than a 200 μm laser fiber [12]. The holmium:YAG laser is the only probe that offers a comparable size and flexibility advantage [13].

In terms of cost, EHL is also the cheapest lithotripter available. The cost of a generator is approximately US$1200 and each disposable probe is US$200 [14]. Usually one or two probes are used in each case, unless a harder stone (e.g. calcium oxalate monohydrate) is encountered.

A major concern with the use of an EHL probe is the damage it may cause to the collecting system. Because, unlike in ESWL, the energy generated by the probe is not focused, the cavitation bubble, can expand and perforate the ureter or renal pelvis. When energy levels greater than 1300 mJ are used, the cavitation bubble expands to over 1.5 cm and places the system at a higher risk of perforation. Thus, when treating a harder stone the risk of perforation is greater. Moreover, given that the expanded cavitation bubble is the inciting event causing injury, the probe need not be in direct contact with the tissue to cause damage [4]. Using a rabbit model, Bhatta et al. reported that an unshielded EHL probe can perforate the bladder with just two pulses of direct contact with the tissue, compared to the six needed by a laser [15]. Even the use of smaller probes carries a risk of perforation. *In vitro* models suggest that placing a 3 Fr probe 0.5 cm from a ureteral wall will induce perforation after an average of 24 pulses from an EHL probe [16]. In clinical practice, the incidence of perforation ranges from 2.9% [10] to 17.6% [17]. Risk factors that increase the likelihood of perforation include stone impaction and poor visualization caused by mucosal edema or hemorrhage [17].

An additional concern with the EHL probe is the extent of retrograde propulsion of stone fragments it causes. Yang and Hong [18] noted in their series of 43 patients with a single mid or proximal ureteral stone that 14% of patients initially treated with an EHL probe required a secondary ESWL to manage stone fragments that were scattered in the kidney. Moreover, the EHL probe tends to fracture stone into larger fragments, especially those greater than 15 mm in size, requiring additional manipulation and travel up and down the ureter [11].

## Laser lithotripsy

Lasers are devices that emit light through stimulated emission of electromagnetic radiation using optical amplification. The term “laser” is itself an acronym for light amplification by stimulated emission of radiation. The energy from a laser is formed when an energy source stimulates an atom. Its electrons are then elevated to an excited metastable orbit. When the electrons relax and return to their natural states, they emit energy in the form of a photon, a discrete amount of light energy. Unlike other devices that emit natural light, lasers uniquely emit photons that are monochromatic (all of the same wavelength), coherent (all in the same phase), and collimated (travelling in courses parallel to one another) [19]. These properties of laser light allow it deliver significant amount of energy in a very concentrated manner.

Different varieties of lasers are named based on the substance that is excited to produce the focused light energy. The coumarin laser was the first clinically utilized pulsed dye laser, employing green coumarin dye as the liquid laser medium [20]. The laser has a reported 80–95% rate of success in fragmenting stones [21]. Despite the major advancement this laser provided, there were drawbacks to the device. First, coumarin is an extremely toxic agent and required careful handling and disposal. Second, the laser was much less effective in fragmenting hard, dense stones, namely calcium oxalate monohydrate and cysteine varieties, limiting its applicability and efficacy. Third, the device and its disposable parts impose a significant upfront cost [21].

### Holmium:YAG laser

The holmium:YAG laser is a modern, widely used iteration of the laser lithotrite and is based on a solid-state laser system that improves on the deficiencies of the pulsed dye laser. The device emits light at a wavelength of 2140 nm and exhibits a pulse duration of 250–350 μs, much longer than the short pulsed dye lasers. This laser's mechanism of action in stone fragmentation appears to be mainly thermal. The laser energy superheats the water and forms a microscopic cavitation bubble at the end of the fiber that then implodes rapidly, creating the shock wave that fragments the stone [22]. The holmium laser energy is also highly absorbed by water, and as a result much of it diffuses into the surrounding tissue. This provides a superficial narrow range for resection or ablation of 0.5–1 mm [23]. As a result, accurate placement of the fiber onto the stone is the predominant method of avoiding urothelial injury. With this system, all stones are fragmented with a success rate of approximately 90% [24].

### Technique

When operating the holmium laser, the fiber should be placed directly on the stone surface before the laser is engaged. The target stone should always be kept under direct vision to minimize the risk of perforation or injury to the collecting system. The laser causes minute stone fragments and debris to develop, obstructing the visual field. Care should be taken to irrigate gently during the lithotripsy process as the flow of fluid can displace the stone, moving it out of reach of the laser [25]. In addition, aiming the laser at either a wire or basket device should be avoided. The holmium laser can easily cut metal, creating iatrogenic debris [26, 27]. The fiber should be extended about 2 mm from the tip of the endoscope in order to prevent damage to the lens, optical system, or working channel of the endoscope. For maximally efficient stone fragmentation, the surgeon should aim to vaporize the stone. To achieve this, the fiber is swept over the broad leading edge of the stone as if painting it. Attempts should be made to avoid drilling deep into the stone as this causes fracturing. In addition, drilling increases the risk of fracturing the tip of the laser as well as unwittingly drilling past the stone and damaging the urothelium [28].

The holmium laser is available in four different sizes: 200, 365, 500, and 1000 μm diameters. The fibers can be either end-firing or side-firing, and only the smaller two sizes, 200 and 365 μm fibers, are pliable enough to used in flexible ureteroscopy. Most commonly, the end-firing fibers are used; they are the standard when performing ureteroscopic lithotripsy. The efficiency with which the holmium laser fragments stones corresponds with the energy density produced, a factor reliant on the pulse energy and the fiber diameter [29]. Energy density correlates inversely with laser fiber diameter: the smaller the fiber, the greater the energy density produced [30]. At the beginning of stone fragmentation, a low pulse energy (i.e. 0.6 J) and pulse rate (6 Hz) are recommended to decrease the amount of stone retropulsion and to maximize the margin of safety of the lithotripter. Increasing the pulse frequency (max 15 Hz) is preferable to increasing the pulse energy (max 1.2 J) when aiming to increase the speed of fragmentation [31].

### Advantages and disadvantages

The benefits of the holmium laser are centered on its safety, efficacy, and versatility. Holium laser energy is quickly dispersed in water, limiting its depth of penetration to ~1 mm [32, 33]. The holmium laser can be active 0.5 mm from the ureteral wall with minimal adverse effects. In a porcine mode, the holmium laser was unable to perforate the collecting system when held 2 mm from the ureteral wall, even at the highest power settings [16]. In direct contact with tissue, however, the holmium laser can cause damage. In one study, it was found that just 2 seconds of targeted contact of the holmium laser with ureteral tissue was enough to cause perforation [23].

The holmium laser is also able to fragment stones regardless of their composition, with success rates ranging from 91% to 100% and stone-free rates following ureteroscopy reported from 87% to 100% [34–40]. The success rates with use of the holmium laser depend on the location of the calculus within the collecting system. In a series of 598 patients with an overall success rate of 97% with laser use, location of the stone within the renal, proximal, middle, or distal ureteral segments yielded stone-free rates of 84%, 97%, 100%, and 98%, respectively [40]. The holmium laser can be employed in both regtrograde and anterograde approaches to calculi. Success rates in PCNL after a single-stage procedure have ranged from

61.4% to 89% [41–43]. Malik et al. have reported that in treating a single 2.5 cm stone via PCNL, the holmium laser provided complication and stone-free rates comparable to those from a pneumatic LithoClast. However, the operative time was significantly longer in patients treated with the laser [44].

Further benefits of the holmium laser are its production of smaller stone fragments as compared to other lithotripters. The finer debris is easily irrigated out of the collection system, thereby reducing the need to manually extract residual fragments with graspers or a basket [45]. Among the different laser fiber sizes, the 200 μm causes the least amount of retropulsion [46].

Disadvantages of the holmium laser include its initial high upfront cost. This is mitigated by its versatility in treating not just stones but a variety of other urologic conditions, which helps offset the initial cost of the device. In addition, the larger 365 and 500 μm fibers exhibit a non-negligible degree of retropulsion [41]. Currently the smallest fibers inhibit the deflection of a flexible ureteroscope by about 20°. Smaller or more pliable alternatives would improve the ability to optimally reach and fragment stones in calyces difficult to traverse. In addition, if the fiber breaks within the working channel, the scope is completely damaged and cannot be salvaged. Increased durability of the fibers may reduce the incidence of these events. Moreover, a theoretical concern of using the holmium laser fiber to treat uric acid stones is the production of cyanide that could cause toxicity. Currently there is no evidence to suggest from clinical experience that the holmium laser is a source of cyanide toxicity [45].

## Ballistic lithotripsy

The first ballistic lithotrite was a Swiss device introduced in the early 1990s named the "LithoClast." This device uses compressed air to propel a metal projectile that is central to its fragmentation mechanism [47]. In contrast, the electric-powered electrokinetic lithotripter houses an electric coil that generates an electromagnetic field that vibrates the probe. Both probes are effective and safe lithotrites with no difference in fragmentation, retropulsion rates, or safety [48, 49].

### Mechanism of action

Ballistic lithotripsy uses the harnessed energy from the motion of a projectile that comes into contact with another object, transferring its ballistic energy. The stimulation of the projectile initially can come from a variety of sources, and once the ballistic energy is transferred from the projectile to a probe, that energy is in turn transferred to the other object with which the lithotripter is in contact, like a jackhammer (Figure 26.2). Objects that receive the probe's energy that are flexible, such as tissue, absorb the momentum, whereas rigid objects that are targeted, such as a stone, are fragmented. The metal projectile in the LithoClast is propelled at a rate of 12 cycles every second, caused by controlled blasts of compressed air at 3 atm [50]. In contrast, the electrokinetic lithotripter operates at a higher frequency of 15–30 cycles per second through stimulation by the generator's electromagnetic field [48].

### Technique

Like all lithotripters, the ballistic probe should be engaged only when both the probe and the stone are in clear view. The probe should be brought into direct contact with the stone before using the pedal to activate the device. Optimally, the stone should be placed in a location where it is not able to move. This is not a challenge in the kidney or the bladder but is more difficult in the ureter. The stones may be fixed with a basket or occlusion balloon if necessary. The end-goal with this device should be to break the stone into fragments <2 mm and small enough to pass spontaneously. Realistically, however, using ballistic probes, larger fragments are generated that will require manual extraction with a basket or graspers.

### Advantages and disadvantages

Ballistic lithotrites are effective in fragmenting urinary stones and exhibit a wide margin of safety. Successful

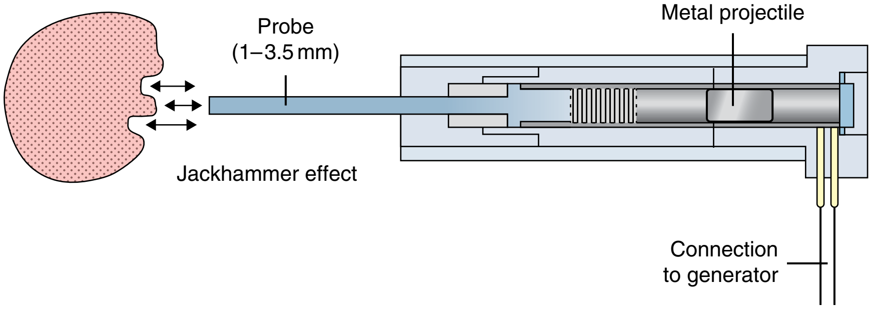

**Figure 26.2** Schematic illustration of a ballistic lithotripter hand-piece mechanism. An oscillating pellet provides ballistic energy to the probe, resulting in a jackhammer-like effect on calculi. *Source:* Matlaga BR and Lingeman JE. *Campbell Walsh Urology*, 10e, 1382–1386. London: Elsevier, 2012. Reproduced with permission of Elsevier.

fragmentation is reported to be between 73% and 100%, a rate that is comparable to that for EHL probes [17, 51–56]. The reported rates of lower efficacy are from studies that have identified deficiencies in the LithoClast that compromise its performance. Knispel et al. [53] noted that when the probe is exercised out of a working channel of a semirigid 6.9 Fr ureteroscope, performance is compromised. These findings are echoed by Zhu et al. [57] who found that the 0.89 mm flexible probe in a flexible ureteroscope was deflected more than 24°. In addition, bowing of the probe is found to reduce the power in ballistic devices [58]. The areas in which ballistic lithotripters are most effective are those in which the stone can be cornered by a rigid device, lending itself better to PCNL and cystolitholapaxy. In these procedure, the stone burden is greater and there is potential to encounter very hard stones, both characteristics that ballistic lithotripters are optimally designed to address. In contrast, it would be disadvantageous to use ballistic lithotripters for ureteral stones or renal stones approached in a retrograde fashion. In these locations and procedures, other modalities provide superior stone fragmentation and clearance rates [59].

Compared to other lithotripters, ballistic devices carry a low risk of perforation. In animal model studies, the ballistic probe was compared to EHL, ultrasonic, and laser lithotripters. Results of these trial revealed that despite direct contact of the probes with bladder and ureteral tissue, ballistic and ultrasound probes did not cause any perforation. On examining the histology of the tissues, it was noted that the LithoClast at most caused partial abrasions of the urothelium [60]. These findings are corroborated by Santa-Cruz et al. who showed that despite 6 minutes of direct continuous contact of a ballistic probe to porcine tissue, no ureteral perforation was noted [16].

From a cost perspective, ballistic probes are an economical option. Although the upfront cost of a generator at around US$30,000 is high, the probe itself costs only US$150 and is reusable [17].

The disadvantages of ballistic lithotrites include the requirement of a straight working channel to be effective. The technology works best in a rigid-probe model, meaning that, as previously stated, its use is limited in flexible endoscopy. These devices are also prone to inducing high rates of stone retropulsion of around 17%, especially in ureteral stones. This is in part attributed to the difficulty in trapping a stone in the ureter [50]. Retropulsion is also propagated because ballistic probes are solid probes that lack a suction channel. The newer LithoVac accompanying suction device works to mitigate that problem. It provides suction to facilitate the evacuation of small <2 mm fragments during lithotripsy when the probe is in place. When the LithoClast is removed from the channel, fragments as large as 3.5 mm can be evacuated as well [61]. Reports on using an 0.8 mm ballistic lithotripter through a 4.8 Fr hollow LithoVac device in a series of 21 patients gave a 95% stone-free rate at three month follow-up. In addition, observationally, the LithoVac was helpful in reducing stone migration and maintaining good visualization [52].

Ballistic lithotripters also usually produce fragments that are larger than 4 mm. Residual stones of this size are large enough to cause obstruction if left untreated [45]. However, fragmenting stones to sizes smaller than 4 mm is a distinct challenge with ballistic probes, especially within the ureter. As a result, additional manipulation is required, such as fetching fragments with a basket or grasper, to reduce the rate of repeat ureteroscopy after the initial procedure [62].

## Ultrasonic lithotripsy

The use of ultrasound vibrational energy to break renal calculi dates back to 1953 when the technique was described by Mulvaney [63]. Ultrasound employs acoustic waves of a frequency above the 20 kHz threshold, which is audible to the human ear. Since the 1950s the technology has matured to become a common and effective and safe means of lithotripsy, especially in treating intrarenal stones in PCNL.

### Mechanism of action

An electric current is used to excite a piezoceramic plate within the ultrasound transducer, causing it to resonate at a certain frequency between 23 and 25 kHz [64]. The vibrational energy of the transducer is transmitted to a hollow steel probe which in turn vibrates longitudinally and transversely (Figure 26.3). With the probe in direct contact with the stone, it stimulates the stone to resonate at a high frequency and fragment. When the probe is directed on the compliant tissues of the collecting system, minimal damage is sustained because tissue does not resonate [1]. The ultrasound probe is also connected to a suction device that is engaged intermittently only when the lithotripter is activated. The pressure is maintained between 60 and 80 cm $H_2O$ to optimize visualization, removal of debris, and irrigation.

The compositions and physical characteristics of stones have an effect of the ability of ultrasound to fragment them. Some stones, particularly harder ones such as calcium oxalate monohydrate, cysteine, and uric acid stones, are more difficult to fragment. However, the the size and surface characteristics of the stone appear to have a greater impact on the efficiency of fragmentation. Smaller, rougher stones are more rapidly fragmented, whereas smooth, larger ones pose more of a challenge [64, 65].

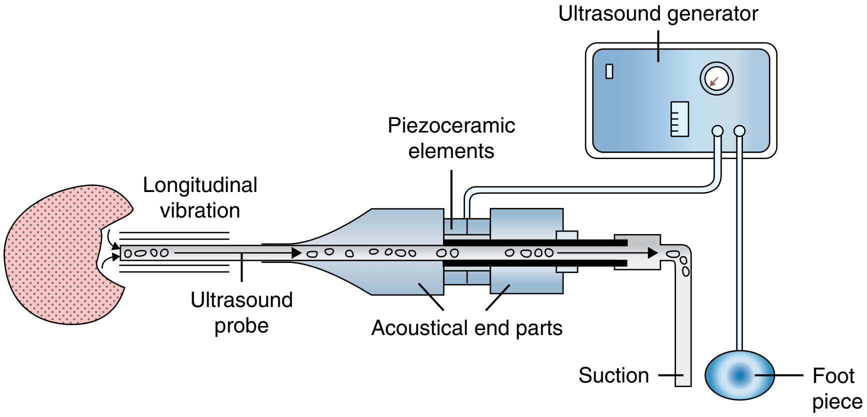

**Figure 26.3** Ultrasound lithotripsy generator and hand-piece. *Source:* Matlaga BR and Lingeman JE. *Campbell Walsh Urology*, 10e, 1382–1386. London: Elsevier, 2012. Reproduced with permission of Elsevier.

The probes are manufactured in sizes ranging from 2.5 Fr to 12 Fr. The larger probes contain a hollow channel through which suction is applied, while the smaller probes (2.5 Fr) are solid and therefore lack suction capabilities. The presence of the hollow channel is a major advantage for the probe. Moreover, the probes are rigid, and if they are torqued or bent during use, the most convex point is a source of energy loss as the vibrations are transformed to heat [65].

### Technique

In PCNL the stone should be pinned against the urothelium. Gentle pressure should be applied while the device is engaged to enhance fragmentation. The surgeons should, however, be mindful to refrain from the use of excessive force as there is a risk of pushing the stone or its fragments through the urothelium. Given the rigid nature of the ultrasound probes ultrasonic lithotripsy appears to be most effective in treating distal ureteral stones. Success rates for ultrasonic lithotripters in addressing proximal, middle, and distal ureteral stones have been reported at 91%, 94%, and 98%, respectively [66]. In ureteroscopic access, the ureter may also need to be dilated to allow the rigid ureteroscope to pass without difficulty. As with other lithotripters, the goal when using the ultrasound lithotripter is to pulverize the stone into small, manageable fragments that can pass spontaneously or be manually extracted during the procedure.

### Advantages and disadvantages

With larger caliber ultrasonic probes, a major advantage is the ability to fragment and remove the stone in tandem. In addition, studies have repeatedly shown that the percutaneous ultrasound treatment of renal stones is effective, with success rates of 84–100% [67, 68]. When the newest iteration of ultrasonic probe, the UreTron® (Med-Sonics, Erie, PA, USA), was compared with competing dual-probe combination lithotripters, it was found to be equally effective and more efficient in treating stones >2 cm. The UroTron gave the highest stone clearance rate compared with the alternative lithotripter cohort (51.9 $mm^2$/min vs. 35 $mm^2$/min, $P = 0.02$) without any differences in stone-free or complication rates [69]. Ultrasound probes are also exceedingly safe. Piergiovanni et al. discovered on a porcine model that perforation was not possible when applying ultrasonic probes on bladder and urothelial tissues without pressure [60]. The authors concluded that in terms of perforation, ultrasonic and pneumatic probes are safer than EHL probes and laser lithotripsy.

Once again, it is important to recognize that a disadvantage of this probe is its limited appeal in tackling ureteral stones. The technology can be used in semirigid ureteroscopes, but a relatively large 5 Fr working channel is needed to accommodate a 4.5 Fr hollow probe. In this setting, success rates have varied from 69% to 100% [70, 71]. Ureteroscopically, the best applications may be for large distal stones or in patients with steinstrasse.

## Combination ultrasonic and ballistic lithotripters

It is evident that both ultrasonic and ballistic lithotripsy have their advantages and disadvantages. Ultrasonic probes offer the suction and optimal irrigation to decrease the extent of stone retropulsion and clear debris and small stone fragments, but they are less effective in clearing dense, hard stones such as calcium oxalate monohydrate. Ballistic probes, on the other hand, outshine ultrasonic probes in this respect. They efficiently tackle hard or very large stones [59, 72], yet they lack the effective suction capabilities of their ultrasonic counterparts.

Thus, the LithoClast Ultra (Boston Scientific, Natick, MA, USA), which combines both ultrasonic and ballistic lithotripsy to optimize stone fragmentation and evacuation was developed. The probe has a hand-piece that incorporates control for the two separate units together. When activated together, the probe maximizes stone fragmention and evacuation capabilities. The first clinical test of the LithoClast Ultra by Haupt et al. in 2001 [73] showed that it was effective in removing renal and bladder stones in 15 patients.

Given the numerous lithotripter options, adding a combined device brings into question whether these devices are equally as or more efficacious in clearing stones than the single-mode devices. *In vitro* assessments were needed to determine the veracity of the manufacturers' claims. Kuo et al. [74] developed a hands-free mechanism to test the LithoClast Ultra. The probe is placed in an upright position and secured by the testing system, and a phantom gypsum stone is placed on top of the lithotripter and compressed with a 63.4 g weight. The aim of this study design is to determine the optimal time for the probe to completely penetrate through the cylindrical phantom stone. Results indicated that using a pneumatic frequency of 12 Hz and ultrasonic power of 100% the stone was penetrated in 9 seconds.

Clinically, the combination lithotripters also perform well. One series investigated 20 patients with symptomatic renal stones who were randomized to PCNL with either a combined lithotripter or standard ultrasonic lithotripsy. The combination device was far more efficient in clearing stones compared to the ultrasonic probe (21.1 seconds vs. 43.7 minutes), and exhibited a greater rate of stone clearance (39.5 vs. 16.8 $mm^2$/min) [75]. In another randomized trial with 30 patients, participants were again randomized to PCNL with either a combined lithotripter or ultrasonic lithotripsy. Here results indicated that both type of devices were equally effective in clearing stones in total (46% and 66%, $P = 0.26$), but once the patients were stratified based on stone composition, it became evident that the combined probe was more efficient in fragmenting harder stones [76].

Other examples of combined lithotripters include the CyberWand (Gyrus ACMI, Southborough, MA, USA), which utilizes a dual ultrasonic probe approach with two coaxial probes, one high and the other low frequency. The dual probes have a synergistic effect that improves on the efficiency of the single-probe ultrasonic probe while maintaining the suction and irrigation capabilities of a traditional single-probe ultrasonic device (see Video 26.1). One study utilized the hands-free *in vitro* testing method previously described by Kuo and associates to assess the stone penetration rate of the CyberWand, and determined that this device is able to completely penetrate the stone twice as fast as the LithoClast Ultra [77]. Clinically, however, results have not shown an appreciable advantage with this device. Krambeck et al. [78] performed a randomized trial in which patients were placed in an arm that tested the CyberWand and another using a traditional single ultrasonic probe. Patients with renal stones >2 cm were treated and no significant difference was found between time to clearance (15.8 minutes vs. 14.2 minutes), or stone-free rates (60% vs. 62.5%) after initial surgery when comparing the CyberWand to a single ultrasonic probe, respectively.

## Conclusions

When choosing a lithotripter to optimally manage genitourinary stones, the patient's anatomy, stone location, stone accessibility, and the planned surgical approach should all be considered. The current options provide the urologist with a number of effective probes to manage these stones, but it is incumbent on the surgeon to combine these factors with a deep understanding of the mechanics and knowledge of the strengths and weaknesses of each in deciding which one to use. The holmium laser is widely considered the most versatile, and it is the most extensively employed method for fragmenting stones ureteroendoscopically. Its flexibility and small-diameter fibers allow for stone management within the entire ureter and the intrarenal collecting system. In patients with significant stone burden undergoing PCNL, however, mechanical lithotripters (i.e. ultrasonic, ballistic, and combination devices) are most effective in safely and efficiently clearing large stone burdens. It is important to note that in a single case, multiple different lithotripsy modalities can be used to ensure complete clearance depending on the situation. Finally, combination devices and other new technologies are promising but require further investigation to ensure that they increase the effectiveness of single-probe systems.

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# 27

# Percutaneous Nephrolithotomy in Children

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## Introduction

Rupel and Brown reported on the first pediatric patient having a renal calculus removed via a nephrostomy tract in 1941 [1], but it was not until 1985 that Woodside et al. presented the earliest series of percutaneous nephrolithotomy (PCNL) in children [2]. In this study, seven patients aged 5–18 years old were treated successfully using adult-sized instruments and equipment. Over the years, the development of smaller nephroscopes and instruments, along with advancements in the form of more efficient energy sources, have resulted in PCNL replacing open surgery for treating both adults and children with large stone burdens, with PCNL monotherapy having stone-free rates approaching 90% [3–5]. Most recently (2015) Lee et al. found PCNL in pediatric patients to be safe and efficacious compared to a matched adult cohort, with similar rates of second-look nephroscopy, length of stay, and complications [6]. There was, however, a higher requirement for a second access tract in the pediatric cohort (15.4%) compared to adults (4.52%). The authors postulated that this was because the small access tracts used in the pediatric cohort made it more difficult to clear the stone burden and another tract was necessary in order to accomplish this without placing too much torque on the tract [6]. PCNL has even been performed successfully in children who have had previous PCNL or open pyelolithotomy, with stone-free rates of 79.17% and only 4.2% requiring blood transfusion [7].

### Indications

Although there are no absolute indications for PCNL in children over any other treatment modality by any current consensus, relative indications include a large stone burden (>2 cm) in the upper urinary tract, lower pole stones larger than 1 cm, an anatomic abnormality which impairs drainage and stone clearance, certain metabolic abnormalities such as cystinuria, or known struvite stone composition [8]. Proper diagnosis is essential as staghorn calculi may be confused with nephrocalcinosis, a condition most often managed nonsurgically [9]. The most recent American Urological Association (AUA) guidelines for treatment of stones in children recommend that PCNL and extracorporeal shock-wave lithotripsy (ESWL) are reasonable treatment options for total renal stone burdens larger than 2 cm. They also recommend that a low-dose, noncontrast computed tomography (CT) scan be obtained prior to PCNL (having the patient in the prone position during CT can be helpful for surgical planning). For patients with questionable function of the renal unit with stones, the panel recommends that a functional study such as a DMSA or MAG3 nuclear renal scan be performed to ascertain if alternative treatment (e.g. nephrectomy) is needed [10].

### Risks

PCNL carries many risks, such as failure to remove all stone fragments, bleeding either immediately post operative, requiring blood transfusion, or delayed renal hemorrhage (both of which may require angioembolization), urine leak requiring stent placement, injuries to adjacent organs (most commonly bowel), inadvertent entry into the chest cavity (pneumothorax, hemothorax, urothorax), and sepsis. A preoperative urine culture should be checked two to three weeks prior to surgery and treated if positive. Broad-spectrum intravenous antibiotics should always be given at the time of the procedure even if the cultures are negative. The AUA guidelines also recommend that a complete blood count including platelet count be obtained before PCNL [10].

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## Pediatric concerns

Although PCNL has been shown to be safe and effective in the adult population, it is not as well established in pediatric populations. Historically, urologists were reluctant to perform this operation in children due to the concerns about parenchymal damage and subsequent insults to renal function from the large adult-size instruments. In the early days of PCNL, smaller/pediatric equipment did not exist. Figure 27.1 demonstrates how the smaller body types of children (Figure 27.1a) have less distance from collecting system to skin (along with total body surface area) than adult patients (Figure 27.1b). Major surgical complications such as bleeding and sepsis when there are fewer invasive options, along with increased radiation exposure from prolonged fluoroscopy, are other considerations that make pediatric providers hesitant to perform PCNL. In addition, there is increased potential for hypothermia along with its sequelae (e.g. coagulopathy) and hyponatremia (e.g. seizures, coma) due to prolonged exposure to irrigation. To decrease the risk of hypothermia, warm isotonic solutions should be used for irrigation, along with warming the operating room, proper draping, monitoring of body temperature throughout the case, and limiting operative times to less than 90 minutes. Warm saline should be used for irrigation whenever feasible, although this would have to be switched to warm water or glycine if an electrosurgical procedure is performed, despite the risk of dilutional hyponatremia.

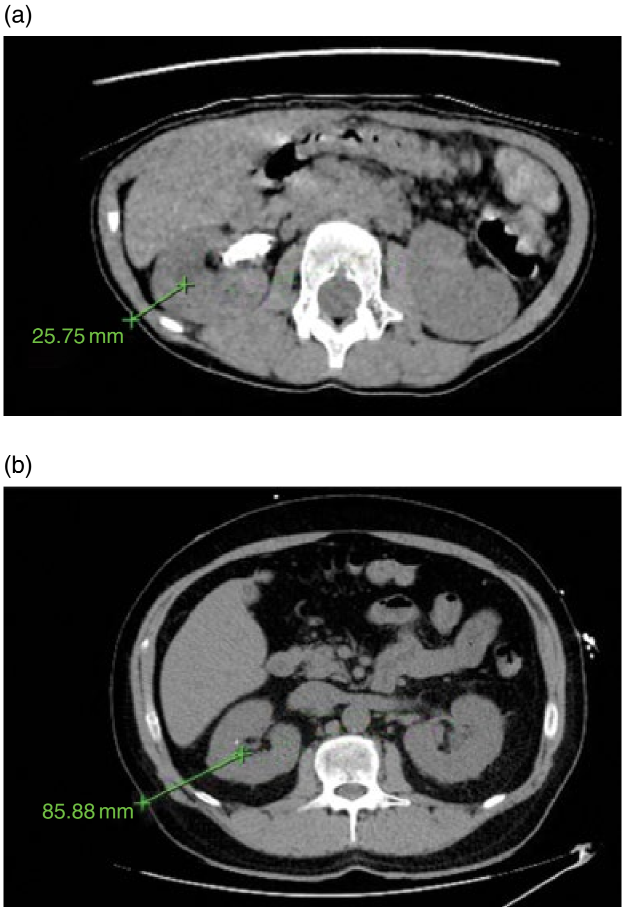


**Figure 27.1** (a) CT scan of a 9-year-old male showing a skin-to-collecting system distance of 2.5 cm, compared to (b) that of a 44-year-old woman with a skin-to-collecting system distance over three times longer (8.5 cm). This demonstrates how the spinal needle should not be inserted as deep during access in younger patients.

## Patient positioning

The procedure is almost always performed under general anesthesia. The patient is first placed in dorsal lithotomy position and an open-ended ureteral catheter is advanced to the level of the proximal ureter (Figure 27.2a). The ureteral catheter size chosen will vary depending on the size of the patient. Figure 27.3 shows the smaller sized ureteral catheters which can be used in children. In the smallest of children, a 3 Fr open-ended catheter is used. The ureteral catheter is left in place with the proximal end within the ureter, and a Foley catheter is placed alongside this for bladder drainage. The patient is then faced prone, with the flank elevated 30° for percutaneous access. Care must be taken to protect and cushion all body parts [11]. If the patient is large enough, they may be placed in the prone position initially with flexible cystoscopy used for ureteral catheterization. This modification obviates the need for repositioning and will aid in decreasing surgical and anesthesia time. Certain patients within the pediatric population who are prone to urinary stone disease offer a special set of challenges in performing PCNL. These patients include those who are wheelchair- or bed-bound, and patients with spina bifida. Patients with spina bifida can have existing spinal hardware which may restrict spinal mobility, impede percutaneous needle placement, and hinder radiographic imaging during the case.

In this patient population, latex-free catheters should be used. Many of these patients may also have limb contractures which makes positioning difficult, and care must be taken to place the extremities in the most comfortable position without excessive flexion and tension on the joints. The risk of pneumothorax is increased with scoliosis, kyphosis, or lordosis due to altered renal anatomy [12]. Patients who are paraplegic or quadriplegic have been shown to have worse outcomes after PCNL, as Danawala and Singh showed, with these patients being three times as likely to suffer a complication from the procedure than nonparaplegic/quadriplegic patients [13].

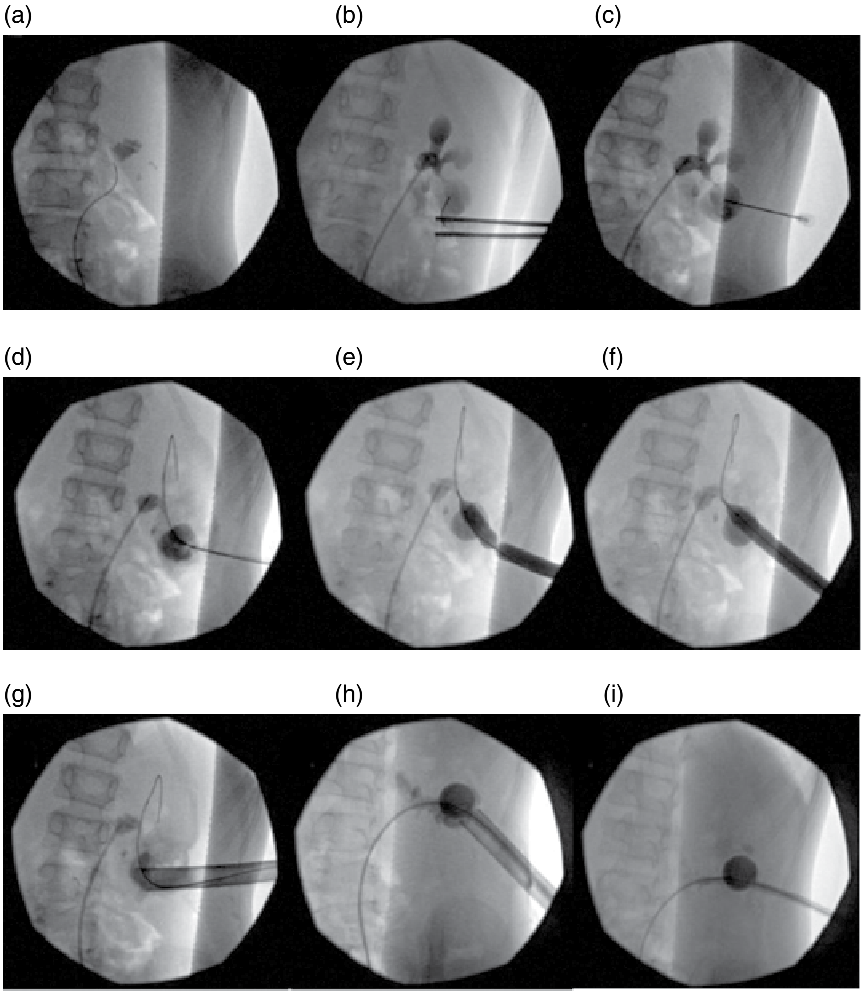


**Figure 27.2** (a) Scout film showing large stone in the renal pelvis with smaller stones in a lower pole calyx, as well as the ureteral catheter after retrograde placement. (b) Lower pole targeted for access after retrograde pyelogram and biplanar fluoroscopy. (c) A 21 gauge spinal needle is inserted with return of clear urine. (d) The guideline is passed through the spinal needle into the collecting system and the tract is serially dilated to 22 Fr. The balloon catheter is then inserted with the distal fluroscopic marker placed into the middle of the lower pole calyx, as shown. (e) The balloon is inflated with waist seen. (f) Continued inflation to 20 atm eliminates the waist. (g) The sheath is placed over the balloon as shown, the guidewire is directed down the ureter into the bladder, and the nephrolithotomy is commenced. (h) A Councill-tip catheter is placed over the wire and balloon inflated to occlude the sheath. Contrast is injected for antegrade nephrostogram demonstrating extravasation and potential injury to the collecting system. (i) A ureteral catheter is placed through the Councill-tip catheter and down the ureter into the bladder while the Councill-tip balloon is placed in the kidney. This is left in place as a nephroureteral stent and secured to the skin. It can be removed later at the bedside after a clamp trial.

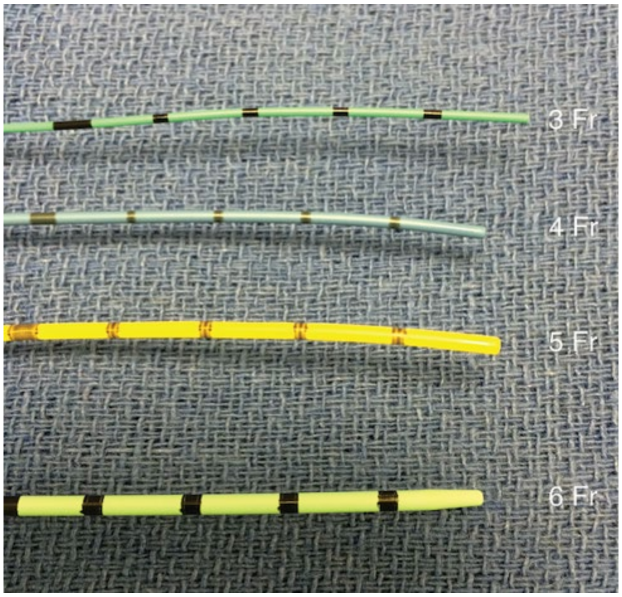


**Figure 27.3** Open-ended ureteral catheters ranging in size from 3 Fr to 6 Fr can be used during pediatric endourology.

Supine PCNL has also been reported, with patients placed in a modified supine position with flexion of the ipsilateral hips and shoulder. Desoky and colleagues were able to achieve stone-free rates of 90.9% with a mean operative time of 65 minutes in 22 children with renal pelvic stones of 2–3 cm [14], while Gamal et al. achieved stone-free rates of 92.5% in 27 children with an operative time of 41 minutes [15]. One patient in each study encountered bleeding that required a blood transfusion.

## Access and tract dilation

A ureteral catheter is placed via the bladder, and is injected with contrast for retrograde pyelography to define the collecting system. Ultrasound guidance can also be used to assist with access to the collecting system, which normally lies in the posterior axillary line. A rotating C-arm is used for biplanar fluoroscopic visualization of the collecting system in the anterior–posterior and oblique positions throughout the procedure. The most optimal tract is determined using the "bullseye" technique (Figure 27.2b). Ideally this would be posterior, and yield direct access, with the shortest distance to the stone, especially when a calyceal diverticulum and/or infundibular stenosis are present. However, for more complex stones or lower pole stones, upper pole access is advantageous as this provides access to both the lower pole calyces, renal pelvis, and ureter [16]. Caution must be taken as this location for access carries increased risk of pneumothorax.

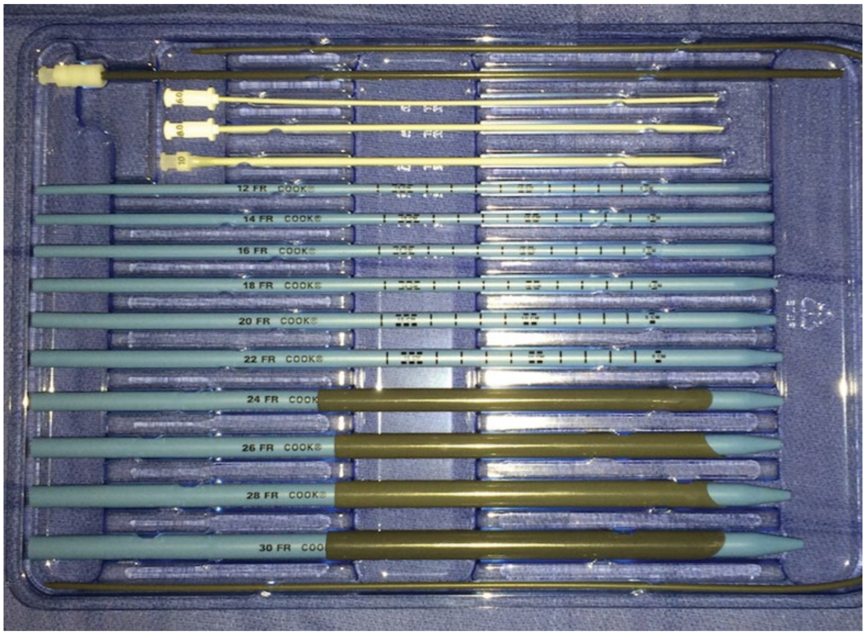
A 21 gauge spinal needle is used to access the desired calyx with return of urine confirming correct placement (Figure 27.2c). A guidewire is passed into the kidney, and through the ureter, and into the bladder. If through and through access is desired, the distal end of the wire in the bladder can be grasped cystoscopically, and brought out through the meatus and placed in a clamp. A small skin incision is made and coaxial dilators (8 then 10 Fr) are placed over the wire into the collecting system, and a super-stiff guidewire is placed and used as the working wire during the procedure. Occasionally, an additional tract may be necessary to perform the procedure, especially if small sheath and nephroscope sizes are utilized, however this is not without additional consequences. Desai et al. found that multiple tracts were associated with lower postoperative hemoglobin decreases and higher transfusion rates [4]. Traditionally, serial dilation has been used with Amplatz dilators (Figure 27.4) over the working wire, followed by a balloon dilator where the distal marker (easily seen on X-ray) is advanced into the calyx (Figure 27.2d). A pressure of about 20 atm should be enough to eliminate the waist seen in the balloon on fluoroscopy (Figures 27.2e,f). The sheath is then advanced over the balloon for simultaneous dilation and tamponade to prevent bleeding and trauma (Figure 27.2 g). Bilen et al. studied different tract sizes (14 Fr, 20 Fr, 24 Fr) utilized during pediatric cases and reported similar efficacy rates in all groups, but there were no transfusions or complications in the 14 Fr group [3]. In our practice, a tract size of up to 30 Fr (same as adult size) can be used with larger teenagers, but in smaller children we dilate to smaller tracts of 20–24 Fr, depending on the size of the child.

## Instrumentation

When PCNL was first used in pediatrics, it was done exclusively using adult-sized instruments and was not performed in children less than 5 years old due to the fear of renal parenchymal damage. It has since been shown that even dilation of the nephrostomy tract up to 30 Fr can be done, and PCNL can be performed consistently and effectively with comparable complication rates, even in very young children less than 5 years of age [3, 5, 17]. Rigid nephroscope sizes used in pediatrics generally range from 10 to 26 Fr (Figure 27.5). Poor visualization and difficulty in the ability to clear larger stone fragments is a downside to using smaller scope sizes. Our preference is to remove the outer 26 Fr sheath of an adult-sized nephroscope (Figure 27.6a) and perform PCNL with just the inner 20 Fr sheath (Figure 27.6b) in children.

After rigid nephroscopy, flexible nephroscopy is usually performed using a 14 Fr flexible cystoscope to inspect

**Figure 27.4** Amplatz straight dilators of sizes 6 Fr to 30 Fr can be used for nephrostomy tract creation. Sheaths in this standard set can be placed over dilators of size 24 Fr or greater.



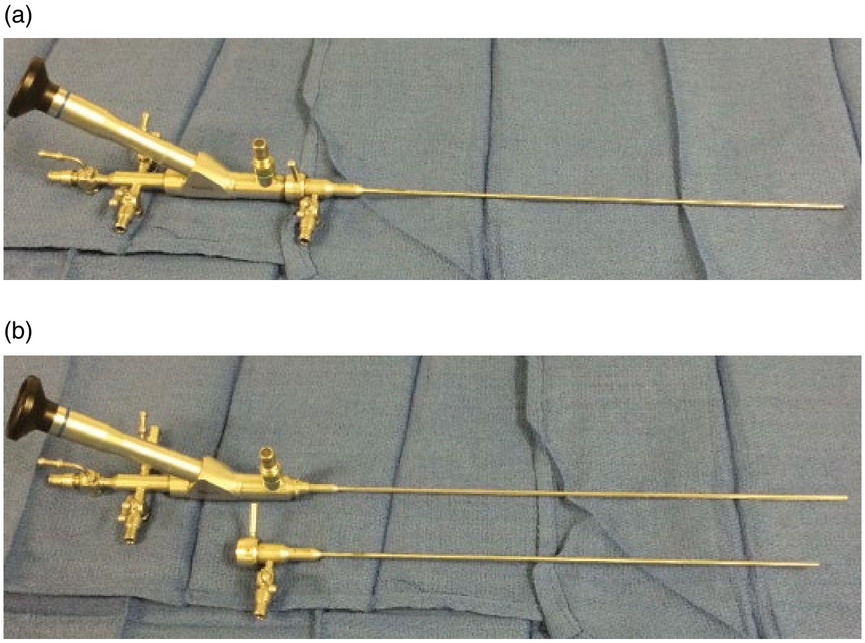


**Figure 27.5** (a) Pediatric nephroscope of size 14 Fr with the outer sheath in place. (b) This can be reduced to 10 Fr after the outer sheath is removed and only the inner sheath is used.

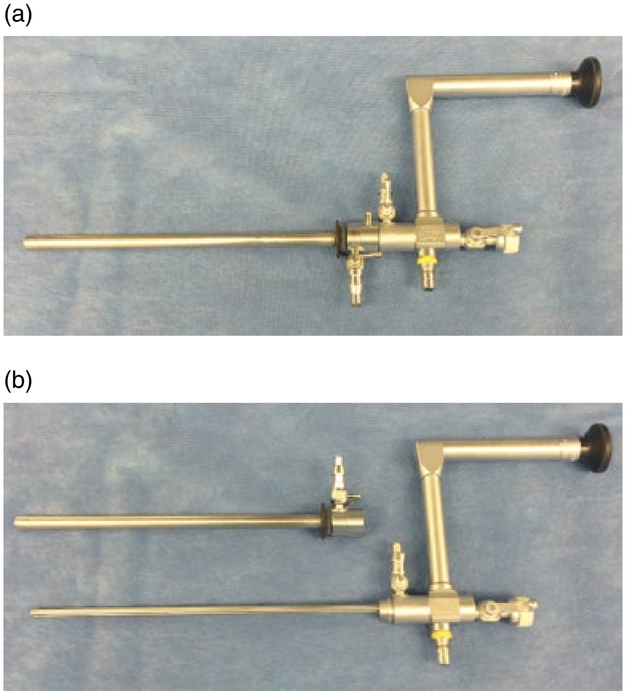


**Figure 27.6** (a) Adult nephroscope of size 26 Fr. (b) The outer sheath can be removed when performing PCNL in children, leaving the inner sheath with a size of 20 Fr. This technique ameliorates the poor visualization and difficult stone removal that occur with pediatric nephroscopes, while still minimizing bleeding from larger tract sizes.

the calyces that may be hard to reach with the rigid scope. Next, ureteroscopy using an 8 Fr flexible ureteroscope may be performed in an antegrade fashion to retrieve any ureteral stones that were pre-existing, or stones that may have dropped into the ureter during PCNL. Mor et al. did not find any evidence of significant scarring nor significant change in differential function on radioisotope scans before and after PCNL in 10 children, and concluded that PCNL performed in children with adult-sized equipment is a safe and efficacious therapeutic option [18]. The larger adult-sized instruments may be more advantageous in children with high-grade hydronephrosis and parenchymal thinning. The larger scopes may help to navigate the larger collecting system, and they may be at less risk of bleeding, as the parenchyma is thinner. Efforts are nevertheless being made in pediatrics to limit unnecessarily large tracts, because they have the theoretic potential for renal damage.

## Mini PCNL

Mini PCNL was first developed by Jackman et al. in 1998, who coined the term “mini-perc” to describe their technique of obtaining access in very young children with large stones. This technique uses an 11–13 Fr peel-away vascular access sheath [19] or a 14 Fr sheath with removable obturator (Figure 27.7) passed over the working wire and through the calyx under fluoroscopic guidance. This system allows instruments to work through the access sheath with enough clearance to allow low-pressure irrigation. The smaller tract sizes afforded with mini PCNL can theoretically improve maneuverability of instruments and decrease blood loss during the case, at the expense of impaired visualization if bleeding does occur. Thus, this technique has been discouraged with larger stone burdens. Large series have shown stone-free rates of 76–91.4% with operative times of 76–109 minutes and

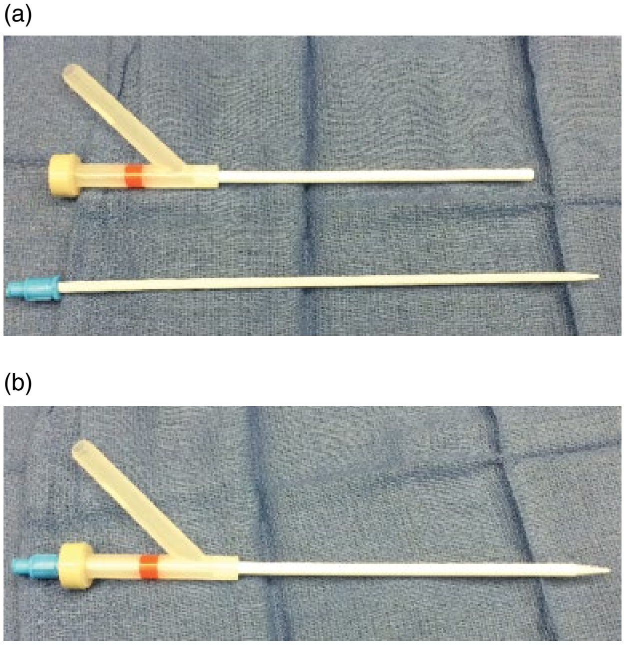


**Figure 27.7** Mini PCNL kit. (a) The set contains a removable obturator and a 14 Fr sheath which can accommodate smaller sized nephroscopes. (b) The obturator is placed through the sheath and subsequently over the guidewire for placement within the nephrostomy tract.

complication rates ranging from 10.6 to 36.3%, with very low rates of high-grade complications according to Clavien classification [20].

Studies comparing standard and mini PCNL in children have shown mini PCNL to have similar stone-free rates with lower hospital length of stay, postoperative pain scores and analgesic requirements, and complication rates, however with longer operative times. Compared to retrograde intrarenal endoscopic surgery, mini PCNL appears to have better stone-free rates, lower operative times, comparable complication rates, but longer hospital stays [21]. Kamal et al. have advocated for the development of equipment that creates even smaller tract sizes for performing PCNL, with sheath diameters reaching as low as <5 Fr ("micro PCNL") [20, 21]. One investigation retrospectively compared PCNL in children using adult (24 Fr), pediatric (18 Fr), and mini (9.5 Fr) nephroscopy, and found stone-free rates of 71.4%, 75.8%, and 78%. The mean hematocrit drop was less in the mini group (0.8) compared to the pediatric (1.7) and adult (1.9) groups as well. Access, total operative time, length of stay, and complication rates did not differ significantly [22].

## Energy sources

Various energy sources can be used for stone fragmentation and retrieval during nephrolithotomy, and there is not much of a difference when performing PCNL in children. Electrohydraulic lithotripsy (EHL) has been studied with 89.8% stone-free rates and a 14% transfusion rate [4]. Salah and associates achieved 98.5% stone-free rates using ultrasonography for fragmentation with only a 0.7% transfusion rate but an 8% rate of urine leak [23]. Holmium laser lithotripsy can be utilized as well, and Bujons et al. reported PCNL to treat staghorn and complex stones using a high-powered holmium:YAG laser in 35 pediatric patients through an 18 Fr tract. Mean stone burden was 4.46 cm, mean operative time was 150 minutes, and in three cases multiple tracts were used. The stone-free rate was 78% after one procedure, and there were two Clavien II complications with no transfusions [24]. Along with fragmentation, stone graspers, baskets, and suction may all be used for stone retrieval. Any residual stones >2 mm should be removed as they can be a nidus for further stone growth and formation.

## Postoperative drainage

At the end of the procedure, an antegrade nephrostogram is performed to identify any residual stones along with assessing for any injuries to the collecting system (Figure 27.2 h). The decision to place a ureteral stent versus a nephrostomy tube are at the discretion of the surgeon and patient. If second-look nephroscopy or a second PCNL is planned, a nephrostomy tube is preferred to allow for direct access to the renal collecting system. A pigtail catheter is useful in children as they are easy to conceal and thus difficult for younger patients to pull on. A clamp trial is performed after two days with subsequent removal if the patient tolerates the clamping without flank pain, nausea, vomiting, fevers, or chills. If an additional percutaneous procedure is not anticipated, a ureteral stent can be placed in an antegrade fashion with cystoscopic removal at a later date in the operating room under moderate sedation (in contrast to adults, in which the stent can simply be removed in the office using flexible cystoscopy with a local anesthetic). Although the data for tubeless PCNL in pediatrics are sparse, one group reported lower pain scores, no intravenous narcotic usage, and shorter hospital stays in 20 children who had undergone tubeless PCNL compared to a matched cohort of children who had PCNL using a tube or stent. One patient with tubeless PCNL had a urine leak [25].

We recommend stenting both the nephrostomy tract and the ureter. A prepackaged nephroureteral stent specifically made for this purpose can be placed. We have found a nephroureteral catheter can be made on the operating table by placing an open-ended ureteral stent through a Councill or Malecot catheter and passing this down the ureter into the bladder while the larger outer catheter's tip is left in the renal pelvis, as both catheters exit from the nephrostomy tract together (Figure 27.2i).

## Staged procedures

In patients with a large stone burden, a staged PCNL may be needed to achieve stone-free status. Typically, the second-look PCNL is done 2–3 days after the initial PCNL during the same hospitalization and through the prior tract. Of note, we do not recommend bilateral procedures to be performed in a single sitting in children. If bilateral stones exist, separate procedures should be done on each kidney at different times to allow for renal recovery after one kidney is addressed surgically. Flexible endoscopy is a useful tool when a second stage is needed, and can be done without using any fluoroscopy. The goal of each procedure should be for the complete removal of all stone fragments. However, in some patients with very large stone burdens, this is sometimes unavoidable [26].

### Sandwich therapy

When additional procedures are needed, the surgeon may elect to utilize "sandwich therapy." This is where ESWL is used following an initial percutaneous procedure to treat any inaccessible stone fragments. Then, if necessary, a second-look PCNL through the prior tract (to remove any residual fragments) can then be performed after the ESWL (which has been "sandwiched" between the two PCNL procedures). This method can be performed during the same or different hospital stays. Mahmud and Zaidi found their stone-free rates after PCNL increase from 60% to 100% after adjuvant ESWL (PCNL + ESWL) was performed. Mean age was 3.8 years and mean stone burden was 2.4 cm [27]. Another large study of 169 children with a mean stone size of 3.1 cm showed stone-free rates increase from 59% to 93.8% after "sandwich therapy" (PCNL + ESWL + PCNL), with a 3.6% transfusion rate [28].

## Complications

Fever in the immediate postoperative period occurs at a rate of 31% and is the most frequent complication after pediatric PCNL, but most often this is transient and non-microbial as the postoperative infection rate is only 6% [3, 20]. However, the high irrigation pressures within the kidney during PCNL along with bacteria that are harbored within the calculi that are released during stone fragmentation place the patient at risk of urosepsis postoperatively. Because of this, all patients are screened preoperatively with a urine culture, and placed on culture-specific antibiotics. An intravenous first-generation cephalosporin such as cefazolin is used during the procedure. Patient should also be covered with antibiotics for the first few days after surgery, and many providers elect to keep patients on prophylaxis until all tubes and stents are removed. There is no consensus on whether or not continuous, daily, low-dose antibiotic prophylaxis is warranted in patients with indwelling or external urinary catheters, but the AUA does recommend a dose of antibiotic be given just prior to stent manipulation or catheter/tube removal to prevent bacterial release from these indwelling structures, which are usually colonized [29]. One prospective randomized study in 95 patients after ureteral stent placement showed no significant differences in rates of symptomatic (10% vs. 9%) and febrile (6% vs. 7%) urinary tract infections for patients, whether or not daily prophylactic antibiotics were used [30]. During surgery, a piece of the stone should be sent for culture, and antibiotic coverage tailored to sensitivities.

If there is an injury to the collecting system and subsequent urine leak (which can be seen as extravasation of contrast on antegrade nephrostogram), prolonged stenting or tube drainage should be employed initially for six weeks. Placement of a perinephric drain may be necessary if a large urinoma develops, and does not resolve with drainage of the collecting system. Injury to the pleural space may occur during attempted access to an upper pole calyx. When suspected, a chest X-ray should be obtained and a chest tube may be required if there is a large pneumothorax, hemothorax, or urothorax.

A drop in hemoglobin requiring transfusion is not uncommon after pediatric PCNL and occurs at rates of 0.4–24%; it occurs more commonly when tract size exceeds 22 Fr [4, 20]. Furosemide is given between units if multiple transfusions are needed. If excessive bleeding is seen in the kidney and nephrostomy tract during the case, a balloon tamponading catheter should be placed through the tract and left in place until bleeding resolves, with a trial of balloon decompression before the tamponade catheter is removed. If the patient requires multiple transfusions, or if the patient presents with delayed bleeding weeks after PCNL, they should be sent for angiographic evaluation for a pseudoaneurysm or arteriovenous fistula. If the source of bleeding is found, superselective vascular embolization can potentially be performed, which is successful in controlling 80% of post-PCNL bleeds [31].

Injuries to adjacent organs vary depending on which organ is harmed and the severity of the damage. If a colonic perforation is diagnosed postoperatively, it is likely retroperitoneal and minimally invasive management can be attempted initially: the nephrostomy tube is withdrawn from the kidney into the colon as a colostomy tube, and an indwelling ureteral stent is inserted.

The patient is placed on bowel rest with total parenteral nutrition. Broad-spectrum intravenous antibiotics including coverage of enteric anaerobic organisms (e.g. with metronidazole) should be employed as well. This may avoid the need for exploratory laparotomy, but general surgical consultation should also be obtained [32].

## Conclusions

PCNL has been shown to be an effective therapeutic option for children with renal calculus disease compared to other modalities. In a large review of over 600 children treated for urolithiasis, PCNL and mini PCNL were found to have superior stone-free rates of 85% and 100%, respectively, compared to ESWL at 68% and ureteroscopy at 66%. Open surgical removal of kidney stones had a higher stone-free rate (94%) than the PCNL group, but the open group also had a threefold higher transfusion rate when compared to PCNL [33]. With further technologic advances, and smaller instruments under development, PCNL will continue to advance as a treatment alternative for children with large stones. Therefore, PCNL can be considered a safe and effective treatment option for large kidney stone burdens in children, even those of a very young age.

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## Part 6 Other Uses of Nephrostomy Access

# 28

# Percutaneous Nephrolithotomy of Calyceal Diverticula, Infundibular Stenosis, and Simple Cysts

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## Introduction

Percutaneous nephrolithotomy (PCNL) is usually performed for large stones, abnormal renal anatomy, and stones not amenable to ureteroscopy (URS) or shockwave lithotripsy (SWL). Advantages of PCNL include superior stone clearance, limited convalescence, and cost-effectiveness [1]. Although major complications are possible, studies have demonstrated overall safety and effectiveness of this technique for complex calculi [2]. Over time, the limits of percutaneous surgery have expanded. In this chapter we review the role of percutaneous surgery in the treatment of three benign conditions: calyceal diverticula, infundibular stenosis with hydrocalyx, and symptomatic renal cysts.

## Calyceal diverticula

A calyceal diverticulum is a congenital, smooth-walled, nonsecretory urothelium-lined cavity that communicates with the main collecting system via a narrow channel. Urine is received by the diverticulum through passive retrograde filling [3, 4]. Calyceal diverticula were first described in 1841 by Rayer [5] and named diverticula by Prather in 1941 [6]. Diverticula occur when small ureteral buds fail to degenerate in 0.21–0.6% of patients, with 3% presenting bilaterally [7–11]. The majority are found in the upper pole (49%) and middle pole (30%) with an average size of 17 mm [3]. Stones occur in 9.5–50% of diverticula [7, 8]. Occasionally, calyceal diverticula can be associated with pain, hematuria, and recurrent urinary tract infections (UTIs) [8, 9]. Complete obstruction of the diverticular neck can lead to sepsis, abscess formation, or hypertension [12].

The cause of diverticular stone formation is controversial. Particle retention due to obstruction and stasis has been proposed, as have underlying metabolic abnormalities in 50–100% of patients [13–18]. Matlaga et al. compared the 24-hour urine studies of calyceal diverticulum patients with calcium oxalate stone formers and normal patients [15]. Although the urinary stone risk parameters of calyceal diverticulum patients were similar to those of the calcium oxalate stone-forming group, urine aspirated directly from the diverticulum of three patients demonstrated significantly lower supersaturation of calcium oxalate compared to urine obtained from the renal pelvis of the same patient, implicating stasis as a contributor to calculi formation.

### Diagnosis

The majority of patients are asymptomatic, with incidental diagnosis on imaging performed for other indications. The differential diagnosis includes renal or parapelvic cysts, hydrocalycosis (hydronephrosis of a calyx) secondary to infundibular stenosis, cystic tumors, and solitary abscess. In appropriate clinical settings, cortical cavitation secondary to renal tuberculosis has similar appearance [12]. In children, calyceal diverticula commonly present with UTIs and association between calyceal diverticulum and vesicoureteral reflux should be ruled out [19, 20].

The workup includes urinalysis, complete blood count, basic metabolic panel, and imaging of the abdomen. A renal ultrasound or noncontrast computed tomography (CT) scan is typically performed. Renal ultrasound will accurately diagnose calyceal diverticulum in 80% of cases [21] (Figure 28.1). The diverticulum without stones will have appearance and echotexture similar to renal cysts. When echogenic material is present, the patient is scanned in different positions to demonstrate gravitational changes of the content, a tell-tale sign of calyceal diverticulum [3]. The classic ultrasound finding of "milk

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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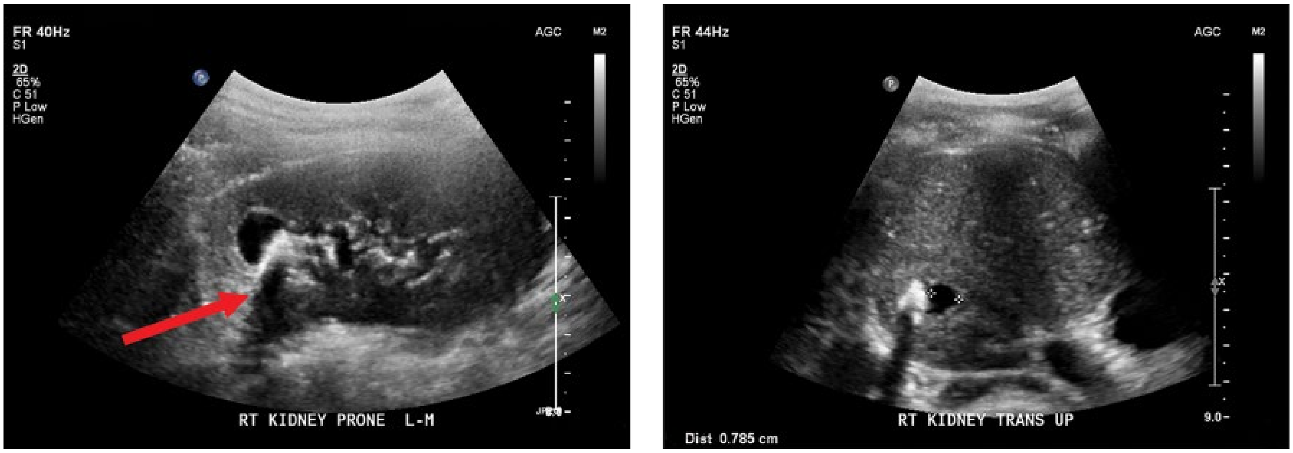

**Figure 28.1** Coronal and axial appearances of calyceal diverticulum on ultrasound. Arrow denotes posterior acoustic shadowing indicating presence of diverticular stone.

of calcium" is a colloidal suspension of precipitated calcium crystals [22]. The milk of calcium will appear as a meniscus-like, semilunar calcification that changes position on upright and lateral decubitus radiographs [23]. Calyceal diverticula are seen on noncontrast CT as a small, round, low-attenuation area adjacent to the calyx or as a dilated outpouching from the collecting system containing a stone [24] (Figure 28.2).

Prior to any treatment, the location of the diverticulum and communication with the rest of the collecting system should be confirmed with a CT urogram or an intravenous pyelogram (IVP). Most calyceal diverticula will opacify if they have a significant communication with the collecting system [8]. Since the diverticulum itself is nonsecretory, the opacification will occur later in the examination as it is filled in a retrograde fashion from the collecting system, necessitating delayed images [3, 25] (Figure 28.3). A retrograde pyelogram can be helpful in locating the neck of the diverticulum. Where the calyceal infundibulum is obstructed, the diverticulum will not opacify with contrast administration and becomes difficult to differentiate from a complex renal cyst. This finding is important for surgical access planning. Notably, the failure to demonstrate the diverticular neck does not detract from the diagnosis [11].

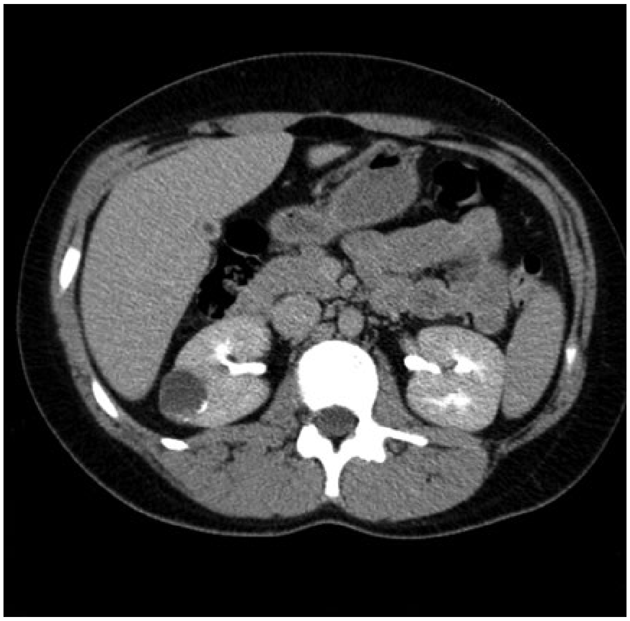

**Figure 28.2** Right kidney calyceal diverticulum with fine stone fragments on CT scan of the abdomen.

## Treatment

Patients with asymptomatic calyceal diverticula do not require treatment. Pain, recurrent UTI, hematuria, symptomatic calculi, or progressive renal damage are indications for intervention [7]. Traditionally, open marsupialization and fulguration of the diverticular cavity or partial nephrectomy were performed. Nowadays minimally invasive options for symptomatic calyceal diverticula include SWL, URS, PCNL, and laparoscopy. Treatment options depend on diverticulum location, stone burden, and size [26].

SWL for the treatment of calyceal diverticula is controversial. Although at short-term follow-up SWL provided symptomatic improvement in 36–70% of patients, stone-free rates were low at 4–20% [27, 28]. The highest reported stone-free rate remains suboptimal at 58% [29]. With longer observation, patients initially rendered symptom-free with SWL will become symptomatic and require retreatment [27]. Thus, SWL is rarely considered as monotherapy for calyceal diverticula. To prevent stone recurrence, eradication of the diverticulum should accompany stone removal, a goal that is

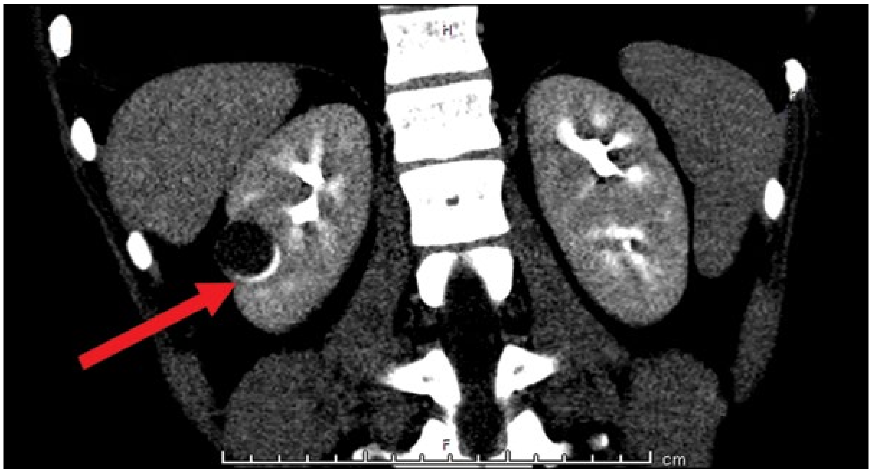

**Figure 28.3** Calyceal diverticulum with classic appearance of semilunar "milk of calcium" deposits on delayed images of CT abdomen.

rarely achieved with SWL [30, 31]. Furthermore, while SWL may be effective in stone fragmentation, the passage of these fragments remains a concern. The narrow diverticular neck that is hypothesized to cause stone formation through stasis in the first place can prevent fragment clearance [3].

Ureteroscopy is more effective at stone clearance than SWL. It is minimally invasive and can allow ablation of the diverticular cavity at the same time. Retrograde URS is a reasonable option for selected patients with a diverticulum in the upper or middle portions of the kidney when the stone burden is small and the diverticular neck is short and easily accessible [3, 30, 32]. Lower pole calyceal diverticula are often at an acute angle that precludes retrograde management. Identification of the diverticular neck can be difficult with a retrograde approach and may account for the lengthy operative times (1.25–4 hours) reported in some URS series [32, 33]. In one series the ostium could not be identified at all in a third of patients [12]. Injection of contrast or methylene blue (with subsequent washout from renal pelvis followed by the slow drainage of the dye from the diverticular ostium) can be useful in identifying the ostium [34]. The diverticular neck is then incised or dilated, allowing stone clearance and cavity ablation with either a holmium:YAG laser or a Bugbee electrode. Stone-free rates for URS range from 19% to 90%, but diverticular obliteration is as low as 18%; furthermore, a significant number of patients demonstrate residual symptoms and require retreatment [31, 33, 35–38]. Bas et al. compared 29 PCNL with 25 URS cases, with similar stone-free rates but higher major complication rates in the PNL group; however the stones in the PNL group were larger [39]. Auge et al. compared 22 cases of PCNL with 17 URS cases and concluded that PCNL was universally better than URS for all stone locations and should be used as a primary modality for calyceal diverticular stones [36].

Laparoscopy is suitable for large anterior diverticula with a thin layer of overlying parenchyma and significant stone burden [40, 41]. Diverticula in ectopic kidneys, where a percutaneous approach will be hampered, are another indication. However, the laparoscopic approach is more invasive than PCNL with lengthy operative times (up to 2.5 hours) even in experienced hands, and should only be considered in select cases [41–43].

Percutaneous treatment of calyceal diverticulum calculi achieves high stone-free rates (87.5–100%) and allows simultaneous obliteration of the diverticular cavity in 76–100% [25, 27, 31, 44–49]. Over 90% of patients report symptomatic relief with percutaneous treatment [27, 36, 44–46, 50], with durable 100% success rates at 38 months follow-up in another study [46]. In a report from Kim et al., operative times were <60 minutes and 20 of 21 patients were sent home tubeless on postoperative day 1 [48]. Typically, percutaneous access is performed directly into the calyceal diverticulum to allow use of a rigid nephroscope as successful treatment of stone-containing diverticulum is contingent on complete stone removal [48]. Direct puncture of a small or upper pole diverticulum can be difficult, requiring puncture of a neighboring calyx. The diverticulum is then entered indirectly by perforating the wall of the diverticulum or by entering in a retrograde fashion through the diverticular neck [51]. However, this "indirect assess" technique has a lower rate of diverticular cavity obliteration (50% vs. 79%) [45, 52]. Finally, percutaneous balloon dilatation of calyceal diverticular infundibula in the absence of stones has also been described [53].

Controversy exists regarding optimal management of the diverticulum following complete stone removal. An existing communication to the collecting system can be dilated and stented or created anew (neoinfundibulotomy), in an effort to promote drainage [27, 38, 45, 47, 50]. Both techniques carry risk of bleeding and require the placement of a nephrostomy tube for a prolonged period to ensure patency. Another treatment strategy is to fulgurate the diverticulum. This can be achieved percutaneously, without ureteral catheterization or infundibular cannulation, with 87.5–100% diverticular ablation rates [46, 48]. Although calyceal diverticulum is lined by a nonsecretory endothelium, most authors advocate fulguration at the time of PCNL [30, 33]. Dilation or incision of the diverticular neck without fulguration results in complete ablation of the diverticulum in only 30% of cases [54], in contrast to the 76–100% ablation rate when fulguration is performed [27, 45, 46, 55]. Others suggest that diverticular wall trauma from the percutaneous dilation process itself is sufficient to ablate the diverticular lumen [44]. If fulguration is to be performed, avoiding infundibular dilation will maximize the chance of diverticular obliteration. Krambeck and Lingeman compared dilation of the infundibular tract with cavity fulguration alone. The “fulguration only” technique had a higher initial stone-free rate (94.2% vs. 77.3%) with shorter length of stay. The diverticulum either disappeared or reduced in size in 89% of patients who had follow-up IVP at three months [56].

## Technique

The procedure is preceded by careful review of imaging to assess the degree of diverticular filling. The percutaneous approach is typically achieved with biplanar fluoroscopy and is thus reliant on visualization of the radiopaque target [57]. If the diverticulum does not fill retrogradely with contrast and/or if the stone is radiolucent, the following steps can be taken. First, contrast can be instilled into the diverticular cavity via a retrograde ureteral catheter (Figure 28.4). Care must be taken to avoid overfill and contrast extravasation, as this makes subsequent fluoroscopic targeting difficult. Second, if the diverticulum does not readily fill with contrast due to stenosed infundibulum, a CT- or ultrasound-guided pre-PCNL opacification of the diverticulum by interventional radiology is an option [25]. A 20G spinal needle is manipulated under radiographic guidance into the diverticulum. Iodinated contrast is gently instilled until resistance is encountered and kidney–ureter–bladder (KUB) imaging is performed to confirm opacification of the target (Figure 28.5). The patient is then transported promptly to the operating room as too long a delay may permit absorption of the contrast and loss of the target. Lastly, ultrasound guidance can be utilized [58]. Unfortunately, it is difficult to monitor guidewire manipulation with ultrasound imaging.

If the target diverticulum is radiopaque, a single-stage procedure is performed where percutaneous access is directed straight onto the stone [48] (Figure 28.6). The patient is anesthetized and positioned prone without an external ureteral catheter. A C-arm is used to visualize the diverticular calculi. When possible, a direct infracostal puncture (to reduce risk of pleural injury) is performed using an 18G diamond-tipped needle and a biplanar fluoroscopic triangulation technique [59]. A 0.035-inch J-tipped movable core guidewire is coiled inside the diverticular cavity, taking care to avoid wall perforation with the stiffer portion of the wire. The flexible distal end of the movable core J-wire can be adapted to the size of the diverticulum, while the wire proximal to the moved core remains stiff enough to function as the

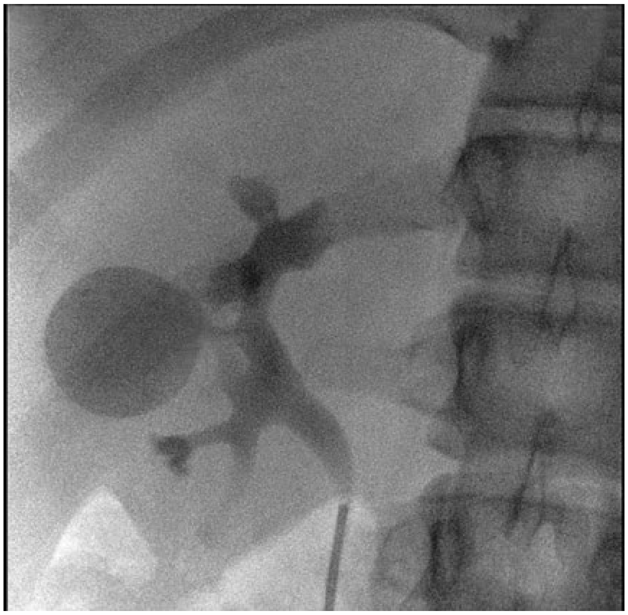

**Figure 28.4** Retrograde pyelogram of a calyceal diverticulum. Contrast instillation allows fluoroscopic targeting for percutaneous access.

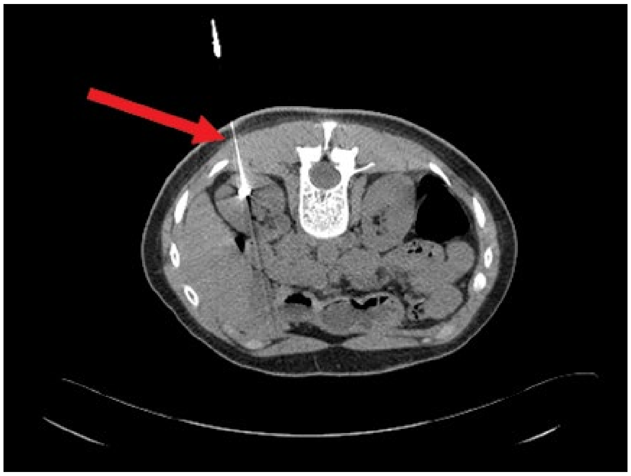

**Figure 28.5** CT-guided contrast instillation to allow fluoroscopic targeting of radiolucent obstructed calyceal diverticulum.

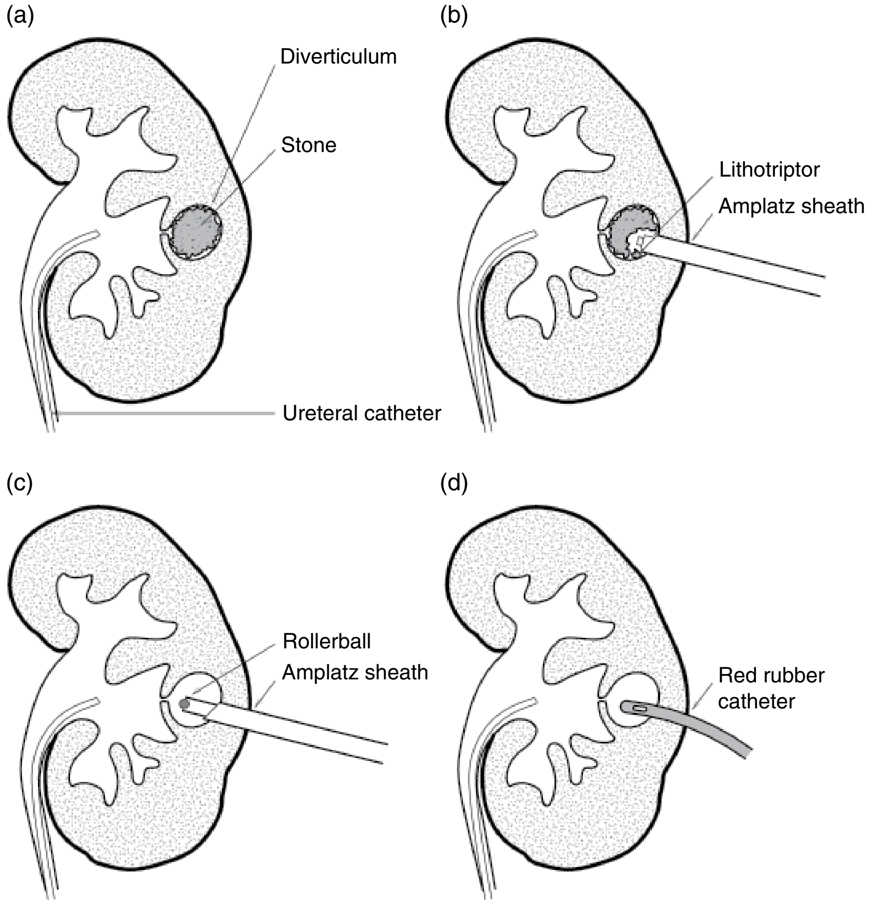

**Figure 28.6** Single-stage percutaneous approach to calyceal diverticulum with stones. (a) Stone in a midpole diverticulum. (b) Placement of Amplatz access sheath and stone clearance using lithotripter. (c) Rollerball electrocautery of diverticular cavity. (d) Red rubber catheter drain placement.

working wire. With the J-wire in place, an 8/10 Fr coaxial dilator is passed over the J-wire in a sequential fashion. The 8 Fr dilator is removed and a second 0.035-inch J-tipped movable core wire is coiled inside the diverticulum and used as the safety wire. The tract is balloon dilated over the working wire, carefully placing the balloon dilator and the wires to avoid perforation of the back wall. A 30 Fr Amplatz sheath is then passed over the balloon dilator under fluoroscopic guidance. The taper on the distal end of the balloon dilator will preclude placement of the sheath directly into the diverticular space unless the diverticulum is large. Next, an offset 24 Fr rigid nephroscope is placed inside the access sheath using normal saline irrigation. Alligator forceps (11 Fr) are used to manually dilate the part of the tract immediately adjacent to the diverticulum, allowing for advancement of the scope and subsequently the sheath into the diverticular lumen. Once inside the diverticulum, ultrasonic lithotripsy or grasping forceps are used to remove the stone burden. Stone culture is obtained by using grasping forceps to transfer a stone fragment directly into the culture cup, where it is ground with a sterile hemostat. After removal of all stone material the entire cavity should be inspected for presence of a flattened renal papilla, indicating an obstructed hydrocalyx rather than a calyceal diverticulum (see Video 28.1).

The irrigant is switched to 1.5% glycine (or sorbitol 2.7% with mannitol 0.54%) to fulgurate the diverticular lining with a resectoscope and a rollerball electrode. Low-energy electrocautery (20 W coagulation, 0 W cut) settings are used. The tip of the rollerball electrode can be bent to aid fulguration of difficult-to-reach areas in the diverticulum or a Bugbee electrode can be used. Fulguration with holmium:YAG laser has also been described [60]. The infundibular communication is neither assessed nor dilated. An 18 Fr red rubber catheter or, in larger cavities, a 10 Fr Cope loop catheter is placed in the cavity. Proper placement of the drainage tube is confirmed by contrast instillation under fluoroscopy. If the diverticulum is small, the red rubber catheter acts as a perinephric drain, as it usually becomes dislodged from the diverticular cavity. The drainage tube can be removed on postoperative day 1 if drainage is minimal. Occasionally, if the communication with the renal collecting system is large, considerable (i.e. >100 ml) drainage from the nephrostomy tube may occur. In this situation the nephrostomy tube is left for one week to allow the tract to mature.

### Potential complications

Complications associated with percutaneous access in general also apply to percutaneous treatment of calyceal diverticula: hemorrhage, retroperitoneal extravasation, pneumothorax, hemothorax, and adjacent organ injury (see Chapters 32–35). Percutaneous access to anterior diverticula has increased bleeding risk due to longer tract distance through renal parenchyma [61]. If infundibular stenosis is misdiagnosed as a calyceal diverticulum and fulguration of a dilated calyx with functioning papillae is performed without infundibular dilation, urinoma with fistula formation can occur. Since only the diverticulum area is treated, we make every effort to place our access site infracostal, thus substantially decreasing the risk of pleural injury and hydrothorax. Use of monopolar electrocautery carries theoretical risk of dilutional hyponatremia, although typically only a short time is spent ablating the diverticular cavity.

Guidewire control is essential, especially with small diverticula. As we do not typically pass guidewires into the main renal collecting system, utmost attention must be paid to keeping the guidewires secure when passing dilators and balloons to avoid loss of access. If serial dilation is performed, a false passage can be created through repetitive insertion and removal of dilators over a poorly secured access wire. If balloon dilation is performed, avoiding advancing the dilator and access sheath too far into the diverticulum will reduce risk of posterior wall perforation and hemorrhage. For small diverticula, we suggest only placing the tip of the balloon dilator into the diverticulum with the access sheath just outside the diverticulum. The remainder of the tract is then manually dilated under direct vision using grasping forceps.

### Posttreatment evaluation

Retrieved stone material is sent for stone analysis. Stone culture specimen is sent as preoperative urine cultures in patients undergoing PCNL have been shown to be unreliable [62]. This stone culture is particularly useful in guiding antibiotic therapy in the rare event of post-PCNL sepsis. Stone-free status is assessed after the procedure with a noncontrast CT scan on postoperative day 1 prior to removal of the drainage tube. Imaging of the collecting system is performed at three months either with CT urogram or an IVP to assess resolution of the calyceal diverticulum. Current literature supports metabolic evaluation for patients with calyceal diverticula calculi as discussed previously.

## Infundibular stenosis

Infundibular stenosis is defined by a dilated calyx draining through a narrowed infundibulum into a nondistended renal pelvis (Figure 28.7). It can be congenital, caused by extrinsic compression (malignancy, retroperitoneal fibrosis) or intrinsic narrowing (infection, stones, iatrogenic injury, or renal surgery) [63–65]. Genitourinary tuberculosis (TB) is the most common cause of infection-induced infundibular stenosis and should be considered in appropriate clinical setting. In children, infundibular stenosis is on the spectrum of pyelocalyceal dysgenesis and can be associated with contralateral multicystic dysplastic kidney in up to 2.5% of patients [66]. Fraley's syndrome, a rare cause, is due to a crossing segmental artery, typically affecting an upper pole calyx [67]. The mechanism is similar to ureteropelvic junction (UPJ) obstruction due to a lower

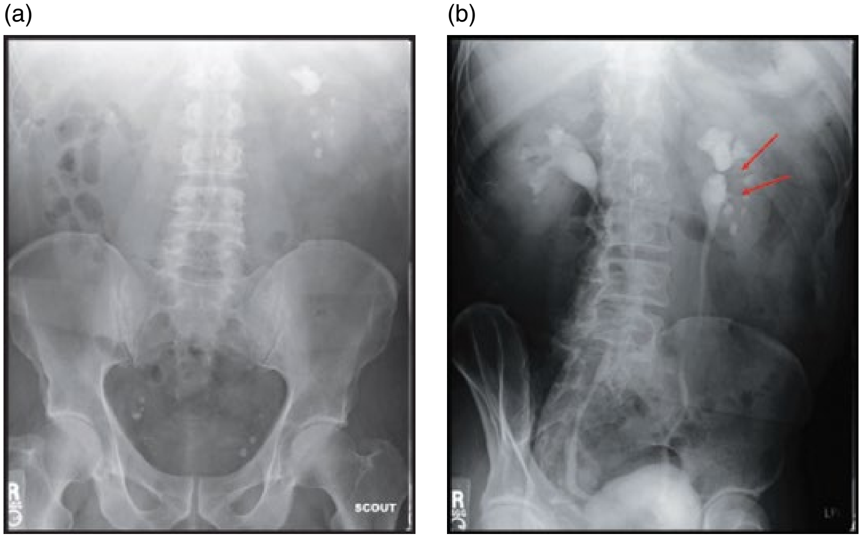

**Figure 28.7** (a) Plain abdominal X-ray of the abdomen and pelvis demonstrating multiple calyceal stones in the left kidney. (b) Excretory urogram demonstrates stenosis of multiple infundibuli leading to the stone-containing calyces (arrows).

pole crossing vessel. Unlike a calyceal diverticulum, urine production continues, resulting in a hydrocalyx. Since infundibular stenosis is so rarely encountered, the true incidence of the disorder is unknown. Occasionally, the stenosis will be so severe that the infundibulum becomes completely occluded; this is termed an excluded calyx.

### Diagnosis

Typically, infundibular stenosis is asymptomatic and discovered incidentally. Acquired infundibular stenosis, even if asymptomatic, can lead to progressive renal failure, with some authors advocating surgical correction [68]. Pain is the most common presenting symptom, followed by hematuria and recurrent UTIs. Stone material may be present in the hydrocalyx [63]. The differential diagnosis includes calyceal diverticulum and renal cyst. While initially suspected on imaging when dilated cystic outpouching of collecting system is seen, true diagnosis requires endoscopic visualization of a papilla in the dilated hydrocalyx. An arteriogram or CT angiogram is useful if a crossing renal artery is suspected, especially for surgical planning [69, 70].

### Treatment

The two indications to treat infundibular stenosis are to relieve obstruction of the dilated calyx and to permit access to a stone or tumor within the calyx. Any reversible causes (e.g. a crossing vessel) should be investigated. Laparoscopic, ureteroscopic, and percutaneous approaches exist.

In general, hydrocalyx with functioning draining parenchyma should not be approached laparoscopically due to risk of urinoma [42]. The ideal candidate is a poorly functioning anterior calyx. The renal parenchyma should be thoroughly fulgurated to destroy any residual functional tissue.

Ureteroscopy is possible if the infundibulum can be seen and cannulated with a wire [69, 70]. It is opened using the holmium laser or balloon dilated, then stented for 4–6 weeks to allow adequate healing. Unfortunately, long-term follow-up studies are lacking. Kieran et al. reviewed experience of 12 URS cases for hydrocalyx, with technical success in most but symptom relief in only half and recurrence in a third. Fortunately, the URS trial did not preclude subsequent percutaneous procedure [71]. As with calyceal diverticula, retrograde flexible ureteroscopic approach is difficult for lower pole obstructed calyces. Percutaneous treatment is possible with direct puncture into the hydrocalyx or by indirect puncture into an adjacent calyx, depending on the anatomy of the affected calyx.

### Technique

Percutaneous access to the calyx is obtained as described above. Retrograde instillation of contrast usually outlines the calyx in question. If the calyx is completely excluded and no stone material is present for fluoroscopic targeting, an ultrasound or CT-guided access is necessary. A needle and then a guidewire are advanced through the calyx towards the collecting system. If the guidewire does not easily traverse the infundibulum, it is coiled in the hydrocalyx, similar to a calyceal diverticulum. After balloon dilation of the percutaneous tract, the access sheath is positioned and the calyx is inspected with a rigid or flexible nephroscope to identify the papilla and the infundibulum. It is important to remove all stones from the calyx prior to infundibular dilation to prevent stone migration into the renal parenchyma. If the infundibulum is not easily identified, retrograde instillation of methylene blue via the external ureteral catheter is useful. In the case of an excluded calyx, a simultaneous URS may be used while the surgeon observes the calyx through the nephroscope. Movement produced by the ureteroscope allows for identification of the main collecting system and may permit successful cut down through the stenosed segment to the wire.

Once a hydrophilic wire is advanced across the infundibulum, it can then either be dilated with a 6 mm × 4 cm balloon or incised with a holmium:YAG laser or a cold knife. Incision is performed away from any obvious pulsations, ideally at the superior and inferior aspects. Multiple superficial cuts are preferred to a single deep cut to limit blood loss [72, 73]. Incision can then be augmented with fluoroscopically guided balloon dilation. Balloon dilation of longer stenotic infundibula reduces the risk of bleeding and extravasation associated with holmium:YAG incision [37].

After dilation of the infundibulum, the hydrocalyx is drained by placing a ureteral stent with the proximal coil in the hydrocalyx and distal coil in the bladder. One or two double-J stents can be used since stent size does not affect subsequent patency of the infundibulum [63, 72]. We prefer an endopyelotomy stent with a larger 14 Fr proximal diameter tapering to 7 Fr distally. Another drainage option is a nephrostomy tube across the infundibulum with coil in the renal pelvis. No study has demonstrated that eventual infundibular patency is affected by type, size, or duration of drainage [63].

In an indirect approach to the infundibulum, access is gained into a calyx adjacent to the hydrocalyx. The flexible nephroscope is then used to identify the stenosed infundibulum that is then balloon dilated or incised with laser. Instilling contrast directly into excluded calyx with either CT or ultrasound guidance can be helpful in identifying the target. Another technique is directing percutaneous needle towards the ureteral catheter positioned in the most likely location for stenosed infundibulum. Once wire is passed into the renal pelvis, a neoinfundibulum is created, serially dilated and then stented [72].

### Potential complications

Complications are similar to those found with calyceal diverticulum treatment. Bleeding and re-stenosis are specific concerns. All efforts to avoid pulsatile vessels should be made at the time of the procedure.

### Outcomes

Data are limited to small case series with calyceal diverticulum patients in the mix. Of the reported series, the success rate is reasonable at 60–80% [63, 74, 75]. No treatment method has been evaluated extensively enough to recommend one surgical approach over another.

### Posttreatment evaluation

Since infundibular stenosis is rare, no clear standardized follow-up protocol exists. We stent the infundibulum (ureteral stent or percutaneous nephrostomy tube) for 4–6 weeks. Urine culture is checked prior to stent removal. If positive for infection, the patient is treated with antibiotics prior to drainage tube removal. Following tube removal, we perform a CT urogram at 4–6 weeks. If there is no evidence of recurrent stenosis, the patient is followed with annual ultrasound imaging.

## Symptomatic renal cysts

Simple renal cysts are noncommunicating fluid-filled structures arising from the renal parenchyma. The incidence increases with age; in one study by the age of 40 years 27% of adults had renal cysts, increasing to 61% by 80 years old [76]. They are occasionally caused by a genetic defect, such as autosomal dominant polycystic kidney disease. Renal cysts are generally asymptomatic and enlarge slowly, although in 2–4% of cases they can cause pain, compression of the collecting system (especially in parapelvic location), infection, or bleeding [77, 78]. Although an association between renal cyst disease and hypertension has previously been suggested, a study of 1526 consecutive patients argued otherwise [77, 79].

### Diagnosis

Simple renal cysts are almost always benign. Complex cysts can harbor malignancy. Although a simple cyst can be diagnosed with an ultrasound, any complex features require a contrast-enhanced CT or magnetic resonance imaging (MRI). The Bosniak classification is used to estimate malignancy risk (Table 28.1) [80]. An excretory CT urogram is useful if compression of the underlying collecting system is suspected. The differential diagnosis of a renal cyst includes calyceal diverticulum, hydrocalyx, UPJ obstruction, and a cystic renal mass. Scanning the patient in supine and prone positions helps differentiate a complex cyst from a calyceal diverticulum with calculi [3, 81], while delayed imaging demonstrating layering of contrast within a "cyst" defines calyceal diverticulum [15]. It is important to rule out malignancy before considering

**Table 28.1** Bosniak radiographic classification of renal cysts and risk of malignancy [80].

| Category | Description | Malignancy risk |
|---|---|---|
| I | Simple, thin walled without septa, calcifications, or solid components | <1%<br>No follow-up required |
| II | Does not enhance with contrast and measures such as water density | 3% |
| IIF | Thin-walled cyst with a few thin (<1 mm) septa with or without fine calcifications. Uniformly high-attenuation (>20 HU) lesions of <3 cm with sharp margins that do not enhance | 5–10%<br>Follow-up recommended |
| III | Multiple thin septa. Septa are thicker than hairline or slightly thick walled. Calcifications may be nodular and thick without contrast enhancement. No enhancing soft tissue elements | 40–60%<br>Surgical excision recommended |
| IV | Intrarenal non-enhancing high-attenuation renal lesions of ≥3 cm | >80%<br>Surgical excision recommended |

*Source:* Adapted from Israel MG and Bosniak MA. An update of the Bosniak renal cyst classification system. *Urology* 2005;66(3):484–488. Reproduced with permission of Elsevier.

percutaneous treatment of a cyst, especially since a neoplasm is more likely to become symptomatic than a simple cyst [82].

### Treatment

Current treatment options include percutaneous aspiration with sclerotherapy, retrograde ureteroscopic puncture, percutaneous resection, and laparoscopic/robotic unroofing. Simple cyst drainage without sclerotherapy has a recurrence rate of 30–80% due to secretory epithelium lining the cyst [77]. Thus injection of a sclerosing agent (ethanol, polidocanol, tetracycline, povidone-iodine, and many others) is preferred, with 75–100% success rates [83, 84]. This procedure is well tolerated with minimal complications, although UPJ fibrosis due to sclerosant extravasation, cyst abscess, fever, pain, and recurrence have been reported [85, 86]. The optimal technique (ultrasound vs. CT guidance), number of treatment sessions, and choice of sclerosant are still being debated [77].

Retrograde ureteroscopic treatment with holmium:YAG laser unroofing and internal marsupialization is limited to parapelvic cysts adjacent to the collecting system. Yu et al. described cure in 26 out of 35 patients and Mao et al. described cyst reduction or elimination in 20 out of 21 patients with this approach [87, 88] with only 25 minutes operation time.

Laparoscopic unroofing is suited to any large renal cyst. A randomized trial of 40 patients revealed similar success of aspiration/sclerotherapy and laparoscopic unroofing despite laparoscopy being more invasive [89].

Percutaneous resection was first reported in 1984 [90]. Multiple follow-up series have confirmed the efficacy and safety of the procedure [84, 91–94]. It is particularly attractive if there are concomitant renal stones.

### Technique

The cyst is accessed using either ultrasound or fluoroscopic guidance. Retrograde installation of contrast allows fluoroscopic targeting, as the collecting system is distorted by the renal cyst. The cyst is accessed percutaneously with triangulation technique and fluid is aspirated to confirm intracyst positioning of the needle. The fluid is sent for cytology and culture. If there is any suspicion of malignancy a core biopsy of the cyst wall should be sent, since cytology alone has a false-negative rate in renal cell carcinoma [95]. Access to the cyst is then achieved in an identical fashion as for a calyceal diverticulum.

Once the access sheath is inside the cyst lumen, the entire cyst wall is examined and fulgurated with a rollerball electrode and 1.5% glycine irrigation fluid. Electrocautery should be set at the lowest possible settings to allow for blanching of the cyst wall without perforation [84]. Bipolar electrocautery with saline irrigant can be used with similar results [96]. A portion of the cyst wall is excised using grasping forceps or loop resection for marsupialization into the retroperitoneum. We do not routinely marsupialize to the collecting system since reports indicate recurrence rates are not decreased with this procedure [84, 97]. An 8 or 10 Fr locking Cope loop nephrostomy tube is left inside the cavity and removed the next day.

### Potential complications

In addition to typical percutaneous procedure risks, cyst recurrence or incomplete obliteration can occur.

### Outcomes

Although earlier studies reported 15–50% recurrence rate [91, 92], Shah et al. reported durable success in 8 patients with 5-year follow-up [97]. Chen et al. describe percutaneous marsupialization technique for renal cysts with ipsilateral renal calculi with no recurrence at mean follow-up of 22 months [93]. Busato and Bettega reported 100% success rate in 32 patients with mean follow-up of 76 months [94].

### Posttreatment evaluation

Although standardized follow-up recommendations do not exist, we perform a renal ultrasound and urinalysis three months post procedure. Since recurrence rates are so low, annual follow-up once cyst is resolved is not required [94].

## Conclusion

Percutaneous treatment of calyceal diverticula, infundibular stenosis, and symptomatic simple renal cysts is a safe and effective option in appropriately selected patients. Long-term data support the role of percutaneous treatment of calyceal diverticula as the initial intervention. Although studies on percutaneous treatment of hydrocalyx associated with infundibular stenosis and symptomatic renal cysts are limited, it remains a minimally invasive treatment option.

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# 29

# Percutaneous Instillation of Chemolytic, Chemotherapeutic, and Antifungal Agents

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## Introduction

Percutaneous instillation of topical agents started when Crowell disintegrated a cystine stone by instillation of alkaline solution into the kidney [1]. Before the advent of miniaturized fiber-optic flexible ureteroscopes and nephroscopes, the nephrostomy tube provided a conduit for direct instillation of topical agents into the collecting system, thus minimizing systemic side-effects. Chemolytic agents for stones were the original and most common agents. Currently, there are two other categories of topical instillation agents used: chemotherapeutic/immunotherapeutic agents as adjuvant treatment for upper tract transitional cell carcinoma (UTTCC) and antifungal agents. The advantages of direct instillation when compared with systemic therapy include increased duration of direct contact of the topical agents with the collecting system, which allows topical agents reach the target organ in appropriate concentrations. This leads to shorter therapy and avoidance of harmful systemic side-effects [2]. In addition, these topical agents can be administered in patients with compromised renal function, inadequate urinary drainage, and high operative risk due to comorbidities [3]. However, it is important to note that there are several contraindications to initiating or continuing percutaneous instillation of topical agents. These include: positive urine culture, febrile patient, persistent flank pain, extravasation of irrigation fluid, or intrapelvic pressure >25 $cmH_2O$ [4].

With recent advances in endourologic technology, indications for instillation of topical agents have evolved and can be very useful for select patients. Although principles of instillation of topical agents into the collecting system are simple, minor errors in technique can result in catastrophic complications. Therefore, in addition to the urologist, both the nursing staff and the patient should be aware of the tell-tale signs of complications and should inform the treating physician immediately to stop the instillation. Therefore, urologists should be familiar with techniques of instillation, indications and contraindications, success rates, and any potential side-effects. In the present chapter, chemolytic agents (for stones), chemotherapeutic/immunotherapeutic agents for UTTCC, and antifungal agents will be reviewed.

## Techniques of irrigation/instillation

Topical instillation of agents into the collecting system depends on the principle of free flow of the solution throughout the collecting system, thus providing a continuous milieu of irrigant solution to the stone, UTTCC, or fungus ball. This can be achieved through several techniques: either retrograde fashion, percutaneous antegrade fashion, or a combination of both.

### Retrograde approach

The retrograde technique is the most simple and least invasive. It is done through a single ureteral catheter that is advanced beyond the level of the lesion or stone. The main disadvantage of this technique is the limitation of outflow through or around this small stent. This can result in a rapid elevation of intrapelvic pressures. Therefore, this technique of irrigation is not recommended. In an attempt to avoid this complication, Kuwahara and colleagues [5] used a computer-controlled, pressure-monitor intermittent pump (Figure 29.1a). This pump infuses fluid for 1 minute, holds for 30 seconds, and then drains for 9 seconds. If the pressure increases beyond the preset limit (15 $cmH_2O$), the infusion stops.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

If the pressure increase is sustained for 5 seconds, the drainage valve opens. This system was not widely used because it was prohibitively expensive; because of this, its safety and efficiency were not properly evaluated. Without such a pump, a single ureteral catheter for irrigation is not recommended.

Several other techniques of retrograde instillation have been described. One technique proposed by Dormia et al. [6] utilizes concentric catheters placed in the ureter to facilitate the outflow from the kidney into the bladder (Figure 29.1b). Another less-efficient technique is by vesicoureteral reflux in a patient with an indwelling

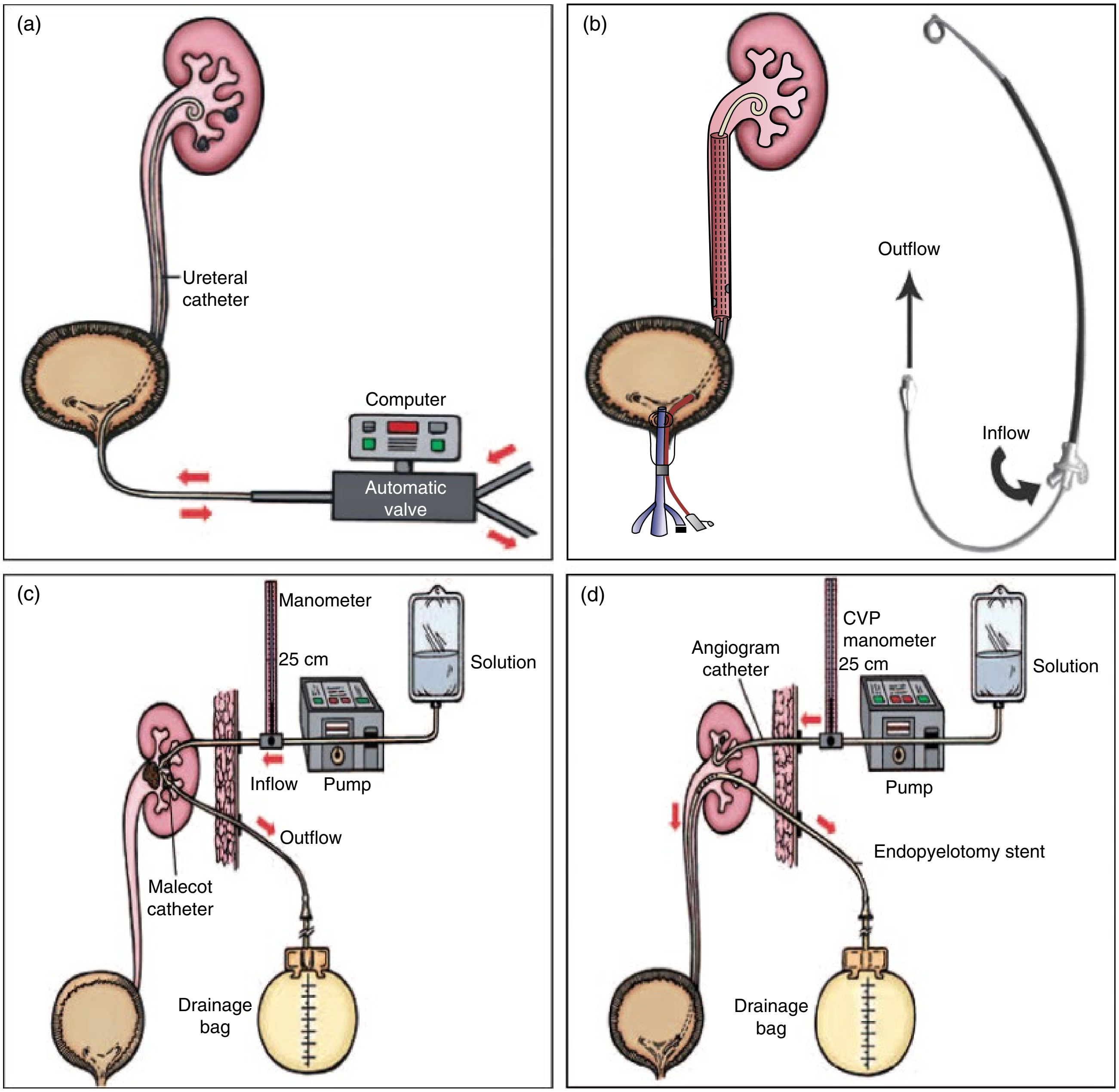
(a)
Ureteral catheter
Computer
Automatic valve
(b)
Outflow
Inflow
(c)
Manometer
25 cm
Solution
Inflow
Pump
Outflow
Malecot catheter
Drainage bag
(d)
Angiogram catheter
CVP manometer
25 cm
Solution
Pump
Endopyelotomy stent
Drainage bag

**Figure 29.1** Irrigation configurations for chemolysis. (a) Retrograde ureteral catheter with computer-driven inflow/outflow. *Source*: Adapted from Fried and Smith [13] with permission. (b) Concentric catheters in kidney, ureter and bladder for transureteral irrigation. *Source:* Adapted from Dormia et al. [6] and Collins et al. [8]. (c) Dual Malecot catheters irrigation. (d) Nephrostomy inflow and universal/endopyelotomy stent outflow irrigation for struvite stones. (e) Circle tube for irrigation chemolysis. (f) Coaxial technique of ureteral catheter through a Foley catheter. (g) Coaxial technique of ureteral catheter through a Foley catheter. (h) Retrograde ureteral catheter inflow and nephrostomy outflow. (i) Constant-pressure renal pelvis irrigation system: a 5 Fr open-end ureteral catheter inserted through a small hole in the urine bag tube while the tip of the ureteral catheter is kept at the end of the nephrostomy catheter. The urine bag tube is placed 20 cm above the kidney while irrigating at 100 ml/h. *Source:* Adapted from Nakamura et al. [21]. CVP, central venous pressure.

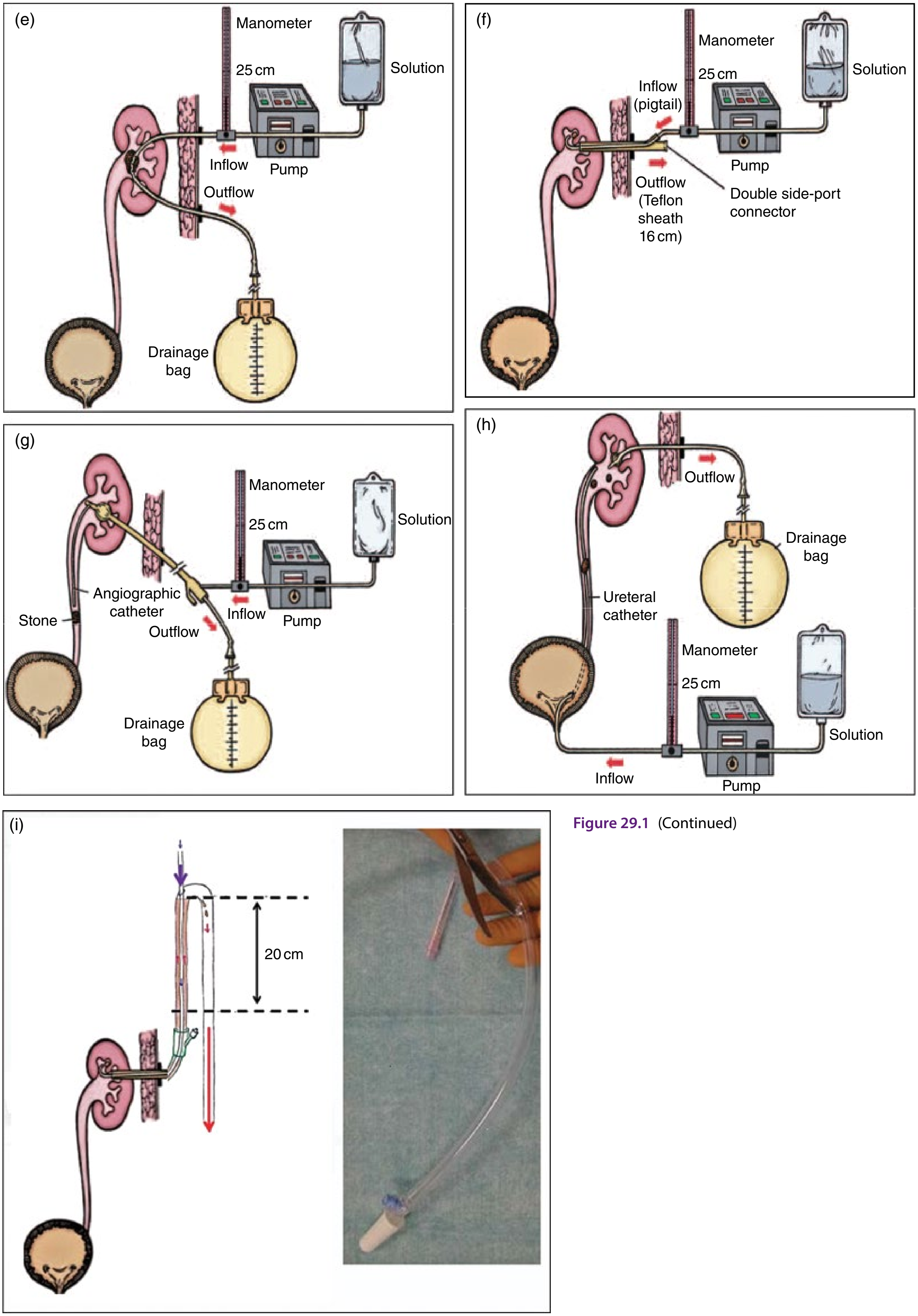
(e)
Manometer
25 cm
Solution
Inflow
Pump
Outflow
Drainage bag
(f)
Manometer
25 cm
Solution
Inflow (pigtail)
Pump
Outflow (Teflon sheath 16 cm)
Double side-port connector
(g)
Manometer
25 cm
Solution
Angiographic catheter
Stone
Inflow
Pump
Outflow
Drainage bag
(h)
Outflow
Drainage bag
Ureteral catheter
Manometer
25 cm
Solution
Inflow
Pump
(i)
20 cm

**Figure 29.1** (Continued)

ureteral stent after ureteral meatotomy [7]. Recently, a high-flow low-pressure irrigation system was described that uses an 8 Fr pigtail catheter through a 12/14 Fr ureteral access sheath (Applied Medical Systems, Rancho Santa Margarita, CA, USA). In an *in vitro* study, this system was found to be associated with significantly higher flow rates and lower pressures when compared with a single nephrostomy tube without ureteral catheters [8].

## Antegrade approach

The ideal inflow and outflow is achieved by percutaneous antegrade fashion through the use of two nephrostomy tubes. For example, two Malecot catheters (16 or 18 Fr) could be used (Figure 29.1c). This configuration is versatile and can be used in most patients. In patients with struvite stones, which tend to form large, irregular pieces on fragmentation, an endopyelotomy stent (14/8.2 Fr) provides excellent two-way outflow, decreases the volume of fragments that enter the ureter and prevent its obstruction [9] (Figure 29.1d). Another method of preventing ureteral obstruction is insertion of an indwelling double pigtail catheter when two Malecot nephrostomy tubes are used. A simpler method of inflow and outflow in antegrade fashion through two nephrostomy sites is the use of a circular tube (Figure 29.1e).

Two coaxial techniques of irrigation have been described. Hare and McOmish [10] described a renal pelvic lavage set to irrigate different areas of the pelvis through a single nephrostomy site allowing both inflow and outflow (Figure 29.1f). Once the Teflon sheath is in place, an inner 6.3 or 8.3 Fr pigtail catheter is directed at the stone for inflow. Outflow, which is limited, occurs through the surrounding sheath and down the ureter. The second coaxial technique of irrigation works well for upper ureteral stones [11, 12]. It is set up by inserting either a 5 Fr ureteral or angiogram catheter over a wire through the lumen of an 18 Fr Foley catheter, which serves as a nephrostomy tube (Figure 29.1 g). The small inner catheter, which provides inflow, can be advanced so that its tip is adjacent to the stone, whereas the Foley catheter provides outflow. This is an effective method for dissolving upper ureteral stones. A simpler technique of irrigating the renal pelvis through a single nephrostomy site is the use of a three-way Foley catheter [13].

## Combined approach

One combination of both antegrade and retrograde techniques can be accomplished through the insertion of a percutaneous nephrostomy (NT) tube and ureteral catheter. The NT acts as an ideal outflow while the ureteral catheter is used for instillation (Figure 29.1 h). However, using the combination of a ureteral catheter, a urethral catheter and a nephrostomy tube severely decreases patient mobility. Therefore, a modified approach can use an NT to instill agents and an indwelling double pigtail ureteral catheter as a drainage catheter. The drawback of this approach is that there is much less efficient outflow through a ureteral catheter than a nephrostomy tube. Therefore, this modification would be ideal for small stones that dissolve in a short period of time, such as uric acid stones.

All the techniques described above should follow appropriate safety principles. Patients should have preoperative urine cultures and be treated with culture-specific antibiotics. Urine cultures should be negative prior to initiating irrigation and patients should be kept on antibiotics throughout the irrigation. In addition, once the tubes are inserted, contrast studies should be performed 24 hours later to rule out extravasation. The irrigation should start slowly with warm saline at a rate of 30 ml/h. When the patient remains pain-free and afebrile, the rate is doubled every 2–4 hours until the target rate of 120 ml/h is reached [13]. After 12–24 hours of saline irrigation, the active agent is instilled at a rate of 30 ml/h and increased sequentially to 120 ml/h. There are several advantages to warming the irrigation solution. It is more comfortable for the patient, it avoids hypothermia, and it may increase the effectiveness of therapy [14–16].

It is important to have an intrapelvic pressure-monitoring system in all of the techniques described. If renal pelvic pressures are uncontrolled, pyelovenous and pyelolymphatic backflow leads to systemic absorption. Subsequently, the patient may suffer agent-specific systemic toxicities or changes in serum chemistries when the irrigant solution is nontoxic [17]. The intrapelvic pressure should not be allowed to rise above 25 $cmH_2O$ in order to prevent pyelovenous backflow [18]. The simplest method is the use of a central venous pressure (CVP) manometer connected to the inflow line. This is readily available and familiar to the nursing staff. Unfortunately, this is an open system that is prone to contamination or overflow spills. Furthermore, it requires continuous monitoring since there is no preset pressure alarm or automatic shutoff for high pressures (>15 $cmH_2O$). A better alternative is a closed continuous infusion pump that provides a continuous display of the intrapelvic pressure and will sound an alarm and shut off if the preset limit is exceeded (CareFusion, San Diego, CA, USA) [6]. Regardless of which pump is used, the patient should be taught how to immediately turn off the pump in case of flank pain or fever.

## New concepts

Small-caliber percutaneous instruments (SCPI) provide a new range of tools for kidney stone treatment. The impact of combined high-pressure irrigation inflow and simultaneous sensor-controlled suction on irrigation turnover and intrarenal pressure in SCPI was recently investigated. A 9.5 Fr Amplatz sheath was introduced through the lower calyx and an 8 Fr ureteric catheter was inserted through the ureter of a nonperfused porcine kidney. Another 8 Fr ureteric catheter was inserted through the upper calyx, and irrigation was performed using a pressure-controlled, combined irrigation/suction pump. Analysis of the intrapelvic pressure was performed by different irrigation pressures with and without sensor-controlled suction through the ureteric catheter [19]. After initiating irrigation flow, the intrarenal pressure reached a plateau within seconds without any pressure peaks during the whole experiment. This sensor-controlled suction increased fluid turnover and decreased intrarenal pressure in SCPI. In addition, such a purging effect prevented collapse or hyperdistention of the collecting system, especially in small-caliber instruments. However, SCPI has not been tested in humans yet.

Similarly, Colli et al. found that application of a 10 Fr ureteral dual-lumen catheter in a porcine model produced adequate retrograde drainage with low intrarenal pressures at high infusion rates (up to 80 ml/min) [20]. This experiment supports the use of separate channels for inflow and outflow during retrograde infusion to maintain intrarenal pressures around 5 $cmH_2O$.

Nakamura et al. reported a novel constant-pressure irrigation technique for a case of a left renal pelvic tumor which developed postradical cystectomy, right nephroureterectomy, and left ureterectomy in a patient with multiple urothelial tumors. The tumor was endoscopically ablated through a nephrostomy tract followed by mitomycin C irrigation [21]. The authors designed a novel constant-pressure irrigation system for effective and safe irrigation into the closed-space renal pelvis. Through a hole in the urinary drainage bag tube, a 5 Fr open-ended ureteral catheter was inserted, and the tip of the catheter was kept at the tip of the nephrostomy tube. The ureteral drainage tube was placed 20 cm above the kidney level to continuously irrigate the renal pelvis with mitomycin C for six-weekly treatments of 1 hour each time. The patient has been recurrence-free for one year (Figure 29.1i).

## Chemolysis of urinary calculi

Stone dissolution through chemolysis remains an option in the treatment of urolithiasis even with the advent of more sophisticated modalities. Chemolytic agents can achieve benefit through either primary or secondary dissolution. Primary dissolution is when chemolytic agents are used as initial therapy to dissolve stones completely or partially. This may be an option in patients unfit for general anesthesia. Secondary dissolution may be useful in patients with residual fragments after some other primary therapy. In this context chemolysis may render the patient stone-free, thus reducing the potential for recurrences or more invasive interventions.

For effective chemolysis, the irrigant and irrigation system must have several important characteristics. First, the irrigant must be compatible with biological tissue and be of limited toxicity. Second, it should have minimal systemic absorption in order to limit potential toxicity. Third, the irrigant should dissolve calculi and their fragments quickly to reduce treatment burden for the patient. Fourth, solutions used for irrigation must not precipitate, causing secondary stone formation. In addition, an ideal irrigation system must provide for free flow of irrigant to a targeted area, while maintaining low renal pelvic pressures to prevent bacteria from entering the bloodstream and to avoid renal damage [17].

Unfortunately, stone dissolution through chemolysis has several limitations. Some stones may require long treatment periods, which may necessitate prolonged hospital admission and patient discomfort. The efficacy of stone dissolution is dependent on many stone-specific factors. For example, uric acid and struvite amorphous minerals dissolve much faster than highly crystalline salts such as calcium oxalate. Likewise, stone size and shape will determine the rate of dissolution. Large stones will dissolve more slowly than the same volume of smaller stones because the surface area is greater in the latter [22, 23]. These variables can make it difficult to predict the necessary length of treatment a priori. In addition, the choice of chemolytic agent will depend on stone type. This requires that stone composition be determined prior to chemolysis. When stone fragments are not available, surrogate methods of determining stone composition, such as CT characteristics or the composition of previous stones, must be used to determine the agent of choice [17, 24, 25].

### Uric acid stones

Almost all individuals who form uric acid stones have persistently low urinary pH (<5.5) and most excrete normal amounts of uric acid [26, 27]. The acid–base properties of uric acid stones render them amenable to dissolution therapy. Uric acid is a weak organic acid with a $pK_a$ of 5.35 in urine at 37 °C. At this pH, half is present as the undissociated acid and half as the urate anion. Since urate is more soluble than uric acid, raising the urinary pH within the physiological range has a profound effect on how much uric acid/urate can be dissolved. For example, a urine sample containing 800 mg/l total urate will have 600 mg/l uric acid at a pH of 5.0 but less than 100 mg/l at pH 6.5. The latter figure is well below the solubility limit of uric acid so that a solution above pH 6.5

can dissolve a uric acid calculus [18]. Any solution above pH 7 is likely to be effective but higher urinary pH solutions may have a tendency to calcify the stone, particularly if sodium bicarbonate is used as the base [28]. Increasing the urinary volume further enhances the therapeutic efficacy of alkaline medications [29]. In addition, decreasing the oral purine load from dietary sources can effectively help treat patients because 40– 60% of excreted uric acid is derived from exogenous sources. Regardless of the method chosen, urine pH should be monitored with pH strips to optimize therapy. Serum and urine uric acid levels are also important to follow, especially in those with recurrent calculi.

To identify those most likely to respond to dissolution therapy, Reichard et al. found that patients with 100% uric acid stones were older, heavier, and had a higher serum uric acid level, and lower urinary pH than those with mixed stones, while urinary uric acid was not significantly different among groups [30]. However, it is unclear whether these characteristics alone will provide enough specificity to predict uric acid stones.

### Systemic agents

Systemic alkalinization is generally achieved with oral or intravenous therapy. The most popular agent is sodium bicarbonate, and the dose is 650–1000 mg three to four times daily. An alternative preparation, if the sodium load is too great, is potassium citrate administered as 15–30 mEq three to four times daily. Specifically, oral alkalization therapy for uric acid calculi has been established in the literature as an effective, totally noninvasive therapy [31]. It is generally effective for stones of 8–52 mm long with success rates of 62–72% in adults within six weeks to six months [32, 33]. Furthermore, oral alkalization is well tolerated and effective in children with uric acid stones, where it eliminates the need for shock-wave lithotripsy (SWL) in up to 73% of those children. One randomized controlled trial (RCT) showed comparable stone-free rates for dissolution therapy and a single session of SWL (72.9% vs. 82.1%, $P = 0.31$). Children undergoing dissolution therapy received potassium sodium hydrogen citrate at a dose of 1 mEq/kg per day for 1–3 months [34]. Several other oral therapies have been suggested to facilitate dissolution therapy. Sterrett and colleagues [35] demonstrated that acetazolamide, a carbonic anhydrase inhibitor, was effective in increasing the urinary pH in patients with uric acid and cystine stone formation who were already taking potassium citrate. Caution must be applied when prescribing acetazolamide, because it could be poorly tolerated and can induce calcium phosphate stone formation. A dose of 250–500 mg is taken at bedtime to maintain urine alkalinity during sleep. In cases of hyperuricosemia and hyperuricosuria, allopurinol should be added to inhibit the production of uric acid through inhibition of xanthine oxidase enzyme.

Intravenous alkalinization is more effective than the oral route. Urinary pH is elevated more quickly, to a higher degree, and is more reliable. This technique, however, is typically reserved for hospitalized patients with acute episodes of (renal) colic and obstruction. One-sixth molar lactate solution has been demonstrated to dissolve uric acid stones even when they are causing ureteral obstruction [36]. Lactated Ringer's solution with one to two ampoules of sodium bicarbonate added per liter is an acceptable alternative. The infusion rate (usually 50–100 ml/h) is titrated to a urinary pH of 7.0–7.5, which occurs within 4 hours. Cardiac and hypertensive patients must be monitored for the large sodium load in these solutions.

### Chemolytic agents

Since the urinary pH can usually be raised to at least 6.5 with oral or intravenous alkaline salts, medical therapy is ordinarily the treatment of choice for uric acid stones [18, 27, 29]. There are clinical situations in which oral or intravenous therapy is not possible, such as in patients who are noncompliant, or have chronic renal failure or an ileostomy. These patients may benefit from direct chemolytic therapy. Additionally, if a large amount of residual fragments is present after an initial therapy, direct chemolysis is a viable option.

The most common alkalinizing agents are sodium bicarbonate solution (pH 7.0–9.0), tromethamine (THAM, pH 8.6), and THAM-E (pH 10.5). Sodium bicarbonate solution is inexpensive and prepared easily by adding 2–4 ampoules (44 mEq each) to each liter of irrigant solution (normal saline solution or water). With this solution, there is no value in increasing the final urinary pH >7.5. In fact, higher elevations may be detrimental to stone dissolution because phosphatic and sodium urate encrustations may form a coating on stones [37]. The THAM solutions are more effective and do not cause such mineral deposits. It has been shown in animal models that THAM results in more rapid stone dissolution than sodium bicarbonate [28]. THAM-E is slightly more effective than THAM because of its higher pH but it is also responsible for more irritation and potential damage to the epithelium [38, 39]. Therefore, for uric acid chemolysis, THAM appears to be the agent of choice [18] (Table 29.1).

If a uric acid staghorn calculus is present, pretreatment with SWL may increase the stone surface area to facilitate dissolution. Unlike struvite and cystine stones, it is unusual to need prolonged irrigation to manage uric acid stones.

## Cystine stones

Cystinuria is an autosomal recessive disorder of dibasic amino acid transport in the kidney that leads to crystallization of poorly soluble cystine in the urine [51].

**Table 29.1** Results of direct chemolysis for uric acid and cystine stones.

| Study | Irrigation solution | Dissolved/ attempted | Duration of irrigation (days) | Adjuvant treatment |
|---|---|---|---|---|
| **Uric acid calculi** | | | | |
| *Chemolysis alone* | | | | |
| Hedgcock et al. [12] | Sodium bicarbonate | 11/11 | 3–21 | |
| Gordon et al. [40] | THAM | 3/3 | 7–10 | |
| Ansari et al. [41] | Sodium lactate | 3/3 | 7–14 | |
| *Chemolysis with SWL* | | | | |
| Lee et al. [42] | Sodium bicarbonate | 5/8[a] | 2–7 | |
| **Cystine calculi** | | | | |
| Schmeller et al. [22] | *N*-Acetylcysteine + sodium bicarbonate | 1/1 | 26 | |
| Smith et al. [43] | | 1/1 | 30 | |
| Aabech and Andersen [44] | THAM-E with/without *N*-acetylcysteine | 2/2 | 3–9 | Surgery with/without SWL |
| Kachel et al. [45] | | 3/9 | – | 3 Partial dissolution, SWL |
| Dretler et al. [46] | | 7/11 | 6–42 | with/without PCNL |
| Kane et al. [47] | Mercaptopropionylglycine | 5/5 | 24–88 | 1 Pyelolithotomy, 1 bladder stone, urokinase added to irrigant |
| Hayase et al. [48] | THAM-E | 0/3 | 25–37 | 3 Partial dissolutio, 1 nephrolithotomy |
| Crissey and Gittes [49] | | 1/2 | 5 | 1 Ureteral, 1 renal stone |
| Stark and Savir [50] | Penicillamine | 1/1 | 180 | 1 Pyelolithotomy |

[a] Three patients had only small clinically insignificant fragments.
SWL, extracorporeal shock-wave lithotripsy.
*Source:* Adapted from Fried and Smith, 2007 [13].

Between 3% and 59% of those who are homozygous for the trait will produce stones [52]. The disease is more severe in men than in women in terms of early appearance and number of produced stones. Although the incidence of cystine stones is only about 0.9%, cystine stones rank third in terms of rate of recurrence [53]. Treatment of cystine stones continues to be one of the most challenging therapeutic dilemmas in endourology because of a high frequency of recurrence, resistance to SWL, difficulty in localization, and the insufficient effect of oral chemolysis [44].

Because of the difficulties in treating cystine stones, much emphasis has been placed on prophylaxis. The solubility of cystine, like all amino acids, is pH-dependent. Therefore, the production of alkaline urine can prevent cystine precipitation in the urine. A significant increase in cystine solubility begins to occur when urinary pH exceeds 7. For example, at a pH of 8, cystine solubility increases to approximately 1000 mg/l [54]. However, a significant drawback of urinary alkalinization is increased risk for calcium phosphate precipitation with pH above 7.5 [55]. For this reason, urinary pH of 7.5 is recommended [54]. It is recommended that this alkaline urinary pH must be maintained at night while the patient sleeps. The use of the potassium salts of citrate and bicarbonate may be more effective than the analogous sodium compounds because the presence of a sodium ion increases cystine excretion in the nephron. Because of this, a low-sodium diet may be useful in the management of cystinuria [56].

Cystine is composed of two cysteine molecules joined by a disulfide bond and its dissolution requires alkalinization and splitting of the disulfide bond. This can be accomplished through either oral therapy or direct chemolytic therapy. D-Penicillamine, the first oral agent used for cystine stones, is a disulfide exchange resin that facilitates separation at the disulfide bond through the thiol exchange reaction, forming mixed disulfides, and also decreases urinary excretion of cystine. The exchange reaction forms penicillamine disulfide–cysteine, which is 50 times more soluble than cystine [57] and is readily cleared through the urine. D-Penicillamine is administered as 1–2 g in four divided doses, starting with a small dose and increasing as tolerated. Side-effects of the drug include leukopenia, thrombocytopenia, gastrointestinal disturbances, skin rashes, proteinuria and nephrotic syndrome, neuropathies, and abnormalities of taste and smell. D-Penicillamine has been reported to dissolve even large stones when combined with alkalinization but its potential side-effects severely limit its usefulness.

α-Mercaptopropionylglycine (MPG) is another disulfide exchange resin with fewer side-effects than D-penicillamine and appears to be more effective [58]. The usual dose of MPG is 600–1800 mg daily in four divided doses. Simultaneous treatment with oral sodium bicarbonate increases the effectiveness of this preparation because the disulfide exchange reaction is more active at higher pH levels.

Oral acetylcysteine, MPG, and D-penicillamine are much more effective in preventing the formation of cystine calculi than dissolving them. When used for direct chemolysis, however, they are potent dissolution agents. During direct irrigation the solution bathing the stone will have a much higher concentration of the active agent. The pH of the solution is likewise more easily controlled, thereby facilitating the thiol exchange reaction [13].

Chemolysis monotherapy would require lengthy durations of irrigation for most stones. Approximately 9 days are required to dissolve a 1 cm cystine calculus. This irrigation time could be diminished when combined with SWL or percutaneous nephrolithotomy (PCNL), which reduce the stone burden and increase the surface area of the remaining fragments. Stones <1.5 cm may be treated initially with SWL since it increases the stone surface area and decreases dissolution time by nearly 50% [22]. If successful fragmentation occurs, repeat SWL or medical management may be sufficient as follow-up therapy. Otherwise chemolysis alone or combined with PCNL is appropriate. For stones >1.5 cm, PCNL is the initial procedure of choice. Residual calculi, which are likely to remain, can be effectively treated with chemolysis and additional PCNL or SWL sessions. Simultaneous oral therapy should be implemented in all cases [13] (Table 29.1).

If the stones appear extremely resistant to therapeutic measures, the possibility of a mixed stone should not be overlooked. Hydroxyapatite, struvite, calcium oxalate, and calcium phosphate contaminants have been found to be present in 14–46% of cystine calculi analyzed in some studies [59].

In summary, although cystine urinary calculi continue to present a formidable challenge to urologists, successful eradication without open surgery may be accomplished with chemolytic techniques in conjunction with minimally invasive fragmentation procedures.

## Struvite stones

Struvite stone formation typically occurs in patients with recurrent urinary tract infection and retained urine. Predisposing factors include urinary tract obstruction, chronic indwelling catheter, urinary diversion, and neurogenic voiding dysfunction [60]. Most commonly, staghorn stones are composed of a mixture of struvite (magnesium ammonium phosphate) and calcium carbonate apatite. In fact, hypercalciuric patients begin with calcium oxalate stone formation and develop superimposed infection with struvite deposition [61, 62]. Struvite calculi are typically referred to as "infection stones" because of their strong association with urinary tract infections caused by such bacteria. Silverman and Stamey [63] identified *Proteus* as the dominant microorganism in 72% of isolates from stone formers. Urease produced by such bacteria leads to hydrolysis of urea to ammonium, hydroxide, and bicarbonate, which increases the pH of the urine (pH >7.2). This alkaline urine, in the presence of trivalent phosphate, results in struvite crystal formation [64]. Other urease producers include *Klebsiella*, *Pseudomonas*, and *Staphylococcus* species [63, 65]. The most ubiquitous uropathogen, *Escherichia coli*, only rarely produces urease and thus is an infrequent cause of staghorn calculi [66].

Struvite stones are characterized by their large size and exceptionally rapid growth. It is not uncommon for a staghorn calculus to involve the entire renal pelvis and calices, nor for it to be formed within a four-week period [60].

Management of struvite stone disease is one of the most frustrating problems in urology as efforts to eradicate such stones often have suboptimal success rates. The problem is not only ridding the patient of the calculi but also sterilizing the urine. Persistence of infection was estimated to occur in approximately 40% and is believed to be responsible for many of the stone recurrences [67]. The presence of small stone particles with embedded bacteria serves as a nidus for new stone formation and rapid recurrences. Therefore, postoperative irrigation therapy has been proposed to potentially reduce struvite stone recurrences [68, 69]. Medical dissolution therapy for struvite and carbonate apatite stones has been described as a second-line treatment option. Oral chemolysis is available primarily in the form of urease inhibitors. Acetohydroxamic acid, the most commonly used agent, was identified as an irreversible urease inhibitor by Fishbein and Carbone [70]. The drug acts synergistically with several antibiotics, sterilizing the urine more rapidly, and its clinical usefulness has been demonstrated in double-blind studies, although serious side-effects precluded its use in patients even though they are reversible and dose-related [71–73]. The usual dose is 250 mg orally three times daily to be reduced to twice daily for mild renal impairment, and it is contraindicated in patients with severe renal insufficiency and in pregnancy. Most common side-effects reported were hemolytic anemia, neurosensory deficits, and thrombophlebitis. Headache, gastrointestinal upset, weakness, and flushing sensation after alcohol ingestion have also been reported [74]. Nevertheless, it is the only US Food and Drag Administration (FDA)-approved urease inhibitor available today [75].

Systemic oral chemolytic agents are seldom effective in reducing stone burden on their own and direct chemolysis of struvite calculi is a far more effective method of dissolution. Suby and colleagues [76, 77] presented the first application of direct chemolysis to struvite calculi where the initial solution was found to be too irritant for urothelium to be clinically used. Suby's solution G, formed by addition of magnesium to the previous formulation, has similar efficacy with decreased mucosal irritability (Table 29.2). Hemiacidrin (renacidin) is a multi-electrolyte solution introduced by Mulvany [78] by modification of Suby's solution. The acids present in this solution provide hydrogen ions and citrate to form soluble complexes with phosphate (phosphoric acid) and calcium (calcium citrate) from the stone (Table 29.3). Magnesium undergoes ion exchange with calcium present in the stone, enhancing dissolution while reducing irritation. The solubility of struvite is markedly increased at a pH <5.5, which occurs with each of the three variants of Suby's solution. This finding was confirmed in a recent *in vitro* study by Jacobs et al. [79]. The success rate of these medications in the literature has been reported to occur in the range of 68–80% [80].

Infectious complications are known to occur as a result of dissolution therapy. Renacidin and Suby's solutions have been implicated as the cause of urosepsis and death, and the FDA banned the use of renacidin irrigation for upper urinary tract stones on June 13, 1963 [90]. Urosepsis is thought to occur due to the release of large amounts of viable bacteria from stones as they dissolve. Therefore, it is critically important to stop treatment if fever occurs and until any infection has been adequately treated.

**Table 29.2** Composition of different chemolytic agents.

| | Suby's solution | | |
|---|---|---|---|
| **Compound** | **G** | **M** | **Renacidin** |
| Citric acid (g) | 32.3 | 32.3 | 28.2 |
| Magnesium oxide (g) | 3.8 | 3.8 | 0 |
| Sodium carbonate (g) | 8.84 | 8.84 | 0 |
| Calcium carbonate (g) | 0 | 0 | 1.0 |
| D-Gluconic acid (g) | 0 | 0 | 5.0 |
| Magnesium hydrocarbonate (g) | 0 | 0 | 14.8 |
| Magnesium acid–citrate (g) | 0 | 0 | 2.5 |
| Water (ml) | 1000 | 1000 | 1000 |
| pH | 4.5 | 4.0 | 4.0 |

*Source:* Adapted from Fried and Smith, 2007 [13].

The presence of catheters and extensive use of antibiotics can also facilitate fungal infection. Replacing the irrigation fluid with amphotericin B (50 mg/500 ml $H_2O$) at a rate of 125 ml/h generally clears the funguria in less than 72 hours. Chemolysis irrigation can resume once urine cultures are negative for 24 hours.

## Calcium stones

Calcium-based calculi constitute about 80% of all urinary tract stone calculi of which about 80% are calcium oxalate stones [91], and yet they are the least amenable to chemolysis. The strong acids required to dissolve this compound cannot be safely used in humans. Only chelating agents have successfully been used *in vivo* to dissolve these types of stones. Ethylene-diamine-tetraacetic acid (EDTA) is the most commonly used solvent, and has shown moderate success in humans [92, 93] in spite of the significant urothelial injury reported [47]. EDTA is a polyvalent molecule which binds calcium through its two amine and four carboxyl groups. This sequestration dissolves the calcium component of the stone, thus reducing stone burden. Complete stone dissolution of over 50% in 260 patients treated with EDTA was reported [94]. Early use of this solution after stone formation is associated with a better response rate. These authors also used 0.25% lyophilized papain to dissolve the matrix component of stones. EDTA solutions are not widely used, primarily because they can cause urothelial injury.

In recent *in vitro* trials, mixed solutions containing natural and synthetic chelating reagents were found to be successful in dissolving calcium oxalate calculi. These solutions consisted of citrate and EDTA ions in addition to ampicillin sodium salt with a pH value of 6.4 [95]. This chemolytic solution seems to destroy oxalate/phosphate and pure phosphate stones including brushite stones. However, there are no reports of clinical studies using these solutions.

Oxalate-based stone dissolution using enzymes appears to be another viable option. Thalji et al. found that the addition of oxalate decarboxylase to calcium oxalate monohydrate crystals resulted in production of highly soluble calcium formate and a 15-fold increase in the solubility of calcium oxalate monohydrate. Moreover, adding formate dehydrogenase increased the dissolution 47-fold when compared with controls [96]. Lysine was also discovered to have a promising place among the major solvents of calcium oxalate stones. Its positive impact on calcium oxalate dissolution was related to lowering supersaturation of human urine [96]. Therefore, lysine injection could effectively prevent the formation or further development of calcium oxalate stones. Finally, both experimental and clinical studies of

**Table 29.3** Results of direct chemolysis of struvite calculi.

| Irrigating solution | Primary (1°) or adjuvant (2°) | Dissolved/ attempted | Duration of irrigation (days) | Comment |
|---|---|---|---|---|
| **Suby's solution G** | | | | |
| Smith et al., 1979 [11] | 1° | 2/2 | 5–9 | Patients had ileal conduits |
| | 2° | 1/1 | NA | |
| Suby and Albright, 1943 [77] | 1° | 3/7 | 10–90 | |
| | 2° | 1/1 | | |
| **Renacidin** | | | | |
| Nemoy and Stamey, 1971 [4] | 1° | 3/3 | 12–30 | Prophylactic irrigation used |
| | 2° | 4/4 | 1–14 | |
| Dretler and Pfister, 1983 [17] | 1° | 16/23 | 6–45 | |
| Spirnak et al., 1988 [23] | 2° | 9/11 | 2–8 | SWL 1.2 times per kidney |
| Silverman and Stamey, 1983 [63] | 2° | 5/11 | 4.5 (avg) | |
| Rudman et al., 1983 [74] | 1° | 2/2 | 14–17 | 9% recurrence at 66 mo follow-up |
| | 2° | 18–21 | 2–26 | |
| Mulvaney, 1959 [78] | 1° | 17/31[a] | NA | Kidney/bladder/ureteral stones |
| Dretler et al., 1984 [46] | 1° | 6/8 | 7–20 | |
| Russell, 1962 [81] | 1° | 2/2 | 10–13 | |
| Kohler, 1962 [82] | 1° | 4/5 | 14–115 | |
| | 2° | 4/6 | 12–120 | |
| Brock et al., 1980 [83] | 1° | 3/4 | 2–9 | Patients had ileal conduits |
| Palmer et al., 1987 [84] | 1° | 7/9 | 6–69 | Outpatient treatment performed |
| | 2° | 7/9 | 3–30 | |
| Blaivas et al., 1975 [85] | 2° | 8/11 | 2–21 | |
| Jacobs and Gittes, 1976 [86] | 2° | 7/11 | 2–22 | |
| Nemoy and Stamey, 1976 [87] | 2° | 2/2 | 8–15 | |
| Kleine et al., 1982 [88] | 2° | 8/9 | 4–34 | |
| Angermeier et al., 1993 [89] | 2° | 3/3 | 1–8 | SWL and PCNL irrigation with pressure control pump |
| Totals | 1° | 65/96 | 14 (avg) | |
| | 2° | 77/100 | 9 (avg) | |

[a] Includes partial dissolutions.

SWL, extracorporeal shock-wave lithotripsy; NA, not applicable; PCNL, percutaneous nephrolithotripsy.

*Source:* Adapted from Fried and Smith, 2007 [13].

hyperoxaluria-associated calcium oxalate kidney stone formers showed that oxalate-degrading microorganisms are capable of and important in regulating urinary oxalate levels. Preliminary experiments suggest that oxalate decarboxylase and oxalate oxidase can actively dissolve calcium oxalate crystals. Therefore, it seems reasonable to start using oxalate-degrading microorganisms with their free enzymes to enhance natural dissolution of calcium oxalate stones [97]. In the future, these manipulations may play a role in dissolution or prevention of calcium oxalate calculi, but they have not yet been proven in clinical practice.

## Summary

In summary, percutaneous chemolysis is an adjuvant treatment option for certain types of stones in highly selected cases. The choice of chemolytic agent and method of administration is dependent primarily on stone composition and should be tailored to the individual clinical scenario. There are several chemical means to increase the solubility of a stone. Manipulation of the pH is most commonly used. However, other modalities include disulfide rearrangement and cation chelation [18]. Manipulation of pH works particularly well for uric acid stones since they are 11 times more soluble at a pH of 6.5 than pH of 5.0 [27, 98]. An effective therapeutic pH of slightly above 7.0 can often be achieved with oral therapy alone but direct chemolysis should be considered for large stone burden [99]. Struvite stones will dissolve at pH of 4.9, but at a rate too slow to be clinically useful [100]. Therefore, other approaches, including systemic chemolysis with urease inhibitors or direct chemolysis with renacidin solution could be considered. The solubility of cystine is increased in alkaline urine, but is higher than that required to dissolve uric acid (pH of 7.5). At a pH of this range, there is an increased risk of secondary precipitation. Therefore, cystine stones can be more effectively treated with direct chemolysis using disulfide exchange resins. Calcium stones are the least amenable to chemolysis, but some success has been shown with EDTA chelation. However, toxicity to the urothelium limits the usefulness of this approach.

Finally, in a cost-conscious healthcare system with rising costs of hospitalization and limited inpatient beds, it is increasing difficult to admit patients for direct chemolysis of stones. Therefore, percutaneous chemolysis for dissolution of calculi is reserved for patients who are poor surgical candidates for minimally invasive endourologic procedures.

## Chemotherapy and immunotherapy for upper tract transitional cell carcinoma

UTTCC accounts for less than 5% of all urothelial cancers and 10% of renal tumors [101]. Nephroureterectomy with excision of a bladder cuff is the gold standard of care for UTTCC, especially for patients with high-grade, muscle-invasive, or multifocal disease with a normal contralateral kidney. Organ-preserving procedures that include ureteroscopic or percutaneous resection and segmental ureterectomy have been reserved typically for patients with solitary kidney, bilateral disease, poor renal function, small tumor burden, and low-grade disease [102]. The advent of improved endourologic techniques facilitates access to any part of the upper tract so that tumor location is no longer a limiting factor. Tumors such as large renal pelvic and proximal ureteral lesions which cannot be adequately treated with retrograde ureteroscopic approach can be resected percutaneously. Although endoscopic approaches for treatment of UTTCC have traditionally been reserved for patients with contraindications to nephroureterectomy, they could be offered to patients with low-grade solitary UTTCC lesions and normal contralateral kidneys [103].

Adjuvant topical immunotherapy or chemotherapy after endoscopic resection of UTTCC has been used in an attempt to reduce the risk of recurrence and progression. Bacillus Calmette–Guérin (BCG), mitomycin C, and thiotepa are the most common agents used. Their use as adjuvant topical agents has been extrapolated from their benefit in the management of superficial bladder transitional cell carcinoma. However, the role of these adjuvant topical agents for the treatment of UTTCC is not well defined [103].

There are several important considerations when using a topical chemotherapeutic agent rather than a chemolytic or antifungal agent. In terms of mode of instillation, the antegrade approach has been hypothesized to maximize contact of the agent with the urothelium and minimize contact interference between the agent and the retrograde ureteral stent [104]. However, this approach predisposes to the theoretical risk of nephrostomy tract seeding. Nevertheless, there are no available data to advocate one approach over another [105].

High pressures in the renal pelvis and extravasation after BCG application must be avoided. For the antegrade approach, the patency of the ureter to the bladder must be verified before each perfusion using contrast media. This also excludes any pyelovenous or pyelolymphatic backflow. If the nephrostomy tract was used for resection of the UTTCC, initiation of adjuvant BCG therapy is usually delayed for 2–3 weeks to allow for healing of the urothelium, thereby decreasing the risk of systemic side-effects. Furthermore, BCG must not be instilled in the presence of gross hematuria for fear of severe systemic complications.

Oosterlinka et al. described a method of instilling BCG in an antegrade fashion into the upper tract. A dose of 360 mg Immuno BCG Pasteur F (Institut Pasteur, Paris, France) or 243 mg ImmuCyst® (Sanofi Winthrop, Meyriez, Switzerland) is dissolved in 150 ml of normal saline. This is the same concentration but three times the dose and volume that is used intravesically. The flask is placed 20 cm above the level of the kidney of the supine patient. A continuous flow of approximately 1 ml/min (15–20 drops per min) is maintained for 2 hours [106]. After the perfusion is finished, the nephrostomy tube is clamped. Patients receive ampicillin prophylactically and are kept under hospital surveillance for one night. BCG instillations are repeated on a weekly basis for six weeks [107].

For the retrograde approach, it is advised not to use ureteral catheters larger than 5 Fr to allow drainage along the ureteral catheter to the bladder. It is very helpful to use fluoroscopy, at least for the first session, to establish proper catheter position and rule out unexpected anatomical difficulties. Free flow of urine from the catheter or retrograde injection of contrast verifies proper position in the collecting system. Ureteral catheters are secured via silk ties to a Foley catheter placed to drain the bladder and brought to rest at the bladder neck. The Foley catheter is either left to straight drainage or elevated over the bedrail to allow some collection into the bladder, depending on whether simultaneous bladder exposure is desired. It may also be capped during treatment if formal intravesical instillation is performed at the same time. The viscosity of the full-dose BCG suspension is such that it will not spontaneously drip under gravity instillation through such a small 4 Fr catheter. Therefore, low-dose BCG (one-third to one-tenth standard dose) plus interferon-α (50–100 million units) in 50 ml normal saline is used with the retrograde approach [102]. The patient is positioned supine and the medication is suspended in an intravenous bag no more than 30 cm above the kidney level. Medication is instilled via micro drip tubing at the rate of 1 drop per 2 seconds, corresponding to a rate of approximately 30 ml/h. The drug is only instilled via gravity and should never be placed on a pump for fear of increased intrarenal pressure. At the end of treatment, the Foley catheter is drained and then removed with the attached ureteral catheters.

A novel approach to gain upper tract BCG exposure was reported by Herr in a patient with grade 3 renal pelvic transitional cell carcinoma and carcinoma *in situ* in an ectopic solitary kidney [108]. After open surgical resection, a freely refluxing pyelovesical anastomosis was constructed. The patient received six-weekly intravesical instillations of BCG and subsequently remained recurrence-free at 13 months follow-up. Ramsey and Soloway [109] reported a similar approach accomplished by creating a freely refluxing system after autotransplantation of a solitary kidney with recurrent pyelocalyceal transitional cell carcinoma. For patients with refluxing urinary diversions, mitomycin C or BCG can be delivered via a catheter placed into the conduit or reservoir.

A substantial proportion of patients with endoscopically managed UTTCC will develop a recurrence. Adjuvant topical immunotherapy or chemotherapies have been used in an attempt to reduce the risk of tumor recurrence and are often reserved for patients with large, multifocal, or residual tumor. The true benefit of topical therapy, either as a primary treatment of carcinoma *in situ* or as adjuvant therapy for endoscopically treated UTTCC, is difficult to assess due to heterogeneous groups of patients receiving such therapy (solitary vs. multifocal disease, primary vs. recurrent, low- vs. high-grade) [102]. These retrospective case series are summarized in Table 29.4. Here we present the three most common agents used.

### Bacillus Calmette–Guérin (BCG)

BCG, a live attenuated strain of *Mycobacterium bovis*, first indicated as a tuberculosis vaccine, has had widespread use in intravesical immunotherapy since the 1970s [130]. It has since then become the drug of choice for treatment of carcinoma *in situ* in addition to being an effective prophylactic agent against recurrences following transurethral resection of high-grade superficial bladder tumor [131–133].

The mechanism of action has been intensively investigated. BCG directly binds to fibronectin within the urothelium, subsequently leading to direct stimulation of a cell-based immunologic response. Numerous cytokines involved in the initiation or maintenance of inflammatory processes, including tumor necrosis factor-α, granulocyte–macrophage colony-stimulating factor, interferon-γ, and interleukins are induced. This immunologic response activates cell-mediated cytotoxic mechanisms that are believed to underlie the efficacy of BCG in the prevention of recurrence and progression [134].

Most patients develop an inflammatory immunologic response to BCG during a typical induction course of six-weekly instillations. Optimal dosing and instillation schedules have not yet been established but some recent trials have demonstrated that a reduced dosing regimen (one-third dose) may be as effective as standard dosing but with fewer side-effects [135–137]. Studer et al. [107] first demonstrated the feasibility and efficacy of using BCG in the upper urinary tract. They treated 10 renal units that had cytologic evidence of carcinoma *in situ* with BCG delivered via a percutaneous nephrostomy tube. In seven of the ten renal units, urinary cytology reverted to negative. Although complications were few, BCG sepsis did develop in one patient, necessitating cessation of therapy. Since then, several other studies have demonstrated the safety and efficacy of intracavitary topical therapy in combination with endoscopic management in UTTCC as shown in Table 29.4 [103, 110–129, 138–142].

There have been no randomized trials comparing endoscopic treatment of UTTCC with or without BCG. Results achieved with intracavitary topical therapy have been varied. Although some authors found intracavitary topical therapy to be beneficial in terms of recurrence and disease-free survival, but not in overall survival, others found no benefit. In one of the largest series of adjuvant therapy for UTTCC, Thalmann et al. [103] retrospectively evaluated the results of BCG therapy in patients not eligible for nephroureterectomy. Thirty-seven patients (22 with carcinoma *in situ*, 15 with Ta or higher after endoscopic resection) were treated with six perfusions of BCG given once a week via a 10 Fr nephrostomy tube. At a median follow-up of 42 months, 14 patients (38%) died of urothelial cancer, 11 (29%) of other causes, and 12 (33%) were alive. Other adverse outcomes included severe septicemia in 2 patients. There was no seeding of the nephrostomy tube tract and dialysis was avoided. Overall median survival was 42 months (range 1–137 months) with median recurrence-free survival of

**Table 29.4** Studies evaluating topical instillation of the topical chemo/immunotherapy for upper tract urothelial cancer.

| Study | Indication | Patients/renal units, *n* | Therapy | Mean FU, mo | Comments |
|---|---|---|---|---|---|
| Thalmann et al., 2002 [103] | Not eligible for open surgery | 37 /41 | BCG | 42 | 87% recurred or progressed; 32% CIS disease-free |
| Eastham et al., 1993 [110] | Adjuvant to endoscopy | 7/7 | MMC | 12 | 2/7 (29 %) recurrence |
| Jarret et al., 1995 [111] | Adjuvant to percutaneous treatment | 17/19 | BCG | 55 | No significant improvement in survival with BCG |
| Elliott et al., 1996 [112] | Adjuvant to endoscopy | 18 patients | Thiotepa, MMC, BCG | NA | No different in outcome between treated and untreated |
| Yokogi et al., 1996 [113] | CIS | 5/8 | BCG | 10–46 | NED in 5/8 renal units |
| Martinez-Pineiro et al., 1996 [114] | Adjuvant to endoscopy | 32 /36 | BCG, MMC, thiotepa, IFN-α | 30.7 | 12.5% recurrence with BCG, 14.2% with MMC, 60% with thiotepa |
| Patel and Fuchs, 1998 [115] | Adjuvant to ureteroscopy | 13/17 | BCG | 14.6 | NED in 15/17 renal units |
| Nishino et al., 2000 [116] | CIS | 6 /8 | BCG | 22 | NED in 8/8 renal units |
| Nonomura et al., 2000 [117] | CIS | 11 patients | BCG | NA | NED in 7/11 patients |
| Chen et al., 2001 [118] | – | 15/23 | BCG/IFN-α | 15.3 | 70% response rate (74% for CIS) |
| Miyake et al., 2002 [119] | CIS | 16 patients | BCG | 30 | NED in 13/16 patients |
| Palou et al., 2004 [120] | Adjuvant to percutaneous treatment | 19 patients | BCG:14<br>MMC: 5 | 51 | 57.9% recurrence in treated patients vs. 26.7% in untreated patients |
| Katz et al., 2007 [121] | CIS, adjuvant to endoscopy | 10/11 | BCG–IFN-α | 24 | 80% complete response, 20% partial response |
| Rastinehad et al., 2009 [122] | Adjuvant to endoscopy | 50 units | BCG | 80.8 | Comparable treated and nontreated groups; 8/50 (36%) recurrence |
| Giannarini et al., 2011 [123] | Adjuvant to endoscopy | 22 units | BCG | 42 | 13/22 (59%) recurrence |
| Keeley and Bagley, 1996 [124] | Adjuvant to ureteroscopy | 19/21 | MMC | 30 | 35% complete response, 27% partial response, and 38% no response |
| Smith et al., 1987 [125] | Adjuvant to endoscopy | 6/6 | MMC (1)<br>BCG (5) | 9.5 | 1/6 (17%) recurrence |
| Schoenberg et al., 1991 [126] | Adjuvant to endoscopy | 9/9 | BCG | 24 | 1/9 (11%) recurrence |
| Clark et al., 1999 [127] | Adjuvant to endoscopy | 17/18 | BCG | 11 | 6/18 (33%) recurrence |
| Jabbour and Smith, 2000 [128] | Adjuvant to endoscopy | 13 units | BCG | 59 | 3/13 (23%) recurrence |

FU, Follow-up; BCG, bacillus Calmette–Guérin; MMC, mitomycin C; CIS, carcinoma *in situ*; IFN, interferon; NED, no evidence of disease; NA, not applicable.
*Source:* Adapted from Rastinehad et al., 2009 [122] and Audenet et al., 2013 [129].

21 months (range 1–137 months). The authors noted that this was a patient population with a poor prognosis, and while BCG extended survival for some patients, it did not provide cure except for some patients with carcinoma *in situ*. Of the patients treated in the adjuvant setting for papillary disease, only 13% remained without recurrent or progressive disease with a median time of recurrence of 10 months. In contrast, treatment of carcinoma *in situ* resulted in 32% of renal units remaining disease-free for a median follow-up of 51 months.

A recent update of this retrospective series with 64 renal units and a median follow-up of 42 months (range: 2–237) showed recurrence of UTTCC in 30 of 64 renal units (47%), including 17 of 42 (40%) patients with Tis and 13 of 22 (59%) patients with Ta/T1 tumors [123]. There was progression of UTTCC in 11 of 64 renal units (17%), 2 of 42 (5%) patients with Tis and 9 of 22 (41%) patients with Ta/T1 tumors. Nephroureterectomy was performed eventually in 7 of 64 renal units (11%), 2 of 42 (5%) with Tis and 5 of 22 (23%) with Ta/T1 tumors. Not surprisingly, patients with Tis had better recurrence-free survival ($P = 0.42$) and significantly better progression-free survival ($P; < 0.01$) and nephroureterectomy-free survival ($P = 0.05$) when compared with patients with Ta/T1 tumors [123]. Since this study did not include any controls, it could not determine whether intrarenal instillation of BCG was associated with any survival advantage.

Orihuela and Smith [139] found a recurrence rate of 80% among patients who did not receive supplemental BCG versus a recurrence rate of 16.6% among those who did. However, an update of their series could not ultimately demonstrate a survival advantage with the addition of adjuvant BCG [111]. Rastinehad et al. [122] retrospectively studied 133 renal units treated by percutaneous resection for UTTCC. Eighty-nine renal units treated primarily by percutaneous resection were then analyzed. Fifty renal units received adjuvant BCG therapy two weeks after endoscopic management for a total of six courses. Recurrence was defined as a positive biopsy result after the third-look nephroscopy. Overall median follow-up was 40.8 months. There was no statistical difference with regard to tumor grade or stage between treated and nontreated groups. Recurrence, time to recurrence, and progression of disease among renal units treated with BCG were subselected by grade and compared with the corresponding nontreated group. There was no statistical significance demonstrated between any of the treated and nontreated groups. The authors concluded that there is no overall oncologic benefit in the administration of adjuvant BCG with regard to disease recurrence, interval to recurrence, and progression of disease in the treatment of UTTCC. The latest analysis of this retrospective series from Smith's group included 141 patients with median follow-up of 66 months [143]. Nephroureterectomy was avoided in 87% of patients. Recurrence occurred in 37% of low-grade UTTCC patients and 63% of high-grade UTTCC patients, with a median time to recurrence of 71.4 versus 36.4 months, respectively. On multivariate analysis, grade was the only predictor of recurrence (HR 2.12, $P = 0.018$). Disease in one patient recurred after 116 months of surveillance, emphasizing the importance of long-term follow-up after endoscopic management of UTTCC. Similar to their previous analysis, BCG and mitomycin did not protect against recurrence, progression to nephroureterectomy, or death over resection alone [143].

Similarly, Martinez-Pineiro et al. [114] have shown reduction in recurrence rates with addition of BCG or mitomycin C following endoscopic treatment of UTTCC. The authors reported a recurrence rate of 50% among patients with grade 2 or 3 disease who were not treated with adjuvant therapy, versus a recurrence rate of 27.7% among a similar group of patients who received some form of adjuvant therapy. They used several drugs in that study, including BCG, mitomycin C, 5-fluorouracil, thiotepa, and interferon-α, from which only BCG and mitomycin C were promising. Finally, Katz et al. [121] published their initial experience with BCG plus interferon-α2b. With a median follow-up of 24 months, 80% demonstrated a complete response, while 20% had a partial response (decrease in tumor size, number, or both). The authors reported that the treatment was well tolerated in the office setting and did not note any complications.

In contrast, other studies have not shown a significant difference between patients treated with adjuvant mitomycin C or BCG compared to those undergoing endoscopic treatment alone [112, 144]. Hayashida et al. [145] reported a 50% disease recurrence rate after a follow-up of 50.9 months using intrarenal perfusion of BCG with endoscopic treatment. This high recurrence rate occurred despite an initial return of cytology results to normal and all of these patients suffered cancer-specific mortality.

There are several known complications of cavitary BCG therapy. Persistent fever after BCG administration has been reported in 3 out of 59 (5.1%) patients in a combined series. However, this resolved in all cases with appropriate antimicrobial therapy [111, 114, 144]. Granulomatous involvement of the upper urinary tract may occur in up to 25% of patients after BCG administration [146]. Therefore, it is important to obtain percutaneous biopsy of renal masses that develop in patients who have received intracavitary BCG prior to deciding on their management [147]. In addition, these renal granulomas could be observed in asymptomatic patients and they may resolve without antituberculous medications [147].

The controversy and variability among studies addressing intracavitary use of BCG as an adjuvant therapy for UTTCC are likely the result of lack of prospective randomized studies and reliance on retrospective case series with their inherent biases in patient selection. Some authors treat all patients with adjuvant therapy while others treat only high-risk patients. Furthermore, it is important to note that there are several products containing different substrains of BCG. There is variability of BCG organisms per milligram of vaccine with different substrains and variability from lot to lot within the same substrain [148, 149]. Thus, the true efficacy of adjuvant BCG therapy for UTTCC has yet to be adequately evaluated. However, secondary effects of therapy seem to be generally well tolerated among patients.

## Mitomycin C

Less information is available on the use of intracavitary mitomycin C topical treatment compared with BCG. Mitomycin C is a 334 kDa alkylating agent that inhibits DNA synthesis. Because of its moderately high molecular weight, there are few problems with transurothelial absorption. Therefore, side-effects such as myelosuppression are rare with mitomycin C. The typical dosage varies from 20 to 60 mg per instillation, and the most commonly used dose is 40 mg in 40 ml of saline or sterile water administered weekly for eight weeks.

Keeley and Bagley [124] reported on adjuvant mitomycin C (40 mg in three divided doses via ureteral catheter) in 19 patients (21 renal units) for high-volume, recurrent or multifocal urothelial carcinoma. No systemic side-effects occurred during or after treatment with mitomycin C. Thirty-five percent had a complete response, 27% had a partial response (reduction in tumor size >50%), and 38% had no response. Tumors with a complete response were of similar size and grade as those that did not respond as well. After a mean follow-up of 30 months, none of the patients suffered local disease progression or died of disease; however, nearly all of the patients required repeat ureteroscopic treatment for residual or recurrent disease. At least one case has been reported of toxic agranulocytosis following absorption of extravasated mitomycin C [114].

An alternative experimental treatment regimen for UTTCC in refractory patients is sequential gemcitabine and mitomycin C. Medication dosage is 1 g gemcitabine in 50 ml phosphate-buffered normal saline, then 40 mg mitomycin C in 40 ml of sterile water. The gemcitabine is instilled followed by mitomycin C immediately afterward. In a group of patients with treatment-refractory non-muscle-invasive bladder cancer, 8 of 37 had upper tract involvement. Gemcitabine alone was effective in only 1 of 14 patients (7%) while sequential treatment with gemcitabine followed by mitomycin C was successful in 13 of 23 patients (57%) [150]. The rationale for sequential treatment is that gemcitabine is too acidic and affects mitomycin C activity if given together. In addition, gemcitabine primarily kills cells undergoing DNA synthesis (S-phase) while mitomycin C is non-cell phase-specific and leads to cell cycle arrest. Gemcitabine is given first followed by mitomycin C to maximize therapeutic efficacy. Some authors feel that improvement of outcome can be achieved by overnight fasting, and the use of sodium bicarbonate to reduce drug degradation, and an increased concentration to 40 mg in 20 ml [151].

### Thiotepa

Thiotepa (triethylenethiophosphoramide) is an alkylating agent and is not cell cycle specific. Introduced in 1961, thiotepa is the oldest and one of the least expensive of the intravesical drugs. Doses range from 30 to 60 mg in 30–60 ml of sterile water or saline. The lower dose appeared to be as effective as the higher one in a comparative study when the concentrations were the same [152]. The Medical Research Council Working Party on Urological Cancer reported that the lower concentration of 30 mg in 50 ml was not effective [153]. The usual regimen consists of six to eight weekly instillations. A low molecular weight of 189 kDa allows partial absorption through the urothelium with possible systemic toxicity. Myelosuppression is a risk, especially with the 60 mg dose. Complete blood count is obtained before each instillation and treatment is delayed if necessary. Thiotepa is evaluated much less than other topical agents as adjuvant therapy after endoscopic management of UTTCC [112, 114].

### Summary

Of interest, renal function was not impaired after instillations of either BCG or mitomycin C. In most cases, the adverse events which could result from administration of such immunotherapy or chemotherapy can be avoided by maintaining low intrapelvic pressures during administration. Although the cumulative experience appears encouraging regarding the efficacy of topical immunotherapy, especially against carcinoma *in situ*, no individual study has shown statistical improvement in relation to survival. This could be the result of insufficient numbers of patients to examine the clinical significance of the drug and inadequate delivery of the drugs in adequate concentrations over a proper period of time to enable a clinical response when compared with lower tract transitional cell carcinoma [7]. There is no doubt that larger prospective studies are needed to settle this issue. It is apparent that most published series regarding percutaneous adjuvant therapy suffer from selection bias secondary to their retrospective design and involve few patients with short follow-up, making it difficult to reach any meaningful conclusion. As yet, no study has shown statistical improvement regarding survival and no protocol of treatment has been accepted. None of the published series have evaluated the role of maintenance therapy, likely because of access problems. Randomized multicenter trials are needed to evaluate the role of adjuvant topical therapy.

## Antifungal therapy

Upper urinary tract fungal infections are rare and are usually associated with diabetes, chronic renal failure, long-term antibiotic usage, immunosuppression, and terminal malignancy. Diagnosis is based on microscopic examination of urine and specific fungal culture. Histopathological examination of fungal balls will demonstrate the fungus. Recently, polymerase chain reaction has been used to detect candidemia in patients with candiduria and to detect candiduria before the culture reports are available [154, 155]. Opportunistic pathogens such as *Candida*, *Aspergillus*, *Mucor*, *Cryptococcus*, and *Histoplasma* are particularly known to infect the kidneys in predisposed individuals with serious complications. These infections are often insidious, and their diagnosis is usually delayed because of the coexisting illnesses [156, 157]. Renal involvement by fungi has been found to be associated with increased morbidity and mortality, particularly in cases of infections by angioinvasive fungi such as *Aspergillus* and *Mucor* [158–160].

Fungal infection may be systemic with secondary involvement of the urinary system or may originate in the urinary tract and then disseminate hematogenously. The use of an indwelling urethral catheter and administration of multiple antibiotics increases the risk of dissemination of urinary fungal infections [161]. These infections of the urinary tract must be diagnosed quickly and treated aggressively. If these infections are improperly treated, they can cause urinary obstruction through formation of accretions called fungal balls [162–164]. Fungal balls cause hydronephrosis, oliguria or even anuria, destruction of renal parenchyma, widespread dissemination of the organism, and death of the patient [165].

Percutaneous antifungal irrigation permits administration of highly toxic antifungal drugs to patients with localized infection, thereby minimizing systemic side-effects [166, 167]. Systemic antifungal agents have been successfully used but in the presence of an obstructed kidney due to extensive fungal infection, drainage of the pelvicalyceal system is mandatory to salvage the kidney. Amphotericin B and its formulations, the azoles (fluconazole, itraconazole, voriconazole, and ketoconazole), caspofungin, and flucytosine are used to treat urinary fungal infections. Schelenz and Ross [2] reported that intravenous antifungal drugs (e.g. caspofungin or amphotericin B) are useful in treating or preventing candidemia during instrumentation such as insertion of nephrostomy tubes in cases of *Candida* pyonephrosis. However, they are unlikely to lead to cure if used as the sole treatment. Conservative management should also include local drainage of pus and fungi as well as instillation of an effective antifungal agent.

The present discussion is limited to the major drugs used as topical urinary antifungals, namely fluconazole and amphotericin B. It should be remembered that fungal infections involving the genitourinary tract are frequently a part of multiorgan systemic disease, often involving an immunocompromised host.

## Fluconazole

Fluconazole is a triazole antifungal agent that is less toxic and more efficient than other imidazole members; it is safe in infants and children. The drug inhibits the cytochrome P-450 enzyme responsible for conversion of lanosterol to ergosterol, which is the major sterol of most fungal cell membranes. Fluconazole is highly water soluble and can be administered intravenously or orally. It is cleared primarily by renal excretion, with approximately 80% of the dose excreted as unchanged drug [168]. Fluconazole administered by mouth or by intravenous route achieves high urine levels [169]. In general, the drug is safe and well tolerated, even in very large doses. The most common adverse reactions are gastrointestinal disturbances.

Systemic fluconazole therapy can be effective in treating candiduria. In one series, orally administered fluconazole (100 mg twice daily for 10 days) eradicated candiduria in 19 of 20 critically ill patients, which was comparable to amphotericin B bladder irrigations [170, 171]. It is important to note that an elevated serum creatinine value is associated with a reduced rate of fungal eradication from the urine with systemic fluconazole therapy. This is likely related to lower urinary levels of fluconazole in patients with reduced renal function [172]. Therefore, in patients with renal impairment direct irrigation may be more effective at treating candiduria.

Fluconazole used as a genitourinary irrigant has been reported as an effective antifungal bladder irrigant [173]. Percutaneous fluconazole irrigation was successfully used to treat candidiasis in nephrostomy tubes that was unresponsive to systemic intravenous form [167]. Fluconazole solution was used as an antifungal irrigant in 20 patients with nephrostomy tube or suprapubic catheter who presented with two positive urine cultures for *Candida*. In 17 patients (85%), *Candida* was eradicated from the urine by the third to sixth day of irrigation. No side-effects were noted [174].

## Amphotericin B

Amphotericin B was first isolated as a byproduct resulting from the fermentation process of *Streptomyces nodosus* and is a member of the polyene macrolide class of antibiotics [175]. Depending on the drug concentration and susceptibility of the organism, amphotericin B may be either fungistatic or fungicidal. It binds to the sterol ergosterol that is present in the cell wall of susceptible fungi, leading to an alteration of the cell wall permeability and thereby causing leakage of cell components, with subsequent cell death. Oxidation-dependent amphotericin B-induced stimulation of macrophages of the host cells also may contribute to its antifungal properties [176]. Amphotericin B deoxycholate has been used in the treatment of most of the fungal infections, with nephrotoxicity being the most common serious chronic adverse effect [177]. Fortunately, this azotemia is usually reversible and sodium loading with intravenous saline and hydration may prevent or reduce the severity of the nephrotoxicity.

In an effort to reduce systemic side-effects, new formulations of amphotericin B have been developed. These formulations encapsulate amphotericin B in lipid vehicles, which are taken up by the reticulo-endothelial system concentrated in liposomes. Monocytes/macrophages in the peripheral blood are thought to take up the drug-laden liposomes and move them to the site of infection. Once these lipid complexes reach the site of action, free active drug is thought to be released through the action of phosolipases [168].

Bladder irrigation with amphotericin B is widely used and has become a standard treatment, although it has not undergone controlled trials [175, 178–182]. Tuon et al. [183] found that amphotericin B bladder irrigation (ABBI) showed a higher clearance of the candiduria 24 hours after the end of therapy than fluconazole. This was confirmed by fungal culture five days after the end of both therapies. The evaluation of ABBI using an intermittent or continuous system of delivery showed an early candiduria clearance (24 hours after therapy) of 80% and 82%, respectively. The use of continuous ABBI for more than five days showed a better result (88% vs. 78%) but this was not statistically significant. Although ABBI has been used in clinical practice, its use is not standardized, and some authors question whether ABBIs have any diagnostic or therapeutic value [184]. Others have advocated that amphotericin B no longer be used in the management of candiduria [170]. Removal of the urinary catheter, if possible, is more beneficial for the patient than instillation of bladder irrigation with amphotericin B [185].

In cases of pyonephrosis, the insertion of a nephrostomy tube for direct irrigation allows urinary diversion with subsequent improvement in renal function and enables the local administration of an antifungal drug directly to the site of infection [186]. Schelenz and Ross [2] demonstrated the limitation of intravenous antifungal agents such as caspofungin as the sole treatment of an obstructive upper urinary tract infection due to *Candida* species. In order to achieve long-term sustained cure from an obstructive pyonephrosis, pus and fungal balls should be drained and an antifungal agent such as amphotericin B deoxycholate instilled locally. An important issue in the management of pyonephrosis caused by such infections is the accumulation of pus and fungi in an obstructed space, such as the renal pelvices. As with other enclosed bacterial infections such as empyemas, drainage of the pus is of fundamental importance and may explain why systemic treatment with antifungals such as amphotericin B, caspofungin, or fluconazole alone have proven to be unsuccessful [167, 187]. Watson et al. [188] reported advantages of percutaneous upper urinary tract drainage as a potentially lifesaving adjunct in the treatment of pyonephrosis. Several case studies highlight the advantage of this maneuver in difficult cases involving obstruction due to extensive fungus.

Bartone et al. [189] reported on five neonates with obstructive urinary tract candidiasis in whom nephrostomy tubes had a major role in management. Eleven nephrostomy tubes were placed in seven patients (two neonates and five adults) who were identified to have renal fungal infections [186]. The nephrostomy tubes allowed prompt microbiologic diagnosis of fungal infection (*Candida albicans* in six patients; *Torulopsis glabrata* in one); urinary diversion with subsequent improvement in renal function, enabling systemic administration of potentially toxic antifungal drugs such as 5-fluorocytosine and amphotericin B (four patients); local irrigation with amphotericin B (four patients); guidewire fragmentation of fungus balls (two patients); and introduction of a Simpson atherectomy device to obtain biopsy specimens from an obstructing ureteral polypoid lesion (one patient).

Untreated or neglected candidiasis may progress to fungus ball or abscess formation. Sonography is commonly used as the initial imaging procedure but retrograde and antegrade pyelographies are used for biopsy, diagnosis, and treatment [190]. The advantages of nephrostomy tubes in this setting include prompt drainage of the obstruction, direct access to obtain specimens from the renal pelvis to confirm the diagnosis, direct irrigation of the fungus balls with amphotericin B, and an access route for fragmentation of fungus balls by guidewire manipulation [186]. Placement of nephrostomy tubes with antegrade amphotericin B irrigation, coupled with systemic antifungal therapy, is the mainstay of treatment for pyonephrosis.

Streptokinase has also been used in conjunction with amphotericin B in the treatment of pyonephrosis. Hutton [191] reported a problematic case in which a very low birth weight infant with obstructing ureteropelvic junction fungal balls that was refractory to standard measures of adequate nephrostomy tube drainage, pelvic irrigation with amphotericin B, and systemic antifungal treatment. In an attempt to avoid potentially difficult open surgery, the author used streptokinase solution (3000 IU/ml) for irrigation. This was successful in clearing the fungal balls, relieving obstruction and rendering the urine sterile. This case highlighted the potential role for streptokinase in cases of renal candidiasis refractory to current treatment protocols.

The role of antifungal agents for upper tract fungal infections will require ongoing investigation. However the relative rarity of this condition may preclude randomized trials. In cases of pyonephrosis the most reported approaches include placement of a nephrostomy tube and local instillation of an antifungal agent such as amphotericin B. The advantage of topical intracavitary treatment is that highly toxic medications can be delivered to the site of infection rather than systemically, which can minimize potential side-effects.

## Conclusions

Percutaneous therapy delivers medications or chemotherapeutics directly into the collecting system and can be highly effective at targeting the pathology. Direct therapy allows high local concentrations to be delivered while avoiding potential systemic complications. Stone dissolution through chemolysis remains an option for patients with multiple comorbidities and high surgical risk for minimally invasive endourologic procedures. Chemolysis is most useful for the treatment of uric acid stones when oral medical therapy is not feasible in the context of a patient who is noncompliant or cannot tolerate oral sodium or potassium salts. Direct chemolysis can also be used for dissolution of cystine and struvite stones. There is no clinically useful irrigant for dissolving calcium oxalate calculi. Chemolytic solutions may be used as primary therapy or as adjuncts to endourologic procedures. Intracavitary immunotherapy/chemotherapy is a useful adjuvant therapy following endoscopic management of noninvasive UTTCC with acceptable side-effects, but no individual study has shown statistical improvement with relation to survival. Percutaneous instillation of topical antifungal agents such as amphotericin B permits administration of highly toxic antifungal drugs to patients with localized infection, thereby minimizing systemic side-effects.

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# 30

# Percutaneous Treatment of Ureteropelvic Junction Obstruction

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## Introduction

Percutaneous endopyelotomy was one of the first minimally invasive surgical procedures to address a reconstructive operation. In patients with ureteropelvic junction (UPJ) obstruction the ultimate goal remains the relief of the obstruction in order to preserve renal function and reduce pain with minimal morbidity. Prior to the introduction of laparoscopic pyeloplasty, percutaneous endopyelotomy rapidly gained acceptance and became widely adopted in the management of UPJ obstruction, replacing open pyeloplasty [1].

However, being totally *endo*scopic, endopyelotomy can only address intrinsic factors of obstruction; extrinsic causes cannot be corrected. In UPJ obstruction, the renal pelvis is usually dilated or redundant. Classically, the volume should be reduced by resecting part of the wall, but this is not possible with a purely endoscopic procedure, neither redundancy of the renal pelvis. This probably explains its inferior success rate compared to pyeloplasty, especially when it is applied without selection [2–5]. As with many pioneering techniques, endopyelotomy has been superseded by newer techniques and is now less often performed (see Prognostic factors, patient selection, and results) [6–8]. It nevertheless retains its status as a landmark procedure, and could be regarded as one of the first natural orifice transluminal endoscopic surgeries (NOTES) to be routinely performed [7].

## Preoperative management

Preoperative evaluation of UPJ obstruction is mandatory with a view to documenting the following critical prognostic factors: the stricture (length, nature, and degree), the involved renoureteral unit (individual renal function, degree of hydronephrosis, remaining ureter), the presence of extrinsic factors (crossing vessels, bands), and the patient themselves (Box 30.1, Figure 30.1).

### Preoperative drainage

Preoperative decompression of the collecting system is advisable in totally obstructed cases, in case of active infection, or when there is a need to evaluate the function of the kidney. Tubular function recuperates in 10–15 days; glomerular function improves more slowly (up to three months). Despite its potential associated morbidity, we favor a small nephrostomy tube inserted under local anesthesia rather than a double-J stent, which commonly induces an inflammatory reaction at the UPJ that may later interfere with healing.

## Antegrade endopyelotomy

### Percutaneous endopyelotomy

For percutaneous endopyelotomy we start with the patient positioned prone in a split-legged position. A flexible cystoscopy is passed through the urethra into the bladder and a hydrophilic tipped guidewire is advanced up the affected side into the kidney. The cystoscope is then removed and a 5 Fr open-ended catheter is advanced up into the renal pelvis and secured. A 16 Fr Foley catheter is placed into the bladder. If this maneuver fails, the endoscopic route should be abandoned, since further attempts to localize an impassable UPJ usually are unsuccessful and an unguided incision is dangerous and may result in total separation of the ureter.

If the catheter is placed with the patient in the supine position, then they should be repositioned prone on the

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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**Box 30.1 Preoperative evaluation.**

**Stricture**

- Length
- Nature
- Degree

**Renoureteric unit**

- Renal function
- Degree of hydronephrosis
- Remaining ureter

**Extrinsic factors**

- Crossing vessels
- Bands, adhesions

**Patient**

- General risk factors
- Habitus
- Informed of procedure and its follow-up

table as for a classical percutaneous procedure Ideally, a posterior calyx is punctured and catheterized. A middle or superior calyx should be selected to secure an adequate working angle to the UPJ. The tract is dilated and the nephroscope is introduced. Secondary calculi are fragmented and extracted at this stage. The UPJ is easily identified by the protruding retrograde ureteral catheter. A second guidewire is introduced from above and down into the ureter. Streem describes placing the ureteral stent in an antegrade fashion prior to performing the incision using an acorn-tip Bugbee. The UPJ and proximal ureter can often be seen to bulge into the renal pelvis, such that a subsequent endopyelotomy is equivalent to a ureteral meatotomy at the ureterovesical junction. Having a stent in place at the onset of the procedure helps to better define the UPJ, and also obviates concern about avulsing the UPJ during placement of a stent after the UPJ has been incised [9] (see Video 30.1).

The best orientation for the incision is still a matter of debate. In a primary UPJ obstruction with no prior pyeloplasty, a lateral incision is made to avoid both a potential posterior and anterior crossing vessel [10]. In a patient who underwent a prior pyeloplasty and had a posterior crossing vessel displaced anteriorly, we prefer to make the incision posterolaterally. The incision is made through the entire thickness of the pelvic wall, the UPJ, and the narrow portion of the proximal ureter, and as far down as necessary to visualize a normal-caliber lumen, essentially performing an endoureteropyelotomy. A significant advantage of the direct percutaneous approach is the possibility of careful visual inspection of the pelvic wall, looking for pulsation transmitted from significant adjacent crossing vessels.

The second guidewire is advantageous to straighten and stiffen the ureter to be incised. Incision of the UPJ can be performed using a cold (straight or hooked) knife railroaded on the track, electric incision, or, more recently, the holmium laser. Equal success has been obtained with these different modalities. When the exact length of the abnormal ureter is in doubt, a dilation balloon is inserted

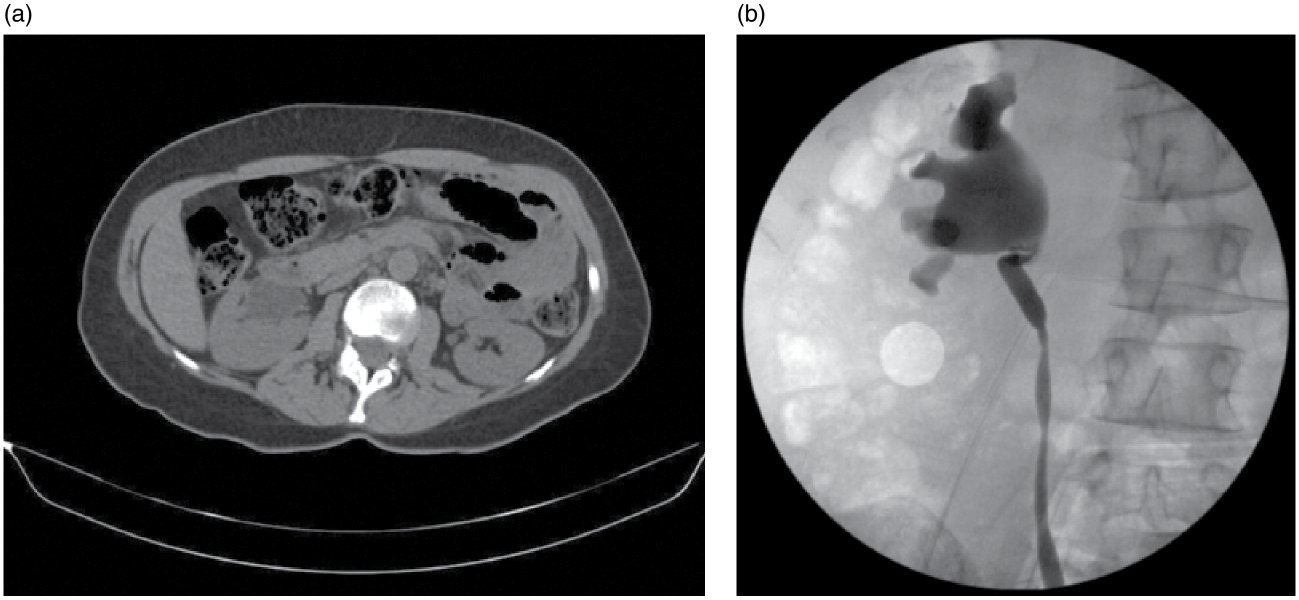

**Figure 30.1** (a) CT scan and (b) retrograde pyelogram showing right-sided hydronephrosis secondary to UPJ obstruction.

over the second guidewire and is inflated with contrast under fluoroscopic control, with care being taken to correct any residual or additional narrowed areas.

Prolonged stenting and drainage are deemed essential, although their exact duration is still a matter of controversy. A convenient drainage system consists of a 14/7 double-J stent, commonly referred today as an "endopyelotomy" stent (Figure 30.2), straddling the incised UPJ. Other drainage techniques including the traditional 8 Fr double-J stent have been used successfully, provided that extravasation is minimal and drainage is adequate. Our own practice has been to leave two traditional 7 Fr stents in parallel in an effort both to hold the UPJ widely open during the healing process and to provide maximum drainage. We typically do not leave a nephrostomy tube but a Foley catheter is placed to prevent reflux and further extravasation of urine through the endopyelotomy incision. In patients with a history of voiding dysfuction or a history of lower urinary tract symptoms, consideration to discharging them home with a Foley cather is made. The internal stent is removed under local anesthesia in the outpatient clinic after 4–6 weeks [1, 11, 12].

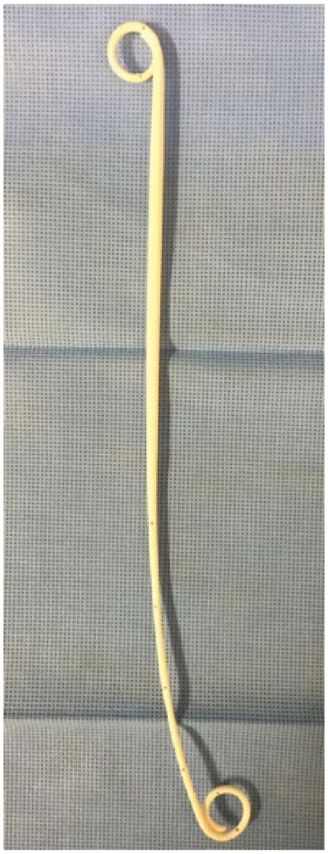

**Figure 30.2** Endopyelotomy stent. The proximal end measures 14 Fr and the distal end measures 7 Fr in diameter.

### Invagination technique

A safe UPJ incision may be facilitated by the modified technique described by Gelet and colleagues. Instead of using a simple open-ended ureteral catheter for the initial retrograde UPJ catheterization, a dilation balloon is used and inflated below the UPJ. After percutaneous access has been obtained, the inflated balloon is grasped from above and pulled inside the renal pelvis, invaginating the UPJ and proximal ureter. Using the holmium laser or a small electrocautery electrode, the double tissue layer (pelvis and ureter) is incised from inside the renal pelvis, down to the plastic balloon. If residual or additional narrowing is suspected, the balloon is reinflated on its way out to calibrate the ureter. When the balloon is deflated and removed from below, spontaneous reduction of the invagination occurs. Drainage and stenting are as in the procedure described earlier.

The invagination technique allows easier incision of the UPJ as the tissue is stabilized on the dilated balloon. It also reduces the risk of damaging crossing vessels, although such complications have occurred [13]. Few series have been reported in the literature, and this technique has unfortunately fallen out of favor to other more commonly practiced techniques.

## Endopyeloplasty

This ingenious procedure is a combination of endopyelotomy and pyeloplasty. Using a custom-made suturing device, a standard vertical endopyelotomy incision is sutured transversely (Heinecke–Miculikz principle). Its primary aim is healing of the endopyelotomy incision by primary intention with accurate suturing, minimizing fibrosis by avoiding urinary extravasation. Preliminary results for this nondismembered procedure appear promising. A totally dismembered procedure using the same suturing technique has been investigated. A feasibility study using a conventional suture with a lengthened 3.5 mm pediatric laparoscopic needle holder via the nephroscope was performed in 10 consecutive patients with promising results [14]. Unfortunately, these original series have not been duplicated, and to our knowledge endopyeloplasty is rarely performed [15, 16].

## Retrograde endopyelotomy

In order to further reduce the morbidity of the procedure, purely retrograde approaches have been devised. They share the advantage of avoiding percutaneous access to the kidney, decreased operative time, hospitalization, and patient morbidity. Modalities used to incise the UPJ include cold-knife, electrocautery, or, more recently, the holmium laser (Figure 30.3). Some of the limitations of retrograde endopyelotomy include difficulty inspecting for pulsation of crossing vessels, or the lack of direct visual control necessary for an exact incision in simple fluoroscopically guided cases [12]. With refinement in this technique over the years, this has become a widely established treatment option for UPJ obstruction [17].

## Ureterorenoscopic approach

In this technique a small-caliber ureterorenoscope is advanced up to the level of the UPJ and a lateral incision is performed under direct vision. The procedure may be facilitated by the preliminary insertion of a double-J stent, which then remains in place for 8–10 days. This maneuver, however, adds to the complexity of this technically difficult procedure, especially in muscular male patients. Most authors recommend the use of the flexible ureterorenoscope combined with the holmium laser. Although patient selection is a critical factor for the success of this technique, in experienced hands, success rates can be as high as 90% [17].

## Balloon dilation and rupture (“endoburst”)

A retrograde ureteropyelogram delineates the upper collecting system. A 24–30 Fr angioplasty balloon is inserted over a guidewire and positioned across the UPJ under fluoroscopic control. The balloon is inflated until wasting completely disappears. Several inflation/deflection cycles are recommended in order to ensure that no residual narrowing remains. An endopyelotomy stent is inserted over the initial guidewire. With few exceptions, long-term success with this technique has been inferior to that with incisional techniques [18, 19]. In a recent study by Xu et al. comparing retrograde balloon dilatation and

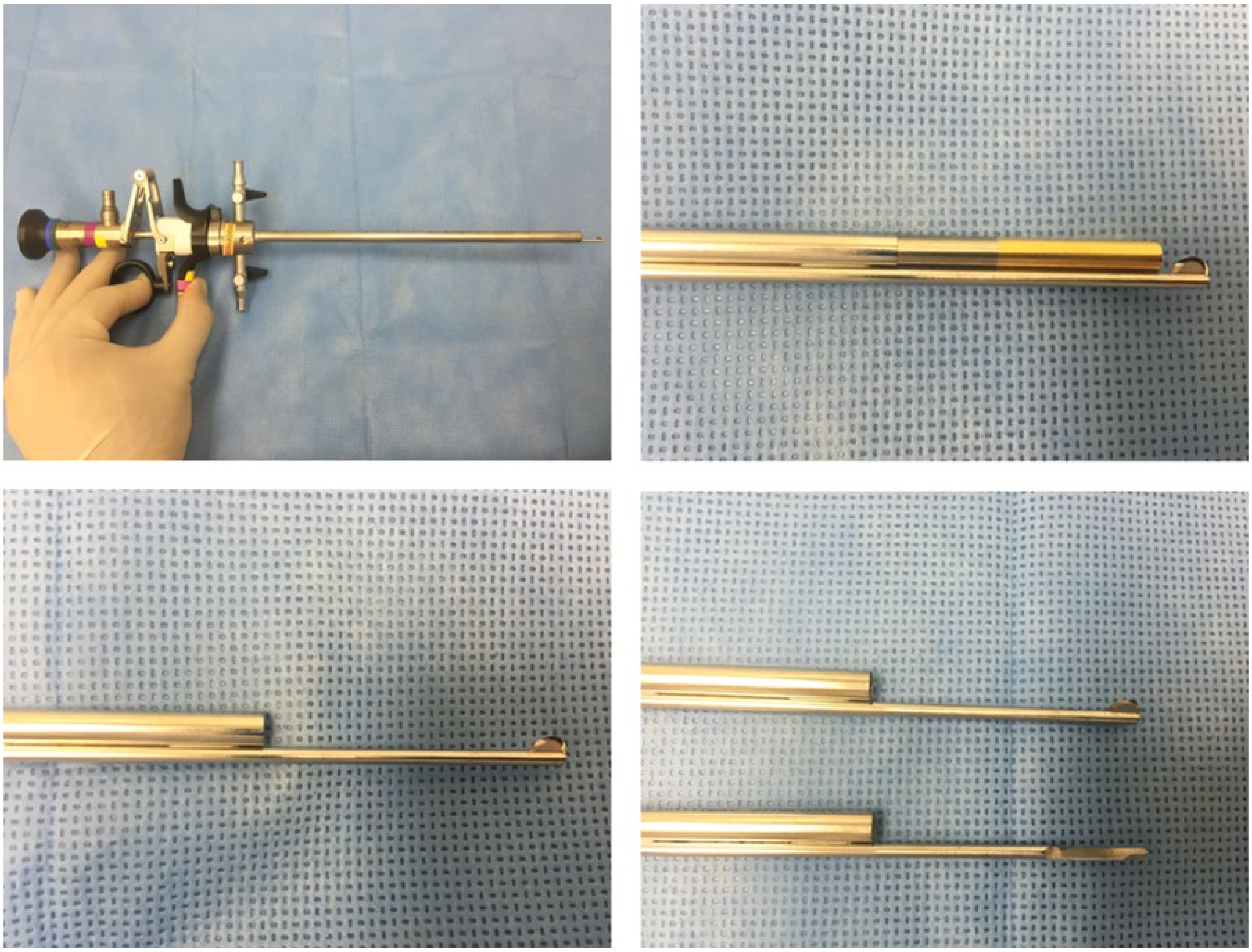

**Figure 30.3** Endopyelotomy using cold-knife. Various blades are available for the incision.

laparoscopic pyeloplasty for the treatment of UPJ obstruction, the 2-year success rate of laparoscopic pyeloplasty was 95.5%, compared to 71% for balloon dilatation alone. The authors recommended balloon dilatation for select patients as a method that is less costly, simpler, and easier to perform [20]. This technique can also be done in concert with an endopyelotomy incision.

### Balloon electrocautery incision: Acucise® endopyelotomy

The Acucise device is a 6 Fr catheter driving a 10/24 Fr low-pressure balloon fitted with an electrosurgical wire active over the 3 cm expendable portion of the balloon. The operative technique is similar to the one described earlier, except that the UPJ is not forcefully disrupted but cleanly cut by the electrosurgical wire that is activated during inflation of the balloon. Extravasation of contrast indicates that the incision has been completed. If there is doubt, flexible ureteroscopy and additional electrosurgical or laser incision under direct vision are recommended. The technique is safe and reliable, especially when the surrounding vascular anatomy of the UPJ has been ascertained by an appropriate imaging study [21]. Although initial results seemed promising [17], success rates in more recent series have been reported to be modest at best [22, 23].

## Laparoscopic and robotic pyeloplasty

The combination of laparoscopic and robotic pyeloplasty adds together the advantages of minimally invasive surgery (reduced morbidity) and open surgery (possibility to correct anatomic factors such as extrinsic obstruction, crossing vessels, and renal pelvis redundancy), and for many it has become the new gold standard. Both intraperitoneal and extraperitoneal approaches have been successful in achieving this goal. Laparoscopic pyeloplasty remains a difficult procedure, requiring considerable expertise; it is difficult to learn and to teach [7, 24]. The recent advance in robot-assisted procedures, albeit still costly, has increased the interest in this approach. Advantages include a shorter learning curve and greater ease of performing the anastomosis with wristed instrumentation and 3D visualization. Several series have reported a marked increase in the number of robotic pyeloplasties performed over the past decade [25, 26]. Today laparoscopic or robot-assisted laparoscopic pyeloplasty has become the procedure of choice for primary UPJ obstruction.

## Prognostic factors, patient selection, and results (Table 30.1)

Results for endopyelotomy fall somewhat short of those for contemporary pyeloplasty (67–95% vs. 95–100%) [3, 5]. As most endopyelotomy series using different techniques report approximately the same results, it is likely that selection criteria play a major role. Risk factors have been identified: the presence of vessels directly crossing the UPJ stands out as a major prognostic factor of outcome; a high degree of hydronephrosis or severely redundant pelvis; type of obstruction (length >2 cm); and renal function <25–30% [27, 28]. In such cases, laparoscopic or robotic pyeloplasty is preferred over endopyelotomy. Long avascular strictures and major alteration of renal function clearly contraindicate the procedure.

Several series have looked at the long-term outcomes of endopyelotomy. Knudsen et al. reported a success rate of 65 and 74% in primary and secondary UPJ obstruction, respectively, treated by antegrade endopyelotomy at a mean follow-up of 55 months. This group highlighted the need for long-term follow-up to identify late failures [29]. Although most failures will present within the first 20 months, late failures are not infrequent but do tend to stabilize after the fifth year [30, 31]. To demonstrate the importance of selection criteria, Butani and Eshghi performed a retrograde cold-knife endopyelotomy in 155 patients with strict inclusion

**Table 30.1** Therapeutic options for ureteropelvic junction obstruction.

| | |
|---|---|
| **Open surgery** | |
| Standard | Pyeloplasty |
| Salvage | Ureterocalycostomy<br>Autotransplantation<br>Transposition of renal vein (right)<br>(Nephrectomy) |
| **Minimally invasive surgery** | |
| Endoscopic | Direct: cold-knife, electrocautery, laser |
| Antegrade endopyelotomy | Indirect: invagination<br>Direct: ureterorenoscopic |
| Retrograde endopyelotomy | Indirect: under fluoroscopic control:<br>• Electroincision with cutting balloon<br>• Dilaceration with angioplastic balloon |
| Endopyeloplasty | Nondismembered<br>Dismembered (experimental) |
| Laparoscopic ± robotically assisted | Intraperitoneal<br>Extraperitoneal<br>(Nephrectomy) |

criteria (stricture length <2 cm, absence of severe hydronephrosis, renal function >25%), and reported a success rate of 96% and 85% for primary and secondary procedure, respectively, at a mean follow-up of 60 months [32]. These criteria likely play a major role in success rates of endopyelotomy.

In our view, now commonly shared but still debated, the presence of significant crossing vessels should be ascertained preoperatively as it significantly influences the outcome. Modern imaging techniques, such as spiral computed tomography (CT), color Doppler, and endoluminal ultrasonography, have replaced the older, more invasive procedures. When a significant crossing vessel has been documented, a classical endopyelotomy is likely to provide inferior results, especially in the presence of a large renal pelvis. When a small artery or a venous channel is encountered, consideration can be given to transection of the crossing vessel [11, 12]. If a major vessel is present, an alternative treatment such as open or laparoscopic/robotic pyeloplasty is preferable. When renal function is poor (<10%), laparoscopic nephrectomy is the first choice.

Today, the major indications for percutaneous endopyelotomy are the combined treatment of UPJ obstruction and concomitant pathology, the most common being secondary renal calculi and secondary UPJ obstruction [8]. This is particularly true in cases where the crossing vessel or fibrous band was addressed at the initial laparoscopic or robotic pyeloplasty. Although several series have reported superior success rates with secondary pyeloplasty compared to endopyelotomy [33, 34], endopyelotomy remains a feasible, less invasive, and effective option in properly selected patients [35]. In addition, several centers with expertise in the procedure continue to recommend the operation in carefully selected patients with primary UPJ obstruction.

## Conclusions

Percutaneous endopyelotomy stands out as a landmark procedure, opening the way to reconstructive NOTES procedures. Like the majority of pioneering techniques, it has now been superseded by newer developments. Nevertheless, it retains specific indications, such as secondary UPJ obstruction and combined treatment of UPJ obstruction and associated anomalies.

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## 31

# Percutaneous Management of Upper Tract Urothelial Carcinoma

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## Introduction

Upper tract urothelial carcinoma (UTUC) is a rare urologic malignancy with an incidence of one to two patients per 100 000 individuals annually. The average age of presentation is around the eighth decade of life, and about 60% of patients have invasive disease at presentation, in stark contrast to the 15–20% of those diagnosed with bladder cancer [1]. Historically, preoperative staging of UTUC depended on cross-sectional imaging and the use of tumor grade as a surrogate, since ureteroscopic biopsies often provided inadequate tissue sampling [2, 3].

Given the advanced stage at presentation, radical nephroureterectomy (RNU) with an ipsilateral bladder cuff excision is the gold standard treatment for UTUC [1]. Radical excision as a cure, however, may be more debilitating than the disease for patients with low-risk characteristics. Moreover, there tends to be multiple competing medical comorbidities in this patient population. RNU has been shown to increase cardiac events [4], significantly reduce renal function [5, 6], and potentially exclude patients from platinum-based chemotherapy, which is treatment necessary for the management of advanced urothelial carcinoma [7]. This presents one of the great challenges in managing UTUC – balancing the morbidity of treatment with acceptable oncologic outcomes.

The endoscopic approach for nephron-sparing management (NSM) is gaining acceptance for appropriately selected patients [8]. Patient selection requires parallel risk stratification of the patient's malignancy balanced with their comorbidities to provide the best outcome. Studies comparing endoscopic UTUC resection against RNU show no difference in overall survival [9], and similar cancer-specific survival in patients with noninvasive low-grade disease [10]. Renal preservation rates of 67–100% are observed, depending on the imperative indication for endoscopic management [8].

In this chapter we discuss patient selection for NSM in the treatment of UTUC, basic considerations/techniques in the percutaneous management of UTUC, and the subsequent long-term follow-up regimen.

## Patient selection

Indications for NSM of UTUC fall into two categories: imperative and elective (Box 31.1). Imperative indications for a minimally invasive approach include an anatomic or functionally solitary kidney, significant renal impairment, bilateral malignancy, and poor candidacy for radical surgery. Although cancer cure may be achieved, these patients would presumably fare worse with radical nephroureterectomy due to their underlying medical comorbidities or resulting renal insufficiency. End-stage renal disease requiring renal replacement therapy (hemodialysis) may significantly reduce life expectancy [11], and is associated with a poor quality of life [12]. Historically, candidacy for NSM was reserved for patients with imperative indications. However, similar to the advent of partial nephrectomy for renal cell carcinoma, improved risk stratification of UTUC has helped identify a cohort of patients who would benefit from elective NSM with comparable oncologic control and preserved renal function.

Elective endoscopic management relies heavily on preoperative risk stratification and patient selection. Traditional staging of UTUC on endoscopic biopsy is poor due to the limited depth of tissue procured, which understages a tumor in up to 54% of cases [2, 3]. The use of larger caliber biopsy forceps (e.g. BIGopsy back-loading biopsy forceps; Cook Medical, Bloomington, IN,

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**Box 31.1 Indications for kidney-sparing surgery.**

**Imperative indications**

- Anatomic or functional solitary kidney
- Significant renal insufficiency
- Bilateral urothelial carcinoma
- Poor candidacy for radical nephroureterectomy

**Elective indications**

- Low-risk UTUC
- Highly selected high-risk UTUC: multifocal, large tumors, with low grade and superficial features

USA) or a basket snare can improve tissue yield and diagnostic accuracy [13]. The thin mucosa, lamina propria and muscularis layers of the ureter and renal pelvis still pose diagnostic challenges. Rouprêt et al. proposed a divergent scheme from classic TNM staging to risk-stratify patients and assess eligibility for NSM [14] (Table 31.1). They identified low grade on biopsy/cytology, noninvasive features on cross-sectional imaging, unifocal disease, and tumor size <1 cm as criteria for low-risk disease. High-grade features on biopsy or cytology, large or multifocal tumors, and hydronephrosis were criteria for higher risk disease inappropriate for elective endoscopic management in patients otherwise eligible for nephroureterectomy.

Unlike tumor stage, clinical grade is more accurately obtained through conventional ureteroscopic biopsies. Yamany et al. showed that ureteroscopic biopsy accurately graded 82% of patients, with 1.3% being downgraded and 16.7% upgraded on final nephroureterectomy pathology [3]. However, only one-third of patients were accurately staged, with nearly two-thirds being upstaged on final pathology, most commonly to pT2 or greater. Up to two-thirds of patients with high-grade disease on biopsy will have muscle-invasive disease [15]. High-grade disease has also been associated with an increased risk of recurrence (HR 2.12, $P = 0.018$) and lower overall survival (42% vs. 69.2% for low-grade disease) in patients undergoing NSM [16, 17]. Likewise, the negative predictive value of a low-grade tumor for the absence of muscle-invasive disease on final pathology is 72% [15]. Given the relative reliability of biopsy grade over stage and the clinical significance of grade as predictive of final pathology, high-grade disease should be the strongest factor of NSM ineligibility.

**Table 31.1** Risk stratification of upper tract urothelial carcinoma.

| Low-risk UTUC | High-risk UTUC |
|---|---|
| Low-grade biopsy | Hydronephrosis |
| Low-grade cytology | High-grade |
| Tumor <1 cm | Tumor >1 cm |
| No invasive features on imaging | Invasive features on imaging |
| Unifocal disease | Multifocal disease |
| Close follow-up possible and acceptable to patient | Failed previous endoscopic treatment |

*Source:* Adapted from Rouprêt et al. (2014) [14].

Tumor multifocality has been associated with poorer outcomes in patients undergoing RNU and long considered a high-risk characteristic in UTUC [18–21]. Interestingly, others have not been able to reproduce these findings in patients specifically undergoing endoscopic management [16]. Multifocality likely represents a predilection for cancer recurrence (pan-urothelial disease) and a greater tumor burden to be managed endoscopically. Multifocality should be considered in the context of endoscopic feasibility and surgeon comfort level rather than an absolute contraindication for endoscopic management. Likewise, tumor size should be given similar consideration. A solitary, low-grade, renal pelvis tumor over 1 cm may be beyond the capabilities of ureteroscopic management but easily accessible and resectable through a percutaneous approach. Rapid recurrence in the setting of multifocal or large tumor volume should still encourage RNU in surgically eligible patients.

Cross-sectional imaging, preferably with contrast urography, provides useful clinical data. Tumor size and location are often identified, which are invaluable for surgical planning. Furthermore, evidence of invasive or infiltrative disease raises concerns for advanced stage, thus discouraging primary endoscopic management. Hydronephrosis is also an independent predictor of high-grade advanced stage (≥pT2), non-organ-confined disease, as well as lymphovascular invasion [22–24]. The mechanism of hydronephrosis is not wholly elucidated but in most cases a result of bulky intraluminal disease. In more advanced cases, mural invasion and narrowing of luminal diameter may be an additional and more ominous etiology.

Lastly, the patient's compliance to a regimented follow-up schedule should be assessed prior to pursuing endoscopic management [25]. Patients treated with endoscopic NSM will need frequent surveillance of their upper tracts, in the form of repeat ureteroscopy under anesthesia and radiographic studies. An unwillingness or inability to comply should be considered against the option of NSM. In describing their institutional 30-year experience with endoscopic UTUC management, Motamedinia et al. described a patient with a primary recurrence 116 months following initial diagnosis. Although a complete resection and durable response is possible, recurrence is common and disease progression needs to be detected early to allow for potentially curative intervention [16]. Similar to bladder cancer, interval visual inspections of the urothelial lining are essential. Office-based or conscious ureteroscopy, although previously described [26], may not be practical or tolerable in all cases.

## Percutaneous tumor resection

Endoscopic management of UTUC is most commonly performed in retrograde fashion via a flexible ureteroscope and most small, low-grade tumors are readily accessible and appropriately managed through ureteroscopy. We have been able to push the envelope with the endoscopic management of UTUC through advancements in digital imaging and improved flexibility of small-caliber ureteroscopes. Modern ureteroscopes and a retrograde intrarenal approach are the workhorse for the visual diagnosis, initial tumor biopsy, and subsequent extirpation of amenable upper tract lesions. However, just as ureteroscopy has limitations in the management of large or complex upper tract stones, the same is true for renal pelvic, calyceal, and selective proximal ureteral tumors. Small-caliber biopsy forceps, snares, and lasers have a limited capacity for tumors greater than 1 cm or those involving a wide "carpeting" of urothelium.

The percutaneous approach for the management UTUC is not common, but is ideally suited for specific clinical situations. Percutaneous intrarenal access allows for the use of larger caliber instruments via a nephroscope, and even a resectoscope with cutting current loop. Higher volume irrigation coupled with suction devices can improve visualization and allow for a more complete resection. Percutaneous access is also favored for patients who have undergone cystectomy, especially with a continent urinary diversion, which would further complicate a retrograde approach.

Presurgical planning for percutaneous access is paramount. A preoperative CT urogram (delayed intravenous contrast phase) or magnetic resonance urogram illustrates the intrarenal anatomy, relative location of the tumor within the kidney, and facilitates the selection of a point of entry. In addition, it rules out invasive disease or nodal involvement, which would disqualify further endoscopic management. We favor a prone percutaneous approach under fluoroscopic guidance as this is also our preferred approach for percutaneous nephrolithotomy (PCNL). However, those who are more comfortable with supine PCNL or ultrasound-guided access should proceed accordingly. A posterior calyx containing a tumor should be directly accessed. If a tumor is located in an anterior calyx, direct access may be more challenging and thus an upper or lower pole puncture may allow for better trajectory into the calyx of interest. Tumors in the renal pelvis or proximal ureter should be approached through an upper or middle pole calyx when feasible, which offers a more direct angle of approach to the ureteropelvic junction. The calyx allowing for the shortest tract will also allow for maximal intrarenal maneuverability with a rigid nephroscope, especially in obese patients or in the setting of large and multifocal tumors.

Dilation of the nephrostomy tract can be performed with coaxial balloon dilation or serial renal dilators. Similar to PCNL, direct access into the renal pelvis should also be avoided due to the proximity of hilar vessels and the propensity for significant hemorrhage [27]. Should the puncture and subsequent dilation cause significant bleeding, the surgeon may consider placing a nephrostomy tube to tamponade the bleeding and to promote tract maturation. A repeat procedure may be conducted at a later date. In addition, great care should be taken to avoid perforation due to theoretical tumor seeding and retroperitoneal fluid collection. Ideal placement of the nephrostomy sheath is at the edge of the entry calyx to allow for complete visualization of the urothelium and reduce the risk of a missed tumor behind the sheath.

Once nephrostomy access tract is established and an assessment of tumor location is completed, we initiate tumor resection. An added benefit of the percutaneous approach is that a standard resectoscope with a monopolar or bipolar cutting loop or rollerball can be used through the percutaneous tract (Figure 31.1). Bipolar

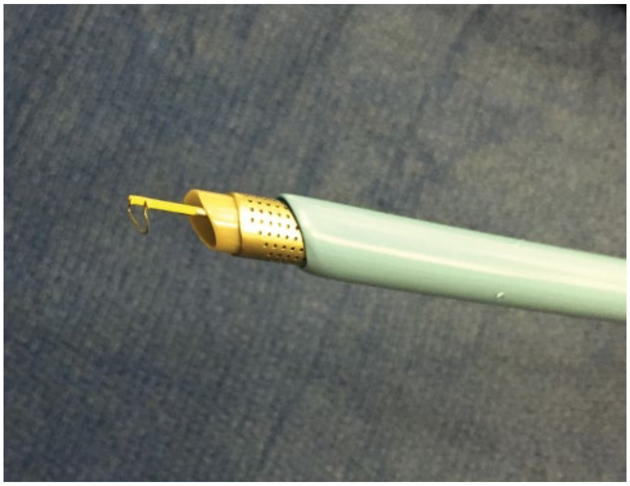

**Figure 31.1** Standard resectoscope (26 Fr) through a 30 Fr nephrostomy access sheath.

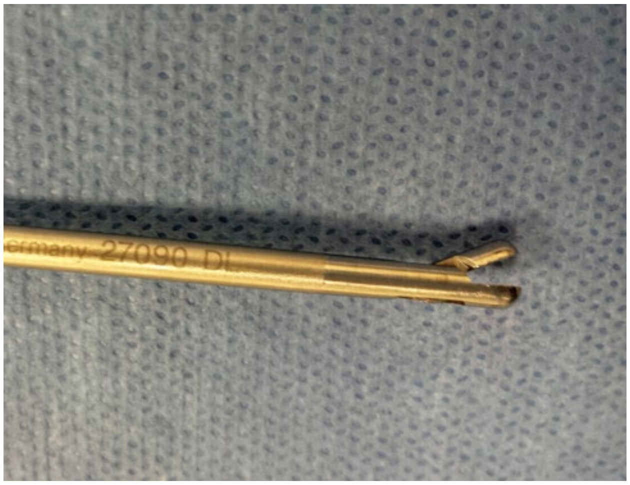

**Figure 31.2** Cold cup biopsy forceps.

energy with saline irrigation eliminates the risk of electrolyte abnormalities associated with the excessive hypotonic fluid absorption possible with monopolar resection. We prefer to first debulk the tumor with cold cup biopsy forceps, especially for papillary neoplasms (Figure 31.2). This allows for tumor removal without cautery artifact. There is also less risk of inadvertent perforation of the collecting system compared to a resectoscope loop when maneuvering in a confined space or approaching a bulky tumor. As the tumor is debulked and larger stalk vessels are exposed, interval hemostasis is necessary to maintain visualization. Our practice is to procure a separate specimen from the tumor base to aid in more accurate pathologic staging, as lamina propria or muscle invasion can best be demonstrated at this level. Careful resection is crucial as the infundibulopelvic urothelium lacks significant muscular backing and can easily be perforated. In addition, second- and third-order renal vasculature branches run parallel to the infundibula.

Use of lasers is also an option. Once the bulk of the tumor has been removed, neodymium:YAG or holmium:YAG lasers can be utilized to ablate the bases. Neodymium:YAG laser with its greater depth of penetration may be useful after a substantial resection as it can induce noncontact coagulation. Holmium:YAG laser with a depth of penetration of 0.4 mm will be inadequate in achieving hemostasis for larger bleeding vessels and has a tendency to accumulate tissue on the fiber tip [27].

In the event of significant bleeding following a deep resection or ablation, continued tissue fulguration or coagulation may be futile and only exacerbate further hemorrhage. A preferred maneuver would be to place a nephrostomy catheter with a balloon to tamponade the site. The procedure should be terminated with a plan for second look after about 48 hours.

The risks for percutaneous UTUC resection are similar to those for PCNL, including: infection, bleeding, collecting system perforation, hemothorax/hydrothorax for supracostal access, and rarely injury to the liver, spleen, or bowel. Risk of bleeding may be higher than that for conventional PCNL given the neoplastic vascularization and need to resect and ablate urothelium as a goal of the procedure. Historic studies have quoted transfusion requirements of 20–50% and vascular complications that correlate to tumor grade [28, 29]. Concern for tumor seeding along the tract is raised as a concern unique to percutaneous management of UTUC. However, only rare case reports have been published on this unlikely complication [30–32]. With appropriate patient selection, percutaneous resection of urothelial carcinoma remains a safe and effective treatment.

## Long-term follow-up

Following percutaneous intervention, in particular bulky tumors, “second look” nephroscopy may be performed two days after to eradicate any residual tumor burden [33]. Second look may be performed during the same hospitalization through the established nephrostomy tract, since matured. Repeat procedures usually afford better visualization and improved hemostasis. In addition to assessing for complete resection of the initial tumor, we advise inspection of the urothelium at the site of access to detect tumors that may have been obscured by bleeding of puncture and dilation. In addition, flexible nephroscopy should be utilized to revisualize all calyces, the renal pelvis, and the proximal ureter for potential missed lesions.

If pathologic analysis of the tissue returns as high grade or presence of muscle invasion, the patient should be counselled toward definitive management with nephroureterectomy. For patients with appropriately low-risk disease, an endoscopic surveillance should be planned within three months. A retrograde ureteroscopic approach is preferred as it is less invasive and is performed in an ambulatory setting. It also provides great flexibility to survey all calyces and allows for concomitant evaluation of the bladder and ureter.

There are no established guidelines for long-term upper tract surveillance following endoscopic resection. Our preferred regimen mirrors the surveillance guidelines for high-risk non-muscle-invasive bladder cancer established by the American Urological Association and Society of Urologic Oncology [34]. Patients undergo endoscopic evaluation (cystoscopy with ipsilateral ureteroscopy) every three months for the first 2 years and every six months thereafter. If the patient is free of recurrence for 5 years, surveillance is performed annually. Urine cytology is checked at each intervention. Cross-sectional imaging with contrast urography is performed annually. For patients with renal insufficiency precluding contrast enhancement, retrograde pyelogram is performed; however, this elevates the risk of missing extraluminal disease [35].

There are no strong data supporting a benefit from intraluminal bacillus Calmette–Guérin (BCG) following UTUC resection [16, 17, 36, 37]. Results utilizing BCG in patients with carcinoma in situ of the upper tract are more promising [37–39]. Ultimately, there are no randomized trials to prospectively quantify potential benefits in either scenario.

## Conclusion

Radical nephroureterectomy remains the gold standard treatment for patient with moderate- to high-risk UTUC. However, strong consideration for renal preservation should be given to patients with low-risk disease, regardless of medical fitness for radical surgery. A percutaneous approach to UTUC resection is ideally suited for calyceal and renal pelvis tumors, or patients who have undergone previous urinary diversion. A stringent follow-up regimen consisting of endoscopic surveillance and cross-sectional imaging is a vital part of endoscopic NSM and should be discussed between patient and practitioner.

See accompanying Video 31.1.

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## Part 7 Exit Strategy and Complications

# 32

# The Access-related Complications of Percutaneous Nephrolithotomy

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## Introduction

Percutaneous nephrolithotomy carries a stone-free rate of over 90%; however, the rate of Clavien I–II complications is almost double those for ureteroscopy and extracorporeal shock-wave lithotripsy (ESWL), at approximately 20% [1, 2]. The rate of Clavien III–IV complications is significantly lower, at a rate of 3.2–3.7% for major complications. Every urologist must be well versed in complications, as the rate of complications has been shown to exponentially decrease with experience [3, 4]. Patients with increasingly complex stones are also significantly more likely to experience a Clavien II–III complication [2]. Of note, patients with morbid obesity, a branched collecting system, spinal deformities, malrotated kidneys, horseshoe kidneys, and a large or complex stone are known to be at increased risk.

Prevention of complications is a complex issue. The astute surgeon should take the following steps prior to every surgery:

- Ensure that anticoagulants are held for the appropriate interval prior to surgery. Aspirin should never be held prior to surgery (Table 32.1).
- Ensure that the patient has adequate imaging for selection of the best access to maximize intraoperative stone removal. This means that the access tract will accommodate stone extraction from the other calyces as well.
- Ensure that the patient has sterile urine prior the procedure. If the patient has colonized urine, use a percutaneous nephrostomy tube to maximally drain the kidney and continue antibiotics. The patient can then proceed with a staged percutaneous nephrolithotomy.
- Ensure that backup equipment is available. If using a lithotripter, a laser or electrohydraulic device should be available in the event that the lithotripter is inadequate. This will prevent intraoperative delays.

Prediction of complications remains challenging. Risk factors (Table 32.1) include anatomic abnormalities of the collecting system, indications for operation, and severe medical comorbidities. Several scoring systems have been used in this patient population in an attempt to standardize stone complexity classification to assist with prediction of complications, success of treatment, and the need for repeat procedures (Table 32.2). To date, no score has accurately predicted the risk of complications postoperatively, although many have been shown to accurately predict the stone-free rate postoperatively [5–7]. Interestingly, poor renal function preoperatively has been shown to predict the risk of worse postoperative outcomes [8].

Approximately 11% of urologists attempt to obtain percutaneous access to the kidney [9]. Many blame this low rate on lack of surgeon confidence. Interestingly, at high-volume centers, the rate of failure to obtain access to the kidney among interventional radiologists may be as high as 9%, while urologists enjoy a 2% risk of failed access, although urologic access may carry a higher risk of bleeding [10, 11]. Therefore, a command of the most common access-related complications and knowledge of how to both prevent and manage them would improve both operator confidence and patient care.

Complications in percutaneous nephrolithotomy (PCNL) often arise in selection of a calyx for puncture, particularly hemorrhage, or from injury to adjacent structures.

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## Problems with initial puncture of the kidney

### Selection of calyx

When selecting a calyx for puncture, focus should be placed on obtaining access through a calyceal fornix rather than the calyceal infundibulum. This will minimize the risk of hemorrhage intraoperatively and postoperatively. Further, access should be attempted laterally as opposed to medially with respect to the kidney. The avoidance of medial access is necessary, as the renal artery and vein and renal pelvis are more easily injured when medial access is attempted. With the patient in the prone position, a retrograde pyelogram is performed. When inspecting the selected calyx to ensure that the puncture was obtained in the desired location, or if one wishes to delineate a posterior calyx, inject $CO_2$, not air, as the use of air increases the risk of air embolism in the event of inadvertent arteriovenous puncture. Care must be taken not to overfill the system, as this may cause extravasation, resulting in a poorly visualized collecting system. Should this occur, the surgeon might need to select a different calyx or merely wait until the contrast is absorbed. Following puncture of a calyx, confirmation of access should be checked by aspiration of contrast or by injection of saline to delineate the contrast. It is critical not to inject contrast material; otherwise, extravasation may occur.

**Table 32.1** Risk factors for complications of percutaneous nephrolithotomy.

| Factor | Example |
|---|---|
| Anatomic | Calyceal abnormalities<br>Malrotated/ectopic kidney<br>Horseshoe kidney |
| Surgical indications | Staghorn stones<br>Upper tract transitional cell carcinoma<br>Uteropelvic junction obstruction<br>Calyceal diverticulum |
| Medical comorbidities | Chronic obstructive pulmonary disease<br>Congestive heart failure/valvular heart disease<br>Morbid obesity<br>Kyphoscoliosis/limb contractures<br>Neurogenic bowel<br>Prior surgeries<br>Metabolic disorders (diabetes mellitus, cystinuria, renal tubular acidosis, sarcoid) |

### Hemorrhage

The overall rate of hemorrhage requiring blood transfusion during PCNL is estimated to be around 2–11% [12]. Most commonly, bleeding is secondary to injury of segmental arteries. Some important risk factors for

**Table 32.2** Scoring of stone complexity.

| Score | Parameters | Correlation with stone-free status and complications |
|---|---|---|
| S.T.O.N.E. Nephrolithometry score (Okhunov et al. [5]) | 1–4<br>Stone size<br>Tract length<br>Obstruction<br>Calyces involved<br>Essence (HU) | Stone-free status ($P = 0.001$)<br>Estimated blood loss ($P = 0.005$)<br>Operative time ($P = 0.001$)<br>Length of stay ($P = 0.001$) |
| Guy's stone score (Thomas et al. [6]) | 1–5<br>I – Solitary stone with simple anatomy<br>II – Solitary stone in upper pole or multiple stones in a patient with simple anatomy<br>III – Multiple stones in a kidney with abnormal anatomy, calyceal diverticulum, or partial staghorn calculus<br>IV – Staghorn calculus | Stone-free rate ($P = 0.01$) |
| CROES PCNL Nomogram (Smith et al. [7]) | Stone burden<br>Body mass index<br>Stone location<br>Stone count<br>Renal anomalies<br>Prior treatment<br>Multiple modalities<br>Case volume | Stone-free rate ($P < 0.01$)<br>If using the nomogram and predicted stone-free rate is 60%, perform PCNL or staged PCNL or use adjunct therapy |

PCNL, percutaneous nephrolithotomy.

intraoperative hemorrhage during PCNL include diabetes mellitus leading to arteriosclerosis, hypertension, stone size greater than 1250 mm$^2$, number of accesses, presence of staghorn calculi, and operative time greater than 58 minutes [12–14].

In most cases, bleeding during PCNL access can be attributed to laceration of subsegmental veins, and use of the Amplatz sheath to apply occlusive pressure will control the bleeding. To avoid tearing the renal parenchyma, once percutaneous access is obtained, the surgeon should avoid excessive up and down movement of the needle. In addition, medial insertion of the needle, which can lead to injury to the renal artery or vein or interlobar vessels, can incur further risk of bleeding.

If bleeding is excessive and the Amplatz sheath does not suffice, a large-caliber nephrostomy tube can be inserted or capped [15]. If that fails, insertion of a Kaye tamponade balloon catheter (Cook Medical, Bloomington, IN, USA) involves insertion of a 36 Fr occlusive balloon over a 5 Fr ureteral stent. This approach allows for drainage of the renal pelvis while tamponading the nephrostomy tract [16]. Once again, if this fails, the patient should be sent to interventional radiology for angiography. In cases in which conservative measures are unsuccessful, the use of super-selective angioembolization will help control the bleeding. Avoidance of perforation of the renal pelvis, which may occur in 7.2% of cases, is also critical [17].

## Guidewire insertion

Appropriate guidewire insertion is crucial to the success of the procedure. Kinking occurs when the tract from the skin to the kidney is not in a straight line. This is commonly related to timing of puncture: while initial puncture occurring during inspiration may lead to caudal displacement of the kidney, tract dilation occurring during expiration will lead to cranial displacement of the kidney, changing the tract trajectory and leading to guidewire kinking. Alternatively, guidewire kinking may result from an angled puncture.

It is essential to monitor the dilation of the tract fluoroscopically to ensure smooth passage over the wire, otherwise kinking of the guidewire is inevitable. When kinking of the guidewire is noted upon introduction, the surgeon should attempt to reposition the wire prior to re-attempting puncture. Never attempt nephrostomy tract dilation over a kinked guidewire, as this will likely lead to dilation tangential to the desired tract and increases the risk of injury to adjacent organs (Figure 32.1). Initially, the guidewire can be pulled back so that the kink is outside the nephrostomy tract. This is only possible if there is sufficient guidewire within the kidney to the ureter. The kink is subsequently straightened and an 8 Fr dilator is inserted over the guidewire to allow for subsequent tract dilation. Another option is to advance a 6 Fr dilator over the wire through the nephrostomy tract. The 6 Fr dilator is more flexible and can often be advanced over a moderate kink. The existing wire can be removed and exchanged for a new, unkinked super-stiff wire, which will allow for tract dilation. If all of the above techniques fail, removal of the guidewire and repeat puncture should be attempted.

## Arterial puncture

Cases of arterial puncture are confirmed with pulsatile bleeding noted from the lumen of the needle; this occurs with a medial puncture or if the needle is advanced too far medially. This can be checked in the 90° position under fluoroscopic guidance (Figure 32.2). A puncture of a vessel by an 18 Fr needle seldom poses a problem. One should merely withdraw the needle and attempt to insert it into the appropriate calyx. In the case illustrated, the surgeon merely had to withdraw the needle approximately 1 cm (Figure 32.2).

## Venous puncture

Occasionally, introduction of the guidewire leads to insertion into the renal vein. This is not all that uncommon. Fluoroscopic advancement of the wire will show the wire advancing into the inferior vena cava (Figure 32.3). Once again, withdrawal of the needle and repositioning is all that is required. If dilation over the wire into the tract is attempted, the renal vein is accessed and can appear to look like the renal pelvis without the calyces in the expected anatomic position. When this

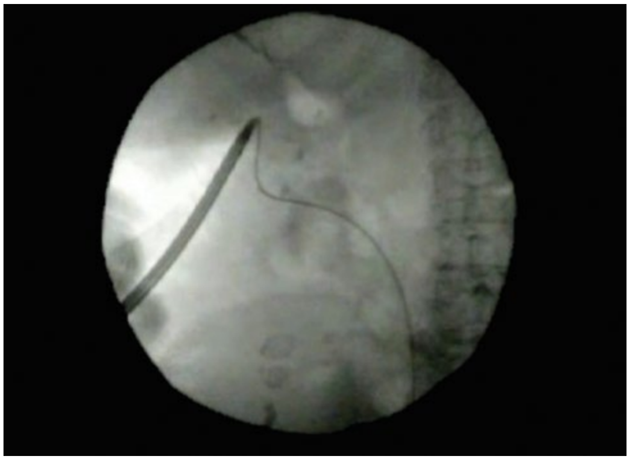


**Figure 32.1** Kinking of the guidewire at the time of obtaining percutaneous access. In this case, the wire was successfully repositioned with the assistance of an 8 Fr open-ended catheter and dilation proceeded without complication.

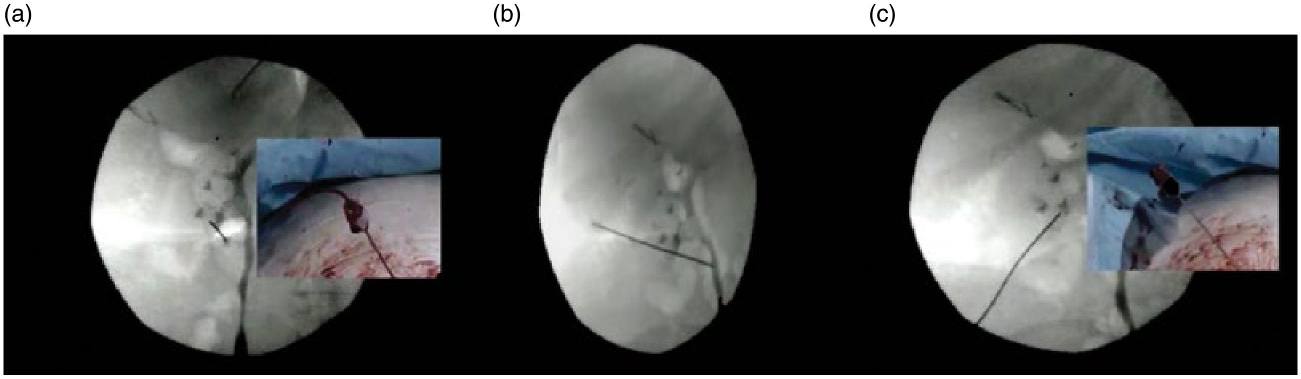
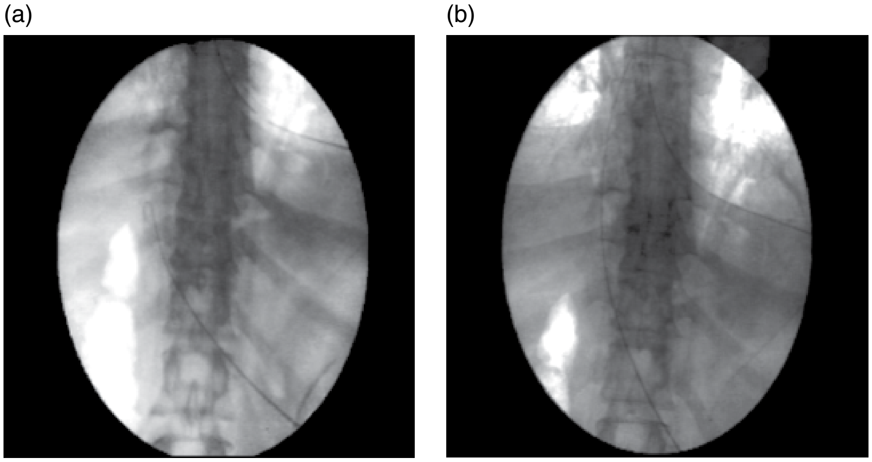


Figure 32.2 An example of inadvertent arterial puncture during attempted percutaneous access. (a) Needle is likely inserted into an interpolar artery. (b) The needle is then de-advanced with (c) cessation of hemorrhage.

Figure 32.3 Inadvertent inferior vena cava (IVC) access at the time of left-sided percutaneous nephrolithotomy. (a) The wire is seen to be crossing the midline, and then (b) entering the IVC.



occurs, remove the nephroscope, gain access to the collecting system, dilate the tract, and insert a Councill catheter, with the balloon of the Councill catheter occluding the laceration in the renal vein. The balloon can be deflated after 48–72 hours.

### Issues encountered with a full staghorn calculus

The patient with a full staghorn calculus remains a persistent challenge at the time of needle placement. If the stone fully occludes the calyx, the needle will meet resistance at the level of the stone. When the needle is removed, the trocar portion of the needle may not be in the calyx and the guidewire cannot be advanced. To counteract this, the trocar (or the sheath of the needle) may be advanced onto the stone and the needle withdrawn. Another alternative is to dilate the tract up to the calyx and then displace the tissue overlying the stone with a grasping forceps. The Amplatz working sheath is then gently rotated until its edges are within the collecting system, and subsequently against the stone itself. Another option is to employ the technique originally described by Clayman et al. [18]. In this technique, ureteroscopic lithotripsy and stone extraction is performed to create space within the renal pelvis and create an appropriate calyx and an unobstructed route to the calyx to facilitate passage of the wire and subsequent percutaneous access.

## Injury to adjacent structures

### Nervous injury

The intercostal nerve and artery are at high risk for injury when supracostal access is attempted [19]. For this reason, supracostal access has been reported to have an increased risk of pain and bleeding. Attempting to access the kidney lateral to the paraspinous muscles within the lower half of the 11th intercostal space may minimize this risk. Occasionally, a bulge in the skin overlying the area of percutaneous access is seen and this is associated with nervous injury. Usually, the bulge resolves over time, and it is due to neuropraxia, but it may persist if indeed there was severe trauma to the nerve.

## Intrathoracic injury

Pleural or pulmonary injury is the most common complication encountered after hemorrhage in percutaneous renal surgery. It remains a rare complication, with incidences estimated to be approximately 0–12% [19–25]. The rate of injury increases threefold with supracostal access [26]. Lower rates of hydropneumothoraces were noted with a subcostal approach. The overall rate of pneumothorax was 1.5%, hydrothorax 0.5%, and hemothorax in 1% of patients. Only 0.5% of patients ultimately required intervention with tube thoracostomy. The risk of these complications increased with supracostal access into the upper pole calyces, which remains the most favorable approach for cases with staghorn calculi, upper pole calculi, or calyceal diverticuli of the upper pole.

When supracostal puncture is performed, it is essential to screen the diaphragm at the end of the surgery. If a pneumothorax or hydrothorax is present, it can be addressed while the patient is anesthetized. In most reports, complications have been managed conservatively or, if necessary, with a chest tube for drainage. Furthermore, in cases in which intraoperative hydropneumothorax is identified, this may be aspirated or drained using a pigtail catheter. In rare cases, thoracoscopy or an intraoperative thoracotomy may be required for patients with loculated effusion, empyema, or pleural effusion not responding to chest tube drainage.

## Injury to liver/spleen

Liver injuries typically occur as a complication of attempting access above the 11th rib. These injuries can be managed with observation alone. Patients should have serial abdominal exams and hematocrit measurements [27]. A follow-up CT scan can be obtained if concerns arise regarding the need for emergent surgical exploration.

Splenic injuries differ from liver injuries, as these injuries will require emergent open surgical exploration due to the significant bleeding often encountered [28]. If attempts to repair the spleen are unsuccessful, splenectomy should be the next step and serves as definitive management of the bleed. There have been several cases of splenic injury, which have been treated conservatively. If the patient is stable, then remove the tube after 72 hours while the patient is in the hospital. The patient should be observed closely for 6–8 hours in the event that urgent surgery is required.

Even less common are the reports of needles inserted at the time of percutaneous access, leading to an injury to the fundus of the gallbladder. In one case, the patient required a laparoscopic cholecystectomy due to biliary peritonitis.

## Injury to bowel

The rate of injury to the colon is reported to be as low as 0.06–0.2% overall [4, 29, 30]. Risk factors for colonic injury include retrorenal colon, renal anomalies (e.g. horseshoe kidney), any history of small bowel resection and diversion, or neurogenic bowel. Most injuries that occur result from lower calyceal punctures [31]. In patients with the aforementioned risk factors, a preoperative CT or laparoscopically guided access should be considered.

When a colonic injury is identified in a patient who does not have symptoms of peritonitis, patients may be managed conservative with placement of a double-J stent to address the ureter and insertion of a nephrostomy tube into the colonic lumen (Figure 32.4). This separation of the urinary and gastrointestinal tract should remove any opportunity for fistula formation. Broad-spectrum antibiotics should be given for 7–10 days with a follow-up nephrostogram to confirm closure of the fistulous tract. Peritonitis mandates abdominal exploration, creation of a diverting colostomy, and placement of an abdominal drain, in addition to closure of the perforation.

Injury to the duodenum is exceedingly rare, and is typically seen when the guidewire used to obtain access to the kidney has perforated through the renal pelvic hilum,

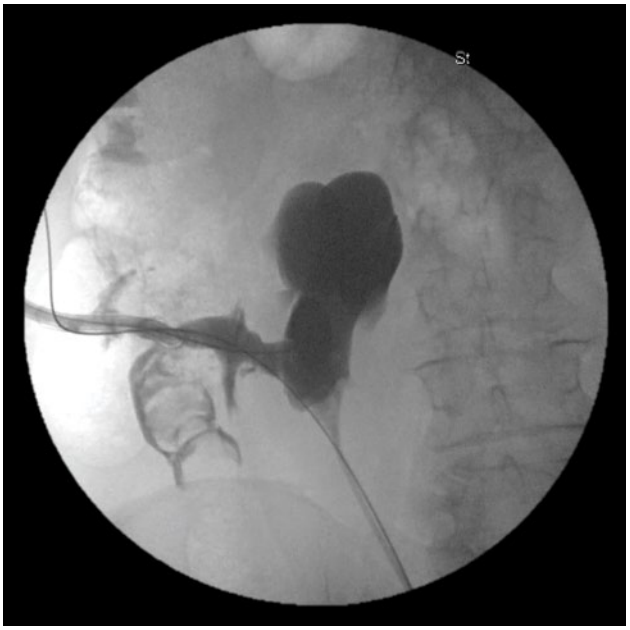


**Figure 32.4** An example of colonic injury at the time of percutaneous access. In this case, a nephrostomy tube was placed in the colonic lumen and a ureteral stent was placed in the ureter for maximal separation. The patient was treated with perioperative antibiotics for 7–10 days and recovered without difficulty.

and thereby penetrates the duodenum. If the injury is small, it can be managed by nasogastric decompression and a nephrostomy catheter. Nutritional status should be maintained by total parenteral nutrition.

## Conclusions

Appropriate technique at the time of obtaining percutaneous access for PCNL is crucial to avoid intraoperative complications. Selection of the appropriate calyx, immediate tamponade of intraoperative hemorrhage, avoidance of guidewire kinking, and careful maneuvering around staghorn calculi are important principles that decrease the risk of hemorrhage and unintentional injury to adjacent organs. Prevention of hemorrhage and organ injury during PCNL is dependent upon excellent technique at the time of creation of the nephrostomy tract. The surgeon can avoid most major complications by ensuring that the needle puncture is attempted postero-laterally, where possible, and that the guidewire is advanced down the ureter without kinking prior to dilation and placement of the Amplatz sheath. In the event of intraoperative hemorrhage or inadvertent injury to adjacent organs, the surgeon must have a command of the necessary techniques to quickly assess and address the problem to ensure an excellent postoperative outcome.

See accompanying Video 32.1.

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# 33

# Hemorrhagic Complications Associated with Percutaneous Nephrolithotomy

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## Introduction

Prior to the advent and widespread adoption of endourologic techniques beginning in the early 1980s, the mainstay of surgical treatment for urolithiasis was open surgery. The risk of bleeding in the era of open renal stone surgery posed particular challenges for perioperative management. For example, in an evaluation of patients undergoing anatrophic nephrolithotomy over a period of 14.5 years, Assimos et al. reported a 6.4% rate of significant postoperative bleeding [1]. A more recent analysis by Al-Kohlany et al., evaluating complications of open renal stone surgery, demonstrated a 24.5% rate of intraoperative hemorrhage requiring transfusion and an 8.9% rate of massive hematuria requiring transfusion [2].

In the modern era, minimally invasive treatments for urolithiasis, such as shock-wave lithotripsy, ureteroscopy, percutaneous nephrolithotomy (PCNL), and laparoscopy, have all but replaced open surgery for large kidney stones in centers with access to such technology and expertise. PCNL, in particular, has had a considerable impact on improving hospital lengths of stay, recovery times, and overall morbidity [3]. However, despite these advances, hemorrhagic complications remain a potent concern during and after PCNL [4–6]. The PCNL Global Study by the Clinical Research Office of the Endourologial Society, which prospectively collected data on consecutive PCNLs performed by centers across the world over a one-year period, found a 7.8% rate of significant bleeding and a blood transfusion rate of 5.7% [4]. Contemporary ranges of bleeding during and after PCNL requiring transfusion are reported to be between 1% and 11% [5–7]. Proper management of perioperative bleeding plays an important role in the safe and effective treatment of kidney stones with PCNL, and the management of such bleeding should be familiar to those performing PCNL as well as those involved in the care of these patients.

The objective of this chapter is to review the various hemorrhagic complications encountered during and after PCNL, the management of these complications, and strategies to reduce their occurrence. This chapter will also discuss perioperative risk stratification and patient optimization, as well as technical considerations during PCNL which influence hemorrhagic complications. It is through the combination of optimizing patient risk factors pre- and perioperatively, executing excellent surgical technique, recognizing bleeding early, and managing bleeding rapidly that hemorrhagic complications during and after PCNL can be minimized and their consequences mitigated.

## Etiology of hemorrhage from percutaneous nephrolithotomy

Bleeding during and after PCNL can occur at any step throughout the procedure, including needle puncture, dilation of the percutaneous tract, excessive torqueing of the renal parenchyma through an established access sheath, aggressive stone manipulation and extraction, from collateral damage to adjacent organs and blood vessels, during nephrostomy tube removal, and in the immediate or delayed postoperative period [8]. Hemorrhage results from either damage to the kidney parenchyma, disruption of the peri- or intrarenal vessels, or injury to adjacent structures.

Renal parenchymal bleeding, believed to stem most commonly from the interlobular vessels, is often mild, apparent during surgery, and frequently can be

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controlled with intraoperative tamponade from the access sheath, and with larger bore nephrostomy or nephroureteral catheters postoperatively. Injury to the larger renal vessels, such as the arcuate, interlobar, lobar, and segmental vessels, is thought to cause more significant bleeding that may limit vision during PCNL and can cause continued significant blood loss postoperatively as well. For vessels in spasm, bleeding may be minor during surgery, but once the spasm abates, bleeding and its effects often become apparent within the first 24–48 hours postoperatively.

Injury to these larger vessels is also believed to be the cause of delayed bleeding. Such delayed bleeding often takes one of two forms: arteriovenous fistulas and pseudoaneurysms. Arteriovenous fistulas arise when a lacerated artery and vein in proximity to each other form a direct connection while healing. Pseudoaneurysms result when surgery injures the wall of a high-pressure artery and blood then leaks into a lower pressure area such as the collecting system, connective tissue, or vein [9]. In both of these cases, significant renal bleeding can present in the early postoperative course or in delayed fashion as late as a number of weeks postoperatively.

## Risk factors associated with hemorrhage during percutaneous nephrolithotomy

Myriad factors have been linked to PCNL-related hemorrhage, and can be grouped together as patient-related factors, operative-related factors, and stone-related factors.

### Patient-related factors

Patient-related factors that have been correlated with increased bleeding risk are numerous and those most consistently shown to increase perioperative bleeding on multivariate analysis include obesity, certain comorbidities such as hypertension, arteriosclerosis and diabetes, older age, patient frailty, higher American Society of Anesthesiology (ASA) classification, renal insufficiency, lack of preoperative hydronephrosis, history of prior renal surgery, renal anomalies, underlying or prior urinary tract infections, and the use of anticoagulants [10–12]. One group has evaluated the effect of prior renal surgery on hemorrhage and has found prior open stone surgery was significantly more likely to be associated with post-PCNL hemorrhage compared to prior PCNL or shock-wave lithotripsy [13]. Interestingly, this contrasts with findings from another group in the same geographic region who found no differences in patients previously treated with shock-wave lithotripsy or open stone surgery [14].

Recent or recurrent urinary tract infections can lead to chronically inflamed tissue, which tends to bleed more easily. Additionally, infection is known to impair effective blood clotting. Furthermore, patient frailty, as measured by Charlson comorbidity index (CCI) and activities of daily living, has been linked to overall patient complications and may be related to increased bleeding risk [15, 16].

### Operative-related factors

Operative and technical factors that have been shown to influence and increase bleeding risk include longer operative duration, larger access tract size, less surgeon experience, use of multiple access tracts, upper pole calyceal access, longer intraoperative time to successful renal puncture and larger bore nephroscopes [10, 17–23]. Compared with smaller access sheaths (≤18 Fr), larger access sheath size was associated with increased hemorrhage risk (threefold increased risk for access sheaths 24–26 Fr and almost fivefold increased risk for access sheaths 27–30 Fr) [24]. Increasing number of access tracts, in particular three or more, routinely appears to correlate with increased risk for higher blood loss and transfusions following PCNL [17, 20–22, 25].

Increasing operative time has also been shown to increase bleeding risk. Though most likely a continuum, surgical duration in excess of approximately 110–120 minutes has been predictive of post-PCNL bleeding [26, 27]. At least one study has suggested that less surgeon experience was associated with an almost threefold elevated hemorrhage risk (0.6% for an experienced endourologist compared to 1.7% for a general urologist or trainee) [18].

A few studies have evaluated the relationship between PCNL-related hemorrhage and hospital case volume, and the evidence remains equivocal as to how hospital PCNL volume influences bleeding risk. One study from the United States used the Nationwide Inpatient Sample and found transfusion rates were highest in the lowest and highest quartile volume centers on univariate analysis, however hospital PCNL case volume was not found to independently predict for transfusions on multivariate analysis [28]. In another study from the United Kingdom, no difference in major hemorrhage events was seen among those hospitals performing low (<10 PCNLs per year; 1.3%), medium (10–20 PCNLs per year; 1.5%), and high (>20 PCNLs per year; 1.5%) volumes of PCNLs [29]. Results from the Global PCNL Global study did show a higher reported rate of bleeding (9% vs. 5.5%), mean hemoglobin change (3.9 vs. 3.5 mg/dl), and blood transfusion rate (5.2% vs. 3.4%) in low volume (<77 PCNLs per year) compared to high-volume (>77 PCNLs per year) centers [30].

Several studies have shown that renal access obtained by a urologist is associated with less bleeding, fewer complications, and a higher stone-free rate than renal access obtained by a radiologist [31–33]. This is thought to be related to the fact that the goals of the radiologist and urologist may differ in these circumstances. The typical tract created by the urologist is often a more direct route, and often more superiorly located (Figure 33.1). It is prudent to assess the radiologist-obtained renal access tract prior to tract dilation, and this can be done with multiplanar fluoroscopy and antegrade nephrostography. If suboptimal access is found, there should be a low threshold for obtaining a new, better access.

### Stone-related factors

Lastly, stone composition and burden have been correlated with increased bleeding risks. In particular, staghorn stone configuration appears to be consistently related to increased risk of perioperative PCNL bleeding. In at least one report, an almost 30% increased risk of bleeding was encountered when more than two access tracts were used to approach staghorn calculi [21].

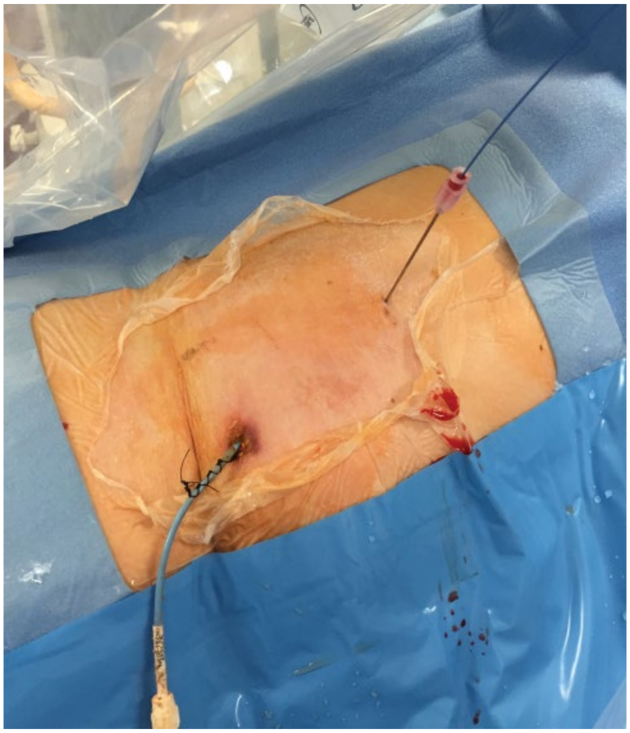

**Figure 33.1** Percutaneous access obtained by interventional radiologist (left side of image) versus percutaneous access obtained by endourologist (right side of image). The endourologist access tract is superiorly located and provides a direct route to renal calculus.

## Preoperative patient assessment and optimization

Absolute contraindications to PCNL include uncorrected coagulopathy and active infection. A complete history and physical examination is important in all patients prior to PCNL, and close attention should be paid to personal and family history of blood dyscrasias and coagulopathic states (clotting factor deficiencies, idiopathic thrombocytopenic purpura, coronary artery stenting, mechanical heart valves, atrial fibrillation, venous thromboembolism, etc.). Medications should be reviewed with the patient with a particular eye towards antithrombotic medications and herbal supplements. Full laboratory evaluation, including complete blood count, serum electrolytes, creatinine level, and coagulation parameters, are important to determine preoperatively. Appropriately screened and cross-matched blood products should be available.

Previous renal and retroperitoneal surgery should be specifically elicited, as previous open renal stone surgery may increase the risk of angioembolization, while prior PCNL may not [34]. Preoperative cross-sectional imaging is recommended to help fully understand renal stone burden and anatomy, and to evaluate for anatomical abnormalities and perinephric organ location. Preoperative negative urine cultures should be the goal, and review of prior positive urine cultures and sensitivities are important in patients with a history of urinary tract infections, as these can influence perioperative antibiotic choices.

Scrutiny of any antiplatelet and anticoagulant medications is paramount as the widespread use of these agents becomes more frequent and the number of agents utilized continues to grow. Determining the indications for such antithrombotics is imperative and can have ramifications on the perioperative management of such medications, including the relative risks of continuing versus stopping them, and whether bridging regimens are indicated. Further details on this topic can be found in Chapter 5.

In the operating room, immediately preceding PCNL, maintaining adequate patient temperature is imperative as efficient clot formation depends on body temperature, and lower core body temperatures are associated with inefficient clot formation [35, 36]. To this end, temperature monitoring in the perioperative period is important, and increasing ambient room temperature and utilizing convective air-warming systems can combat rapid body temperature losses associated with clothes removal and anesthetic induction prior to the start of surgery. During patient positioning alone, core body temperatures can fall by approximately 1°C [36, 37]. Furthermore, it is important to use warmed irrigation fluid when available.

## Intraoperative hemorrhage: recognition and management strategies

Intraoperative hemorrhage is typically not subtle, and can happen at any step during PCNL, from initial percutaneous access to final urinary drainage. It is thought that the moments of greatest hazard are: (i) during initial access and percutaneous tract dilation, when any of the perinephric organs or vascular structures is at risk for nonvisualized (blind) puncture injury, and (ii) during excessive torqueing of the sheath or nephroscope during the procedure, which can result in renal parenchymal shearing and tearing.

The first step to minimizing bleeding begins with the initial renal puncture. The preferred approach involves an "end-on" calyceal puncture, where the access needle passes centrally through the longitudinal axis of the targeted posterior calyx. Moreover, the preferred access should traverse Brödel's avascular plane along the shortest and straightest track from the skin to the collecting system, thereby minimizing the amount of renal parenchymal disruption. Excessive medial advancement of renal dilators should be avoided and careful note should be made to pass or situate dilators just to the forniceal–calyx junction. Creating as straight and short a percutaneous track as possible is advised, as is dilating in as straight a manner as possible between skin and target calyx; this will reduce the possibility of guidewire kinking which can hinder the passage of subsequent catheters, dilators, and sheaths. These strategies are thought to reduce the risk of injury to the interlobar, segmental, and main renal vessels, and to reduce the risk of renal pelvis perforation [36, 38–42]. Routine use of flexible nephroscopes, when available, can help reduce overly aggressive torqueing of the nephroscope and access sheath, which can lead to renal parenchymal tearing and resulting increased bleeding [43].

When significant bleeding is encountered, especially during percutaneous access and tract dilation, the anesthesia team should be notified immediately so that preparations can be made for closer hemodynamic monitoring and possible transfusion of blood products. Bleeding in these instances is frequently self-limited, and can usually be managed with tamponade from the access sheath once it is properly positioned across the renal parenchyma. In most cases, PCNL can then proceed as planned.

During stone manipulation, the access sheath should remain positioned across the renal parenchyma to avoid repeated shearing and loss of tamponade, both of which will increased bleeding and obscure vision. Removing stones or fragments too large for the access sheath can lead to sharp and everted deformation of the working sheath, which can lead to tract tearing and increased bleeding upon sheath removal. Severe bleeding has been reported following rupture of a renal working sheath [44]. To prevent these issues from arising, excessive force should be minimized when removing calculi, and attempted removal of stones that are too large should be avoided.

If significant bleeding or the passage of blood clots persists through the sheath, visualization may be impaired. When visualization is too poor to continue safely, it is best to place a large-bore nephrostomy tube and return at a later date, after bleeding has ceased. Bleeding severe enough to cause early termination of PCNL is infrequent, reported in about 0.2% of cases [45, 46].

Hemodynamic instability, often evidenced by tachycardia, hypotension, and potentially increasing vasopressor requirement from the anesthesia team, are concerning and should alert the surgeon to the possibility of large blood loss. Good communication with the anesthesia team is critical in these instances.

It should be noted that intraoperative assessment of blood counts (hemoglobin, hematocrit) may underestimate the degree of blood loss in the acute setting and initiating blood product transfusions should be considered when signs of hemorrhagic shock exist despite a higher than expected blood count intraoperatively. Similarly, a steady but still significant blood loss may be underperceived due to irrigation fluids, and this can often manifest itself as gradually worsening hypotension and tachycardia as the PCNL proceeds. This is most common during longer PCNLs, and is one of the reasons certain stone centers terminate PCNLs after a set duration of time (often 2–3 hours), and stage the procedure thereafter if more work is still necessary.

When heavy bleeding is encountered, vision can be improved by moving the access sheath closer to the stone or collecting system wall. Irrigation pressure can also be increased, but this should be done with caution as it can lead to increased pyelosinus, pyelovenous, and pyelolymphatic fluid absorption and may increase the risk for infection and sepsis. If vision remains limited or bleeding persists, a large-diameter catheter (e.g. Councill tip) can be placed over a wire and through the sheath into the kidney. The catheter balloon can be inflated (approximately 3–5 ml) to provide additional compression in the renal parenchyma to supplement the sheath's tamponade on the tract. After approximately 5 minutes, the balloon can be deflated and the bleeding reassessed. If the bleeding persists, the catheter can be advanced or withdrawn slightly within the renal parenchyma and the balloon reinflated with a view to achieving hemostasis. At this point, the procedure can be terminated if it is felt that the risk of further bleeding outweighs the benefits of continuing. The sheath can be removed and the catheter can be left in place for urinary drainage and to facilitate subsequent renal access. Another option is to use a large-bore nephroureteral catheter or re-entry tube to provide tract tamponade and maintain access to the collecting system and ureter.

A Kaye tamponade balloon catheter (Cook Medical, Bloomington, IN, USA) can be advanced over a wire into the renal pelvis under fluoroscopic guidance and provides excellent control of tract bleeding while maintaining collecting system access [47, 48]. This catheter provides balloon tamponade along the entire length of the tract and retains entry and access to the pelvicalyceal system. In the absence of a Kaye or other suitable catheter, the balloon dilator used for initial tract dilation and access sheath placement can be repositioned and inflated along the length of the access tract.

These techniques allow for compression along the entire length of the access tract. Moreover, they usually provide adequate tamponade of less common sources of bleeding such as subcostal or intercostal vessels and bleeding stemming from unintended organ injury during initial renal puncture and dilation (e.g. spleen, liver). Such infrequent sources of PCNL-related hemorrhage usually manifest at the conclusion of surgery, just after removal of the access sheath, or at the time of nephrostomy tube removal.

Refractory bleeding, significant blood clots emanating from the nephrostomy catheter, or hemodynamic instability after any of the above maneuvers suggests ongoing, often arterial, bleeding (Figure 33.2). Attention should be paid to the patient's vital signs, and if there is concern for impending hemorrhagic shock, blood product transfusions should be initiated, the procedure should be aborted, and a low threshold should exist to transfer patients directly from the operative suite to angiography for possible angioembolization. In the absence of hard signs of hemorrhagic shock, the patient may be monitored with frequent vital signs assessments and serial assessment of blood counts. In instances where bleeding is believed to be from an intercostal vessel, a small incision and cutdown directly onto the caudal aspect of the involved rib, allowing for vascular control, may be considered [36].

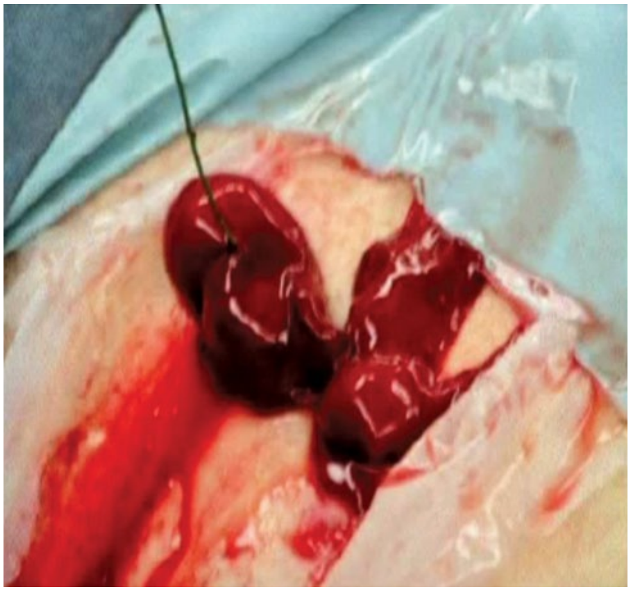

**Figure 33.2** Significant blood clots emanating from the nephrostomy tract suggests ongoing, often arterial, bleeding.

Catastrophic bleeding in the setting of severe hemodynamic instability may preclude safe transit for angioembolization. This can result from injury to the main renal vessels and usually occurs during overly forceful tract dilation or too medial placement of initial puncture needle and tract. Very occasionally, though, this may result from overly aggressive nephroscope and renal manipulation. Thankfully, main renal vessel injury is rare (0.4%) [45, 49].

Strategies to avoid this complication include ensuring urine return through the puncture needle prior to tract dilation, withdrawing the needle and choosing a different puncture if blood is aspirated during initial needle puncture, and directing a stiff guidewire down the ureter prior to tract dilation or heavy stone manipulation to direct dilation forces down the ureter and away from the renal hilum. These instances of life-threatening hemorrhage appear rare in contemporary PCNL series. When this is encountered and the patient cannot be safely transferred for angioembolization or this resource is not available, then retroperitoneal renal exploration can be attempted to achieve vascular control; however, this often results in nephrectomy.

## Alternatives and adjuncts to tract tamponade

Modifications to conventional catheter tamponade for tract bleeding have been proposed, and include a variety of hemostatic inducing agents, an antifibrinolytic (tranexamic acid), electrocautery, and cryoablation. Fibrin glue, porcine-derived absorbable gelatin compressed sponges (Gelfoam, Pfizer, Inc., New York, NY, USA), oxidized cellulose (Surgicel, Ethicon, Somerville, NJ, USA), fibrin-soaked porcine gelatin sponges (Spongostan, Ferrosan Medical Devices, Copenhagen, Denmark), sterile equine collagen matrix coated with human thrombin, fibrinogen, and fibrin glue (TachoSil, Nycomed, Zurich, Switzerland), and bovine collagen granules (FloSeal, Baxter Medical, Deerfield, IL, USA) have been used in an attempt to reduce post-PCNL bleeding events. Descriptions exist of using these agents alone or in combination with various catheters to help target delivery of the hemostatic agent to only the percutaneous renal tract.

One of the more elaborate methods includes a hemostatic "sandwich" consisting of gelatin matrix hemostatic sealant interposed between two Councill tip nephrostomy tubes, each with inflated balloons [50–55]. For uncomplicated PCNL without refractory bleeding, Abbott et al. proposed the use of a hemostatic sealant as an adjunct to "tubeless" PCNL [56], whereby the nephrostomy tract is occluded by thrombin-soaked absorptive gelatin (Gelfoam) and the skin closed without a percutaneous drainage catheter. A similar technique was earlier described by Kaufmann et al. [57], who used FloSeal to similar effect.

More recent meta-analyses evaluating the role of hemostatic agents provide no convincing evidence that the use of such agents along the access tract provides any significant benefit in terms of blood loss, transfusion requirement, complications, fevers, or analgesic requirement [58, 59]. Overall, it appears the use of hemostatic agents is safe, but comes at considerable cost and does not appear to meaningfully change the bleeding risk.

At least one randomized controlled prospective study with 200 patients has analyzed the effect of tranexamic acid, an antifibrinolytic, on bleeding following PCNL [60]. In this initial study, blood transfusion rate was significantly lower (2% vs. 11%; $P = 0.018$) and operative time was significantly less (48 minutes vs. 71 minutes; P 0.0001) in the group receiving tranexamic acid. Though encouraging, further studies are necessary to better understand the true advantages and disadvantages of this approach.

Cauterization of the percutaneous access tract has also been explored, primarily in an effort to achieve successful tubeless PCNL. A retrospective study found a statistically significant decrease in blood transfusion rate among patients who underwent electrocautery of the PCNL tract compared to those who did not [61]. However, the authors point out care must be taken to avoid inadvertent injury to other perinephric structures.

Okeke et al. proposed cryotherapy of the nephrostomy tract as another hemostatic alternative [62]. In this technique, a cryoprobe traverses the nephrostomy tract and a single 10-minute freeze–thaw cycle was applied (Figure 33.3). It was found that the cryotherapy group had significantly shorter hospital stays, decreased rates of delayed bleeding, and decreased urinary leak rates. However, use of the cryotherapy system was found to be cumbersome and led to longer operative times, thereby calling into question the potential benefit.

## Management of postoperative and delayed hemorrhage

In the postoperative period, patients should be monitored for changes in vital signs and for hematuria, both from the nephrostomy tube and per urethra. Bleeding

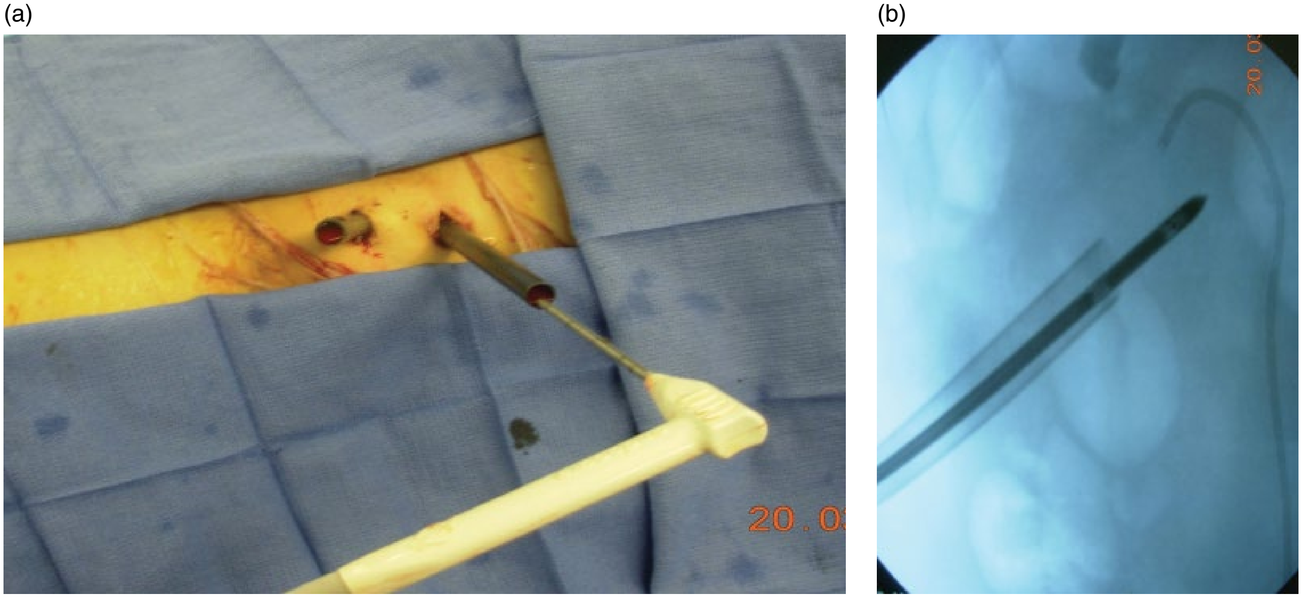

Figure 33.3 (a) Cryoprobe introduced through percutaneous nephrostomy access sheath. (b) Fluoroscopic image of cryoprobe within tract during freeze–thaw cycle.

originating from the parenchyma usually manifests as hematuria through the nephrostomy tube and or urethral catheter, while bleeding from the percutaneous tract can present as bleeding around the nephrostomy tube. Moderate hematuria can often be managed by clamping the nephrostomy tube temporarily or elevating the nephrotomy drainage bag above the level of the ipsilateral kidney, both of which aim to facilitate clot formation within the kidney and potentiate internal tamponade.

Heavy tract bleeding or hematuria in the immediate postoperative period can often be managed through a combination of local compression and nephrostomy tube clamping. Local compression becomes particularly important in instances where no nephrostomy tube is placed (i.e. in “tubeless” PCNL). This can be accomplished by repositioning the patient completely supine, which allows the overlying organs to provide anterior pressure, and placing a 3-liter fluid bag underneath the ipsilateral flank, which increases posterior compression (Figure 33.4). Alternatively, hands or fists situated over the ipsilateral abdomen and back can provide direct pressure.

Following the immediate postoperative period, persistent or worsening hematuria should raise suspicion for hemorrhage that may require intervention. The color of hematuric urine from the nephrostomy tube and urethral catheter provide some approximation of the degree of ongoing bleeding. When heavier hematuria or clot passage is noted, clamping the nephrostomy tube for a number of hours postoperatively is advised. When the nephrostomy tube is unclamped later, light pink to clear urine output suggests severe bleeding has abated.

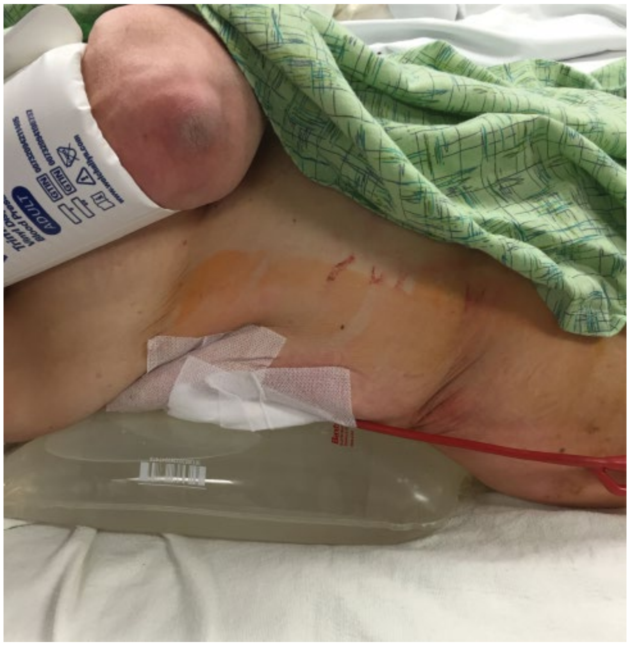

**Figure 33.4** Placing the patient supine with 3-liter fluid bag underneath the ipsilateral flank can assist with local compression for hemostasis.

Occasionally, heavy bleeding arises with nephrostomy catheter removal. This often stems from an open arterial branch that was occluded by the nephrostomy catheter or by a vessel that was in spasm but opens with catheter removal. Rapid catheter reinsertion and external tract compression are recommended in this scenario, with consideration for subsequent renal angiography and possible embolization, especially when accompanied by signs of hypovolemia and hemorrhagic shock [36, 45].

When the above-described measures are unsuccessful in controlling bleeding or when the severity and acuity of bleeding are more drastic, renal angiography with the option of selective or superselective embolization is recommended. In centers where the technique is available, it is often the preferred first-line procedure as it can be both diagnostic and therapeutic in the same setting (Figure 33.5). In general, indications for renal angioembolization include the need for repeated transfusions, ongoing hemoglobin decrease, hemodynamic instability, repeated bladder clot evacuations, and imaging (e.g. Doppler ultrasound or computed tomography) suggestive of vascular lesions [19, 45, 63]. Patients who continue to show significant hematuria, large blood clot passage per urethra or accumulation of clots within the bladder (Figure 33.6), ongoing hemoglobin loss with hypotension and tachycardia in the few days following PCNL, as well as those who return within a week to a month after hospital discharge with similar symptoms and signs should be routinely considered for renal angiography and possible embolization.

In these situations, the most common vascular lesions encountered are arterial pseudoaneurysms and arteriovenous fistulas, and less frequently arterial lacerations. Vascular wall injury during PCNL can lead to pseudoaneurysms in high-pressured vessels. Arteriovenous fistulas develop when high-pressured arteries form an inappropriate communication with and drain directly into the lower pressured veins. Arteries that heal with a direct communication to the collecting system may present as intermittent, severe hematuria, clot passage, and flank pain [5, 9]. Contemporary reviews show an approximately 1–1.5% incidence of renal angioembolization following PCNL, and increased experience with this technique has almost completely obviated the need for partial and total nephrectomy to control bleeding in centers with available angioembolization technology and expertise [5–8, 33, 64, 65]. The most common

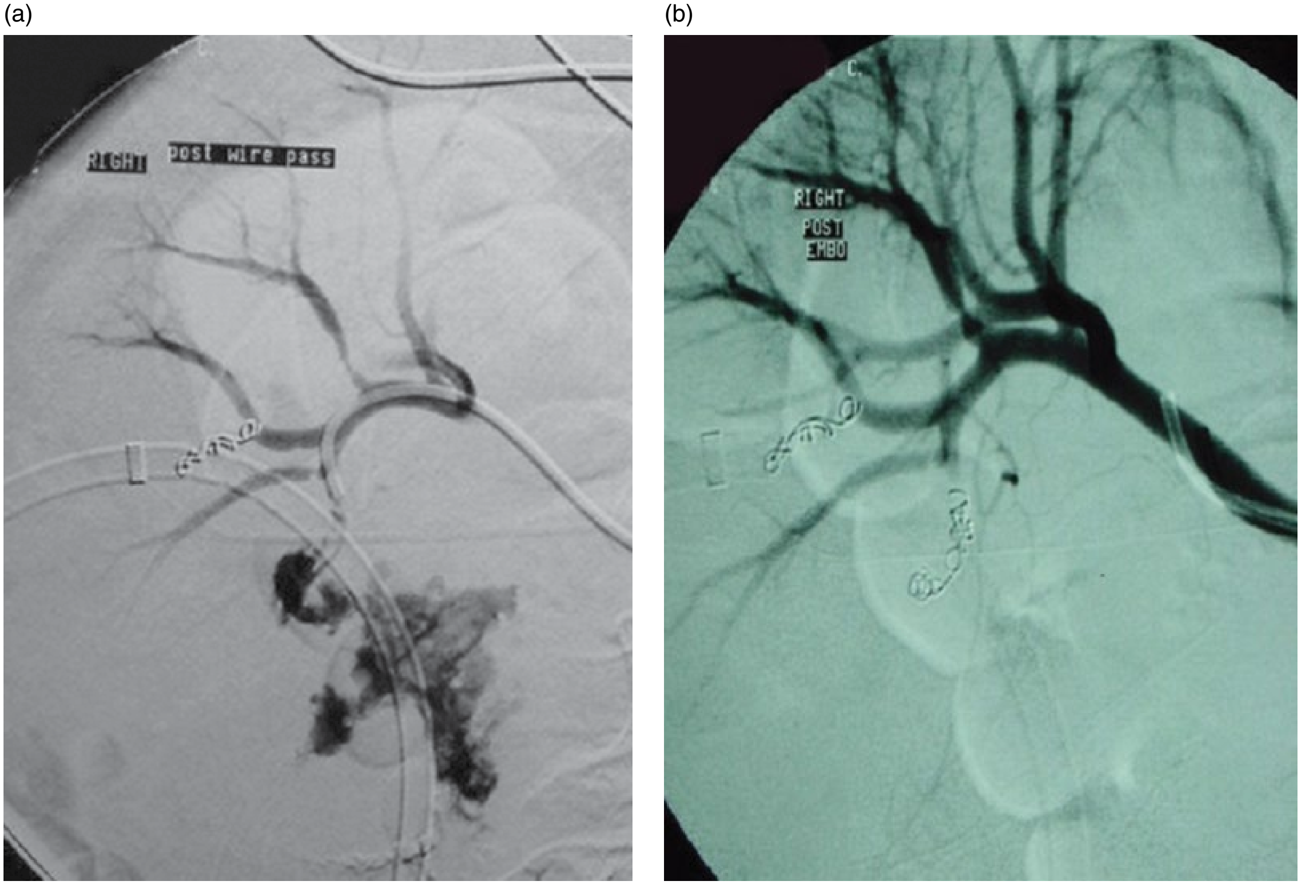

**Figure 33.5** (a) Angiography demonstrates vascular extravasation in arterial branches supplying kidney. (b) Post-coil angioembolization results in cessation of extravasation and control of bleeding.

site of vascular injury requiring angioembolization is variable and appears to coincide most with the preferred calyx of access rather than an obviously anatomically increased incidence with one location relative to another [18, 19, 66].

Bleeding associated with pseudoaneurysms and arteriovenous fistulas is often referred to as delayed bleeding, as the average onset of hemorrhage appears to be one to two weeks after surgery. However, delayed bleeding can present as much as a month or longer following PCNL [33, 35, 36]. Initial selective renal arterial embolization is successful at controlling renal bleeding 80–90% of the time [6, 66, 67]. In one series reviewing initial angioembolization failures, renal arterial embolization was found to initially fail in approximately 10% of cases (12 out of 117 patients), with successful hemorrhage control during second embolization in 8 out of 12 patients, during third embolization in 3 out of 12 patients, and a single patient went on to require nephrectomy [67].

When analyzing risk factors for failed initial angioembolization, multiple bleeding sites and multiple percutaneous tracts were found to correlate with angioembolization failure. In a 12-year review from a single institution, superselective angioembolization was found to have an initial success rate of 85% (35 out of 41 patients) and of those who failed, two patients went on to undergo nephrectomy for persistent bleeding [66]. In each case, multiple punctures (>3) were performed for a large-burden staghorn calculus. In other instances, failed angioembolization eventually leading to nephrectomy was associated with underlying, and previously unrecognized, malignancy (renal cell carcinoma or upper tract urothelial carcinoma), and a high index of suspicion should be maintained in cases of failed initial superselective angioembolization [6, 68].

Following superselective renal angioembolization, the vast majority of patients (up to 90%) can experience some combination of flank pain, nausea and vomiting, and leukocytosis, collectively referred to as postembolization syndrome [68, 69]. Pain can be severe following embolization of large swaths of renal parenchyma, and anti-inflammatories, and in some instances steroids, may be used prophylactically. Loss

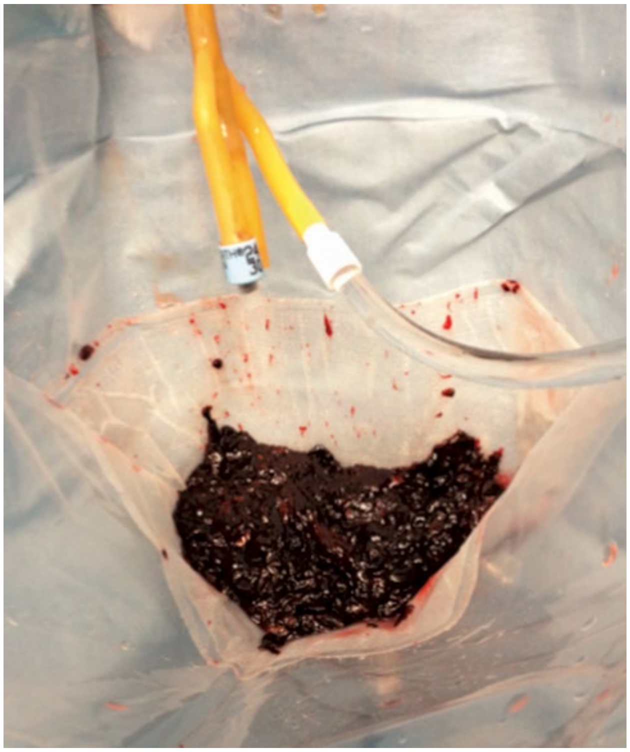

**Figure 33.6** Significant hematuria and clot burden from the bladder that persists after PCNL may indicate arterial bleeding that may require angioembolization.

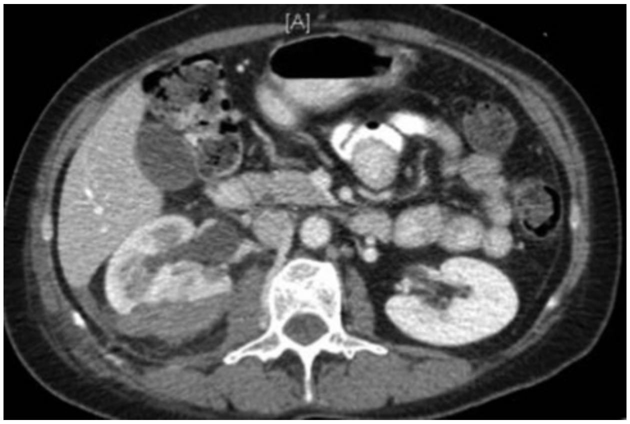

**Figure 33.7** Cross-sectional axial CT demonstrating right-sided perinephric hematoma, which can occur in up to one-third of patients undergoing PCNL.

of renal function following angioembolization has been evaluated, and it appears the effects are most pronounced in patients with solitary kidneys with one-third (3 out of 9 patients) showing increased serum creatinine but none requiring dialysis in one study. Interestingly, in the same study, 20% of patients (6 out of 30) showed no photopenic areas on renal scintigraphy, and renal function in these ipsilateral renal units was seen to significantly increase from 25% to 34% at mean follow-up of 3.9 years [70]. Coil migration, albeit rare following superselective renal angioembolization, has been described and is seen most commonly in the lung or urinary tract with resultant urinary tract obstruction [71, 72].

Rarely, lumbar artery injury can be the source of significant bleeding after PCNL, and angioembolization has been employed successfully to manage this complication as well, although this requires a limited aortogram and should be considered if the initial renal angiogram shows no bleeding [73, 74].

Perinephric and subcapsular hematomas may occur in up to one-third of PCNLs, and are usually clinically silent with fewer than 1% requiring intervention with selective angioembolization (Figure 33.7). Prior shock-wave lithotripsy predisposes to perinephric hematoma. Perinephric hematoma should be considered when post-PCNL hemoglobin continues to drop despite clear urine drainage. The use of triphasic CT in these situation can help make the diagnosis and help distinguish active renal bleeding from urinary leak and urinoma formation [75, 76]. In rare instances, a perinephric hematoma may lead to a "Page kidney," where incomplete or delayed resorption of the hematoma causes renal compression and relative hypoperfusion and the subsequent development of hypertension. In these instances, percutaneous drainage of the perinephric hematoma is suggested [63, 75].

## Conclusions

Hemorrhagic complications associated with PCNL remain common and are often associated with larger stone burdens, prolonged operative times, surgeon inexperience and multi-tract procedures. Most bleeding-related complications can be managed with conservative measures. Numerous techniques are available to address intraoperative and postoperative hemorrhage. For serious and life-threatening hemorrhage and for persistent bleeding refractory to conservative measures, superselective renal angioembolization has proven itself as an excellent technique to control post-PCNL bleeding with relatively minor associated morbidity. Early recognition and management of bleeding complications require attention to both technical and patient-related factors, and are critical to executing safe and effective percutaneous nephrolithotomy.

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## 34

# Diagnosis and Management of Thoracic Complications of Percutaneous Renal Surgery

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## Introduction

Percutaneous nephrolithotomy (PCNL) is the recommended treatment modality for renal stones greater than 20 mm in size, staghorn stones, infection-based stones, and a variety of other indications such as percutaneous renal tumor treatment, stones in kidneys with utereropelvic junction (UPJ) configuration, and for treating stones in patients with urinary diversions [1, 2]. The concept of percutaneous stone surgery was first described by Rupel and Brown in 1941. The authors inserted a cystoscope through a percutaneous nephrostomy tube track in order to treat a renal stone in a solitary kidney [3]. Fernström and Johannson later described the technique of using serial dilation to percutaneously treat a renal stone in 1976 [4]. Since these early descriptions, experience and techniques have expanded and now PCNL is widely performed worldwide. The percutaneous approach means there is a certain risk of injury to structures surrounding the kidney. Therefore, successful utilization of this approach relies on methods to minimize complications and maximize the ability to treat the pathology. Percutaneous access to the kidney is obtained for a number of other indications aside from stone management, such as antegrade management of UPJ obstruction, antegrade management of upper tract urothelial cancer, and percutaneous ablation of renal masses.

There are many possible complications with this approach, yet the proximity of the kidneys to the diaphragm and pleura make thoracic complications a unique and important complication to consider. This chapter discusses the type of thoracic complications that are possible as a result of percutaneous renal surgery. We also review the relevant literature regarding the incidence and management of thoracic complications so that the reader gains an updated management algorithm.

## Anatomic considerations

The kidneys are located in the superior aspect of the retroperitoneum, in close proximity to the diaphragm and pleura. The superior pole of the right kidney is typically located slightly superior to the 12th rib, while the superior aspect of the left kidney is often located just beneath the 11th rib [5]. The intercostal spaces are located between the ribs and are named for the rib superior to the space. Therefore, the 11th intercostal space is located between the 11th and 12th ribs. Figure 34.1 demonstrates the anatomic relationships between the kidneys, ribs, and parietal pleura.

The lungs are enveloped by two layers of a thin, serous, membrane called the pleura. The parietal pleura lines the internal aspect of the thoracic cavity while the visceral pleura directly surrounds each lung. These two layers of pleura are generally in close proximity with only a small amount of pleural fluid between them that serves as a lubricant, allowing the two layers to slide past each other with minimal friction. The potential space between these two layers is called the pleural space. Thoracic complications arise when significant air or fluid fills the pleural space, causing irritation or compression of the lungs [6].

Posteriorly, in the midscapular line, the parietal pleura attaches to the internal aspect of the 12th rib [7]. At the midaxillary line, the pleural is approximately at the level of the 10th rib and anteriorly, the parietal pleura is approximately at the level of the 8th rib. Posteriorly, the 12th rib curves downward, yet the pleura continues in a relatively horizontal plane, crossing the 12th rib at the lateral border of the erector spinae muscles of the back. In some individuals, the 12th rib is difficult to palpate through the subcutaneous layers, making accurate identification on physical exam difficult [6].

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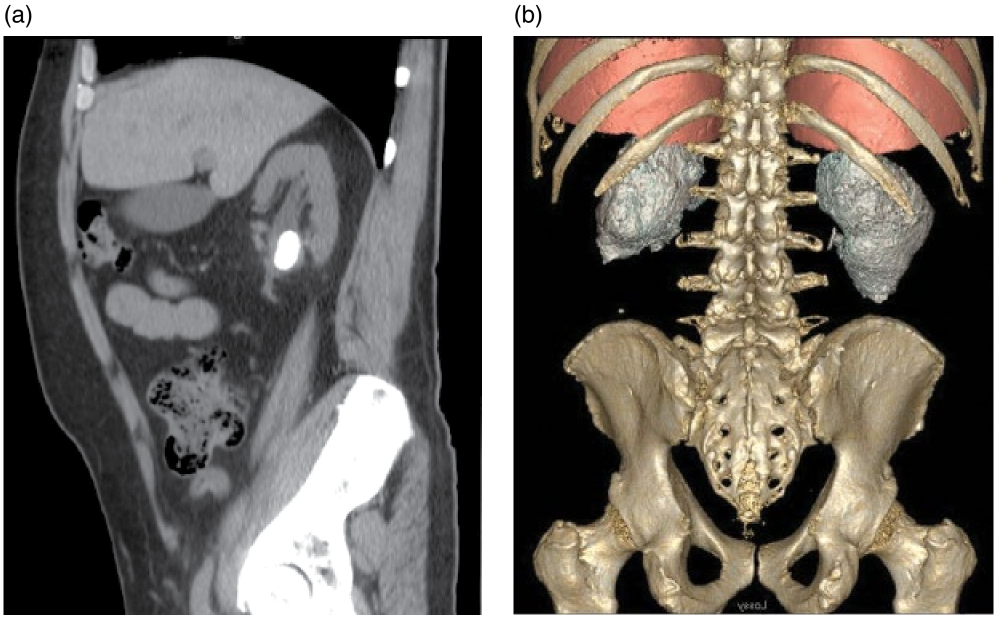

**Figure 34.1** Relationship of the kidneys, pleura, and ribs. (a) CT image in sagittal section showing the pleural reflection extending down to the 12th rib. Notice that supracostal access would violate the pleura in this patient. (b) Three-dimensional CT reconstruction of the same patient showing the relationship of the pleura, ribs, and kidneys. The parietal pleura has been colored pink, and the kidneys are gray. Notice that the pleura crosses the 12th rib approximately half-way along its length.

The relative levels of the kidneys and parietal pleura in relation to the ribs means that in many patients the superior aspects of the kidneys are covered by parietal pleura posteriorly [6]. This relationship is an important consideration since many urologists approach percutaneous surgery of the kidney from the posterior aspect.

## Incidence, etiology, and risk factors of thoracic complications

Percutaneous nephrolithotomy techniques have improved since the early descriptions, with modern data showing an incidence of Clavien grade III or higher complications of about 5% [8–10]. There is variability in the reporting of thoracic complications. Some studies report all complications detected, many of which are incidentally discovered on postoperative imaging, while others report only complications that were diagnosed based on symptoms. One multicenter study reported the outcomes of 197 patients who underwent PCNL and showed that 111 (56%) had CT evidence of chest pathology on routine follow-up imaging. However, 88 of these were atelectasis that resolved with conservative measures and only one patient required a chest tube for a hydrothorax [11]. Nevertheless, thoracic complications constitute a significant percentage of the overall complication rate following percutaneous renal surgery with an incidence of 1.8–3.1% [8–10, 12]. The etiology of thoracic complications involves the introduction of air or fluid into the pleural space during or following the procedure.

The proximity of the kidneys to the diaphragm and pleura directly correlate to the risk of thoracic complications. Therefore, the risk of injury to the pleura increases with higher intercostal space access to the kidney. Table 34.1 shows the results of selected studies demonstrating the risk of thoracic complications in relation to the level of access. Munver et al. categorized thoracic complications by site of entry, showing a rate of pleural injury of 4.5% for subcostal access versus 16% for supracostal access. In the supracostal group, 35% of the patients with access above the 11th rib had a pleural injury [13]. Lojanapiwat and Prasopsuk reported a 15.3% hydrothorax rate for supracostal access versus 1.4% for subcostal access. However, only 10 of these patients required drainage. In contrast, nine (5%) of the patients in the supracostal group required drainage [14]. The Clinical Research Office of the Endourological Society (CROES) published data from 5803 patients across 96 worldwide centers showing an overall rate of thoracic complications of 1.8%, all of which were hydrothoraces [10]. These data were then analyzed to evaluate the risk of thoracic complications between patients with upper pole access versus patients with lower pole access. The upper pole access group had a hydrothorax rate of 5.8% whereas the lower pole access group had a hydrothorax rate of 1.5%. This equated to a hydrothorax odds ratio of 0.4 (0.19–0.85) for lower pole versus upper pole access.

**Table 34.1** Review of selected publications regarding thoracic complications following percutaneous renal surgery.

| Reference | Study years | Number of patients | Pleural complications | Findings |
|---|---|---|---|---|
| De la Rosette et al. [10]<br>CROES Data | 2007–2009 | 5660 Total<br>948 Supracostal<br>4712 Subcostal | 104 (1.8%) | All hydrothoraces |
| Tefekli et al. [15]<br>CROES Data | 2007–2009 | 3515 Total<br>403 Upper pole<br>3112 Lower pole | | Lower pole access has 60% lower odds of hydrothorax vs. upper pole<br>Access above the 11th rib has a 5.6× higher risk of hydrothorax compared to access above the 12th rib |
| Semins et al. [11] | 2007–2008 | 197 Total | 17 (8.6%) | Only 1 pt required a chest tube |
| Bell et al. [16]<br>Lojanapiwat and Prasopsuk [14] | 2006–2014<br>2006 (publication date) | 491 Total<br>346 Supracostal<br>145 Subcostal<br>464 Total<br>170 Supracostal<br>294 Subcostal | 24 (4.9%)<br>22 (6.4%)<br>2 (1.4%)<br>30 (6.5%)<br>26 (15.3%)<br>4 (1.4%) | 13 Hydrothoraces<br>11 Pneumothoraces<br>Hydrothorax in 26 pts (15%) with supracostal vs. 4 pts (1.4%) with subcostal access<br>10 pts (2.2%) required drainage |
| Muslumanolgu et al. [17] | 2002–2004 | 275 Total<br>23 Supracostal<br>252 Subcostal | 2 (0.7%)<br>2 (8.4%)<br>0 | Both hydropneumothoraces |
| Sukumar et al. [18] | 2000–2007 | 565 Total<br>110 Supracostal<br>455 Subcostal | 10 (1.8%)<br>10 (9.1%)<br>0 | All hydrothoraces |
| Mousavi-Bahar et al. [19] | 2000–2006 | 671 Total<br>199 Supracostal<br>472 Subcostal | 5 (0.7%)<br>5 (2.5%)<br>0 | Pneumothorax (*n* = 3)<br>Hemothorax (*n* = 2) |
| El-Assmy et al. [20] | 1999–2003 | 1121 Total<br>141 Supracostal<br>980 Subcostal | 2 (0.2%)<br>2 (1.4%)<br>0 | Both hydrothoraces |
| Netto et al. [21] | 1995–2000 | 119 Total | 2 (1.7%) | 1 Pneumothorax and 1 hydrothorax |
| Munver et al. [13] | 1993–1999 | 300 Total<br>98 Supracostal<br>202 Subcostal | 8 (2.7%)<br>7 (7.1%)`<br>1 (0.5%) | 5 Hydrothoraces (4 in pts with supracostal access)<br>2 Nephropleural fistulas (both with supracostal access)<br>1 Pneumothorax (supracostal access) |
| Desai et al. [12] | 1991–2008 | 773 Total | 5 (0.6%) | All pneumothoraces |

The odds ratio of hydrothorax for access above the 11th rib versus above the 12th rib was 5.6 (1.97–15.8) [15].

These data have led some surgeons to prefer lower pole access when possible as it has a much lower rate of thoracic complications and flexible nephroscopy can be used to treat upper and middle calyceal stones [22]. Proponents of upper calyceal access cite improved access to the ureter and better stone clearance rates. Upper pole access is often preferred to treat urinary stones in the proximal ureter, stones associated with UPJ obstruction, upper calyceal diverticulum stones, renal anomalies, and complex staghorn stones [14, 15, 23]. However, the benefits of upper calyceal access must be weighed against the risk of thoracic complications, as upper calyceal access requires a supracostal approach in approximately 70% of patients [15].

When access superior to the 12th rib is preferred, staying lateral to the midscapular line may reduce the risk of pleural injury. Recall that the 12th rib curves downward, while the pleura maintains a mostly horizontal course along the posterior chest. Therefore, staying lateral to the paraspinal muscles may allow supracostal access while decreasing the incidence of pleural injury.

Another risk factor for the development of a hydrothorax is premature withdrawal of the percutaneous access sheath. The percutaneous renal access sheath offers several advantages, it diverts urine and irrigation from the renal collecting system through the center of the sheath and out of the body. This helps to decrease the intrarenal pressures while operating and helps to minimize extravasation of fluid out of the kidney into the retroperitoneum. In terms of thoracic complications, if a pleural injury occurs and fluid is allowed to extravasate, this can travel through the pleural defect and accumulate in the pleural space. This can be done inadvertently when the nephroscope is withdrawn during the procedure.

Therefore, care must be taken to ensure that the sheath is not displaced during the surgery. Occasionally the sheath is withdrawn to allow access to nearby calyces. It is recommended that this be done near the end of the procedure to help minimize any extravasation that may occur.

There does not appear to be a significant difference in the rate of thoracic complications for access obtained by a urologist versus a radiologist. El-Assmy et al. performed a retrospective review of 1121 PCNL surgeries; 661 (52%) were obtained by a urologist at the time of the PCNL and 612 (48%) were obtained by an interventional radiologist prior to the PCNL. There were two hydrothoraces requiring drainage in the cohort, with one being in the urologist access group and the other in the radiology access group. The small numbers of pleural complications did not demonstrate statistical significance between the groups. Interestingly, the urologist group used multiple access points in 230 of the cases and performed a supracostal access in 112 (17%) of the cases. In contrast, the radiologist access group obtained supracostal access in only 29 (4.7%) of the cases [24]. Watterson et al. performed a retrospective review during a similar time frame. The study included 103 patients with 54 patients who had access obtained by an interventional radiologist and 49 patients who had access obtained by a urologist. Again, each group demonstrated one pleural complication during the study which did not show a statistical significant difference between the urologist-guided group versus the radiologist-guided group [25]. In studies of this nature, one criticism is that interventional radiologists may be asked to obtain access in the more complicated patients. In addition, in some of the patients who had access obtained by interventional radiologists this may have been done to drain the kidney and not necessarily to access the kidney in a way to best treat the offending stone. However, it is notable that in both studies mentioned, the urologists obtained a higher number of accesses and in the El-Assmy study did so using a supracostal approach and yet maintained the same complication rate.

The risk of bleeding and hemothorax is similarly increased by supracostal access as thoracic bleeding is often caused by intercostal vessels. Since the neurovascular bundle runs just inferior to each rib, if supracostal access is used, needle access should be done on the superior aspect of the rib below to minimize bleeding [26]. Multiple puncture sites have also been shown to have a higher incidence of bleeding, which may contribute to a hemothorax [17].

There are data to support that operative time, fluoroscopy time, and even overall complication rate decreases with surgeon experience. However, it is unclear if the rate of thoracic complications specifically is affected by surgeon experience [27–29]. There does not seem to be a correlation between dilation method and rate of thoracic complications [30].

Body mass index (BMI) does not appear to have an impact in thoracic complications. Fuller et al. analyzed the CROES database and found no difference in pulmonary complications in relation to patient BMI [31]. Other studies have also corroborated these results [32, 33], and some data have even shown that increasing BMI corresponds to a lower risk of thoracic complications [16]. This is likely because the higher amounts of visceral fat push the kidneys more cephalad, thus creating a greater distance between the diaphragm in the collecting system. Patients who have certain anatomic variations such as horseshoe kidney, pelvic kidney, and malrotation tend to have lower risks of thoracic complications as the kidney is located more caudad [34]. In a study of 54 cases done on horseshoe kidneys, none of them experienced a thoracic complication [35].

Special consideration should be given to patients that have alteration of normal anatomical landmarks such as patients with severe scoliosis, spinal cord injury, and other musculoskeletal deformities. It is often difficult to position these patients on the operating table and the relationship of the pleura to the kidneys is often distorted due to their physical deformities. CT or ultrasound imaging should be considered when obtaining access in these patients to decrease thoracic complications [36].

The risks of a thoracic complication are higher when upper pole access is used as this often violates the pleura. However, this approach offers many ergonomic advantages and allows for superior access for a multitude of conditions. The risks of upper pole access must be carefully weighed against the benefits of this approach. Each patient should be assessed for the optimal access carefully and no one approach will work for every patient.

## Descriptions of thoracic complications

### Pneumothorax

Pneumothorax is the accumulation of air within the pleural space (Figure 34.2). A pneumothorax results from the introduction of external air into the pleural space as a result of a pleural violation during surgery. Most commonly this occurs during the surgical procedure as air is introduced during renal access or tracks along the access sheath during the procedure. In this instance the source of the air is from outside of the patient's body. Rarely, injury to the lung parenchyma can occur when obtaining percutaneous renal access. This can result in a tension pneumothorax where air continues to escape from the bronchial tree or alveoli that

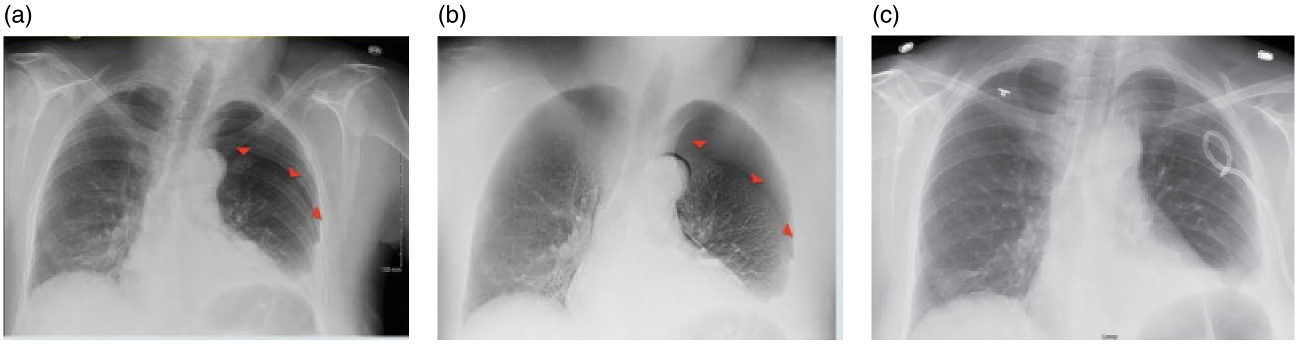

**Figure 34.2** Pneumothorax. (a, b) Chest X-rays of the same patient in different windows showing a pneumothorax. Arrowheads mark the edge of the lung parenchyma. Notice the lung parenchyma does not extend to the chest wall and there is a significant collection of air superior to the lung. (c) Chest X-ray of the same patient after placement of a chest tube with resolution of the pneumothorax.

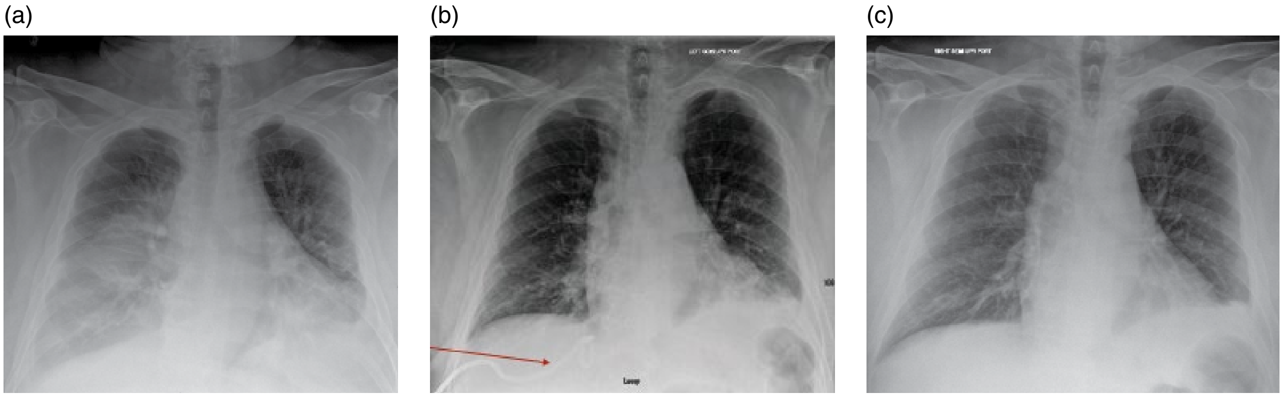

**Figure 34.3** Hydrothorax. (a) Chest X-ray showing blunting of the costophrenic angle with fluid. The patient had undergone right PCNL the day prior via an upper calyceal access. He was experiencing significant pleuritic chest pain and requiring 15 l/min of supplemental oxygenation. (b) The same patient after insertion of a pigtail chest tube in the dependent portion of the pleural cavity (arrow). The patient ultimately drained approximately 1.5 liters of fluid from the thoracic cavity. The creatinine was similar to the patient's serum creatinine and no bacteria were demonstrated on Gram stain or culture. (c) Chest X-ray after two days of chest tube removal, demonstrating resolution of the hydrothorax. Notice the presence of a clear costophrenic angle and the clear demonstration of lung markings that continue to the edge of the chest wall.

becomes trapped in the pleural space. Both etiologies can generate a compressive effect against the lung parenchyma if air continues to accumulate in the relatively fixed space of the thoracic cavity.

## Hydrothorax

Hydrothorax is the accumulation of fluid within the pleural space (Figure 34.3). The fluid can be a variety of substances, including surgical irrigation, urine, or reactive serous fluid. In the case of surgical irrigant or urine, the fluid extravasates through the dilation tract of the kidney and subsequently passes through the pleural defect caused by the percutaneous access and into the pleural space. Urine can accumulate in the pleural space during or after the procedure and is referred to as a urinothorax. If the collection of urine continues to re-accumulate through a fistulous connection, this is referred to as a nephropleural fistula. This connection allows for urine to continue to fill the pleural space. Although this is a less common form of hydrothorax, Lallas et al. reported a rate of 2.3% [37].

Occasionally, serous fluid can accumulate within the pleural space as a result of a reactive effusion. This results from irritation of the diaphragm that occurred during the surgical procedure or from a nephrostomy tube that was placed at the end of the procedure, causing a reactive serous fluid accumulation in the pleural space.

## Hemothorax

Hemothorax is the accumulation of blood in the thoracic cavity. This is most commonly the result of injury to an intercostal vessel which causes bleeding that can accumulate in the pleural space [26]. Alternatively, bleeding emanating from the kidney itself can traverse through a

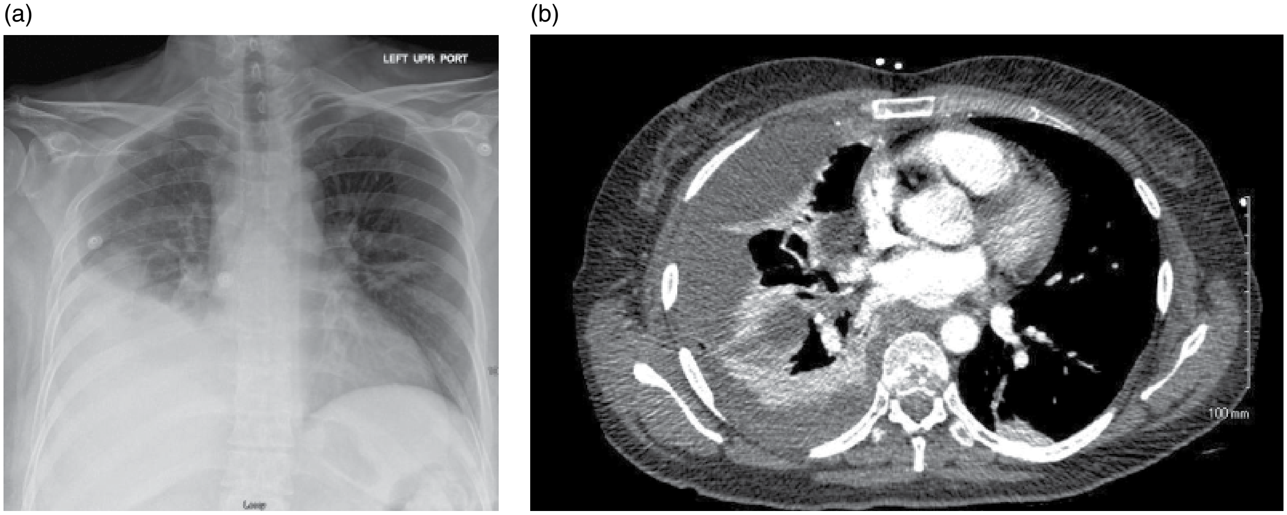

**Figure 34.4** Empyema. (a) Chest X-ray and (b) chest CT from a patient with a history of pyelonephritis who underwent right PCNL for a staghorn calculus. The patient later developed leukocytosis, fevers, and had purulent fluid emanating around her nephrostomy tube. A chest tube was placed with return of pus. Notice on the chest X-ray the dense accumulation of fluid obscuring the right lung. The CT of the chest demonstrates a dense, loculated, fluid collection with areas of enhancement indicative of a complex empyema. The patient failed to respond to chest tube drainage alone and video-assisted thoracic surgery was performed with subsequent improvement in clinical status.

pleural violation and accumulate in the thoracic cavity [27]. Hemothoraces may present immediately at the end of the case after the sheath is removed or in a delayed fashion, depending on the etiology of the bleeding.

### Empyema

Empyema is the presence of pus within the pleural space (Figure 34.4). This can occur either as a secondary infection of sterile fluid that enters the pleural space or as a result of infectious fluid that accumulates within the pleural space. In the former example, an uncomplicated hydrothorax or hemothorax may become infected if bacteria are able to take up residence and replicate within the fluid. In the later example, infected fluid extravasates from the kidney and enters the pleural space. The treatment of renal stones also has a known risk of releasing any bacteria that are associated with the stone being treated. These bacteria may then travel via surgical irrigant and/or urine into the pleural space, where they can grow and result in an empyema. An empyema may also result from a nephropleural fistula if associated with a urinary tract infection [26].

## Diagnosis of complications

The symptomatology and sequelae of thoracic complications can vary depending on the amount and type of fluid that accumulates as well as the patient's overall health status. The thoracic cavity is confined by the boney rib cage, which limits its ability to expand. Therefore, accumulation of air or fluid causes compression of the lungs which can compromise respiratory function. This results in the typical symptoms that are seen with thoracic complications.

The diagnosis of most thoracic complications is based on a combination of clinical symptoms and chest radiology. Complications can be detected intraoperatively or postoperatively depending on the timing of the complication and the severity.

### Intraoperative signs of thoracic complications

There are several changes that may be noticed during the procedure that can indicate a thoracic complication is occurring. Urologists should communicate to their anesthesia colleagues to be cognizant for any changes in ventilation, such as an increase in peak airway pressures [8]. Since the ribs create a relatively fixed structure to the chest wall, any additional air or fluid accumulation compresses the internal organs of the chest, most notably, the lungs. This is particularly problematic when the patient is in the prone position, as expansion of the thoracic cavity is limited in this position and the patient's weight further reduces the expansive capability of the chest wall. Furthermore, when the patient is in the prone position, it is difficult to observe any expansion of the thoracic or abdominal cavity. Narrowed pulse-width pressures may be noticed during hemodynamic monitoring as a result of air or fluid compressing venous return to the heart.

When venous return is compromised, the stroke volume of the heart is decreased, causing a decrease in the systolic blood pressure. This creates a smaller gradient between the systolic and diastolic blood pressure, thus creating a lower pulse pressure difference.

If a nephrostomy tube is placed at the end of the procedure, many urologists inject contrast to ensure proper placement. If contrast is seen communicating with the pleural space, this indicates that a pleural violation has occurred [8].

## Radiologic diagnoses of thoracic complications

Radiologic evaluation of the patient after the procedure is recommended, especially after upper calyceal access [26]. Some urologists perform intraoperative imaging of the chest at the conclusion of the procedure to evaluate for thoracic complications, while others delay chest imaging until the recovery room. Ogan et al. evaluated intraoperative chest fluoroscopy versus postoperative chest X-ray versus postoperative chest CT and found that intraoperative chest fluoroscopy is sensitive enough to detect clinically significant thoracic air or fluid accumulations [38]. Performing intraoperative radiographs has the advantage that if a significant intrathoracic air or fluid collection is encountered, percutaneous aspiration or the placement of a chest tube can be accomplished while the patient is under anesthesia [39].

Alternatively, chest imaging can be obtained in the recovery room. Plain chest radiography is less sensitive than transthoracic ultrasound or chest CT, however, it is less expensive and usually readily available. Furthermore, it can usually detect clinically significant amounts of air or fluid.

Chest X-rays can detect as little as 50 ml of fluid in the lateral view, whereas volumes of 200 ml are typically needed to view blunting of the costophrenic angle on anteroposterior films, and the diaphragm becomes obscured at a volume of 500 ml [26, 38]. Ultrasound may also be used to evaluate for pleural fluid accumulation and can visualize as little as 50 ml of fluid [26]. CT scan is the most sensitive modality, however this is the most costly of the imaging techniques. In addition, the small air and fluid accumulations it detects may not require intervention and can often be safely observed. Semins et al. reported on 197 patients who underwent PCNL and had a CT scan within 24 hours of surgery and found that 23 patients (12%) demonstrated a pleural complication. However, only one of these patients required a chest tube and the remaining recovered with conservative measures [11]. Therefore the increased sensitivity may not be necessary and certainly introduces an increased cost and radiation exposure and may complicate the management of these pathologies [38].

## Symptoms of thoracic complications

Patients with a thoracic complication may complain of pleuritic chest pain or shortness of breath and may demonstrate hypoxia or decreased breath sounds on the affected side [8]. These symptoms should be closely followed and imaging should be performed (if not done already) to evaluate for thoracic pathology.

## Differentiating between thoracic pathologies

A pneumothorax can be easily differentiated from forms of hydrothoraces by the presence of air in the pleural space. Air appears black on plain radiographs and CT and in the case of pneumothorax will often rise to the most superior position of the chest, which can vary depending on the position of the patient. The lung parenchyma will typically demonstrate dense linear markings that normally extend to the periphery of the chest wall. When there is a gap between the chest wall and the lung parenchyma this indicates a pneumothorax is present. Figure 34.2 shows an example of a pneumothorax.

Hydrothoraces will demonstrate a hazy appearance in the dependent portion of the chest that obscures the costophrenic angle of the pleural reflection as it continues from the lateral chest wall onto the domed shape of the diaphragm. The relative position of the fluid will vary depending on the patient's position. Figure 34.4 shows an example of a hydrothorax.

Differentiating between types of hydrothorax may require aspiration of the pleural fluid. Visually, the fluid can be assessed and one can differentiate between simple-appearing fluid, blood, or frank pus. If simple fluid is encountered, this should be sent for creatinine, Gram stain, and culture. If the fluid creatinine is higher than the serum creatinine, this indicates the presence of urine in the fluid. The Gram stain and culture can determine if there is a concomitant infection in the fluid even if there is not frank pus. If there are findings consistent with infection, an empyema may develop and this can affect management (see Figure 34.4). We discuss this in detail in the section on Management of thoracic complications.

If a urinothorax is diagnosed, one must consider if this was urine that accumulated during the procedure or if a nephropleural fistula is present. The diagnosis of a nephropleural fistula is more likely when the patient has a delayed presentation of fluid. In addition to the diagnostic techniques mentioned earlier, a few other modalities may be helpful in this diagnosis. As previously mentioned, if a nephrostomy tube is still present, a nephrostogram may demonstrate extravsation of contrast from the collecting system into the pleural space.

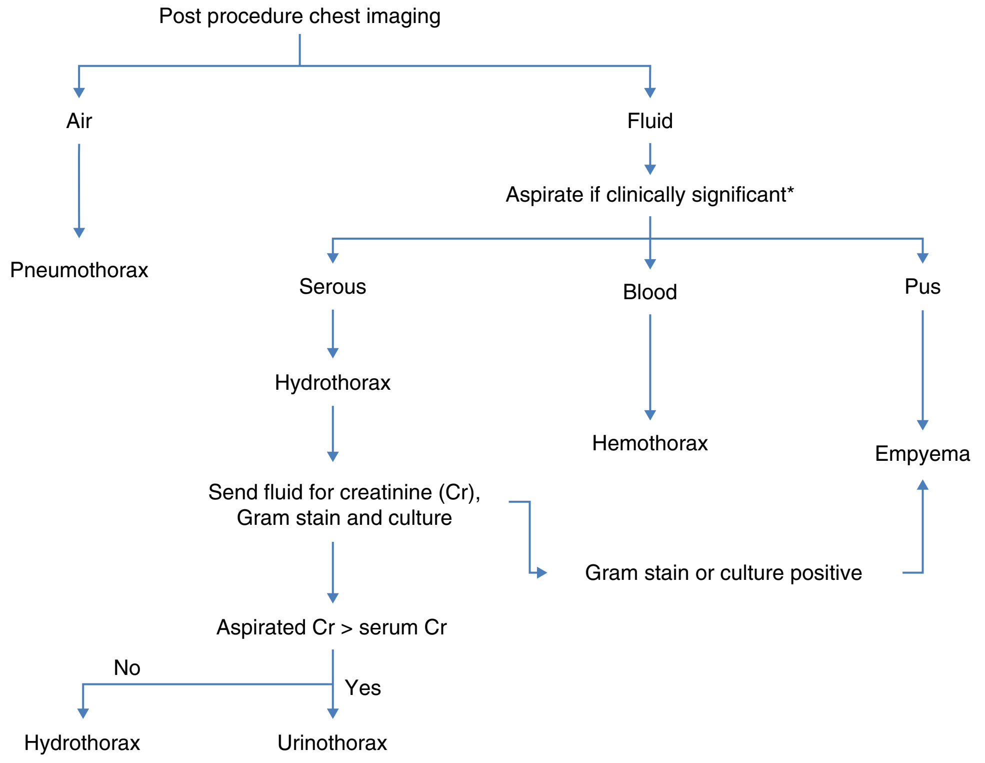
Post procedure chest imaging
Air
Fluid
Aspirate if clinically significant*
Pneumothorax
Serous
Blood
Pus
Hydrothorax
Hemothorax
Empyema
Send fluid for creatinine (Cr), Gram stain and culture
Gram stain or culture positive
Aspirated Cr > serum Cr
No
Yes
Hydrothorax
Urinothorax

**Figure 34.5** Diagnostic algorithm for thoracic complications following percutaneous renal surgery. *Aspiration can be separate procedure or part of chest tube insertion.

A retrograde pyelogram may also be beneficial in the evaluation, diagnosis, and management of nephropleural fistula, particularly when there is no nephrostomy tube. Contrast extravasation may be seen extravasating from collecting system into the pleural space in a similar fashion to the findings seen on antegrade nephrostogram. If a nephropleural fistula is diagnosed, the patient should be evaluated for distal obstruction such as from a distal stone fragment or edema [26]. CT, kidney–ureter–bladder, retrograde pyelogram, or a nephrostogram may be useful in this evaluation. If an obstruction is demonstrated, this kidney should be drained, as discussed in the section on Management of thoracic complications.

Hemothorax is diagnosed by radiographic evidence of blood in the pleural space or by visualizing blood upon aspiration of the thoracic fluid collection. Bleeding may be noticed during the procedure which can raise the suspicion of a hemothorax if a fluid collection is demonstrated postoperatively. In addition, a decrease in the patient's hemoglobin and hematocrit may also serve as a clue that bleeding has occurred. Significant bleeding may also be noticed once the sheath is removed during the procedure. The source of bleeding may be from an intercostal vessel or from the kidney itself. While the source of bleeding may not be entirely clear, the urologist should be aware that this bleeding may track into the pleural space if pleural violation has occurred.

Fluid, pus, blood, urine, and air can all accumulate within the pleural space after PCNL. These can be differentiated based on a combination of clinical history, radiology and visualization of the fluid. Figure 34.5 shows a diagnostic algorithm that illustrates this process.

## Management of thoracic complications

The management of thoracic complications is largely determined by the patient's clinical status. Small volume of air and fluid in the pleural space may be observed when the patient is minimally symptomatic. Intervention is therefore indicated if the patient is having significant symptoms, or when significant volumes of air or fluid are seen [9]. Figure 34.6 demonstrates a management algorithm for thoracic complications following percutaneous renal surgery.

Chest drainage is the treatment for thoracic complications. The type and size of the chest tube depends on the pathology being managed. Small chest tubes are usually adequate to drain air and simple fluid collections, whereas larger tubes may be needed to optimally drain hemothoraces and empyemas [40]. Chest tubes are

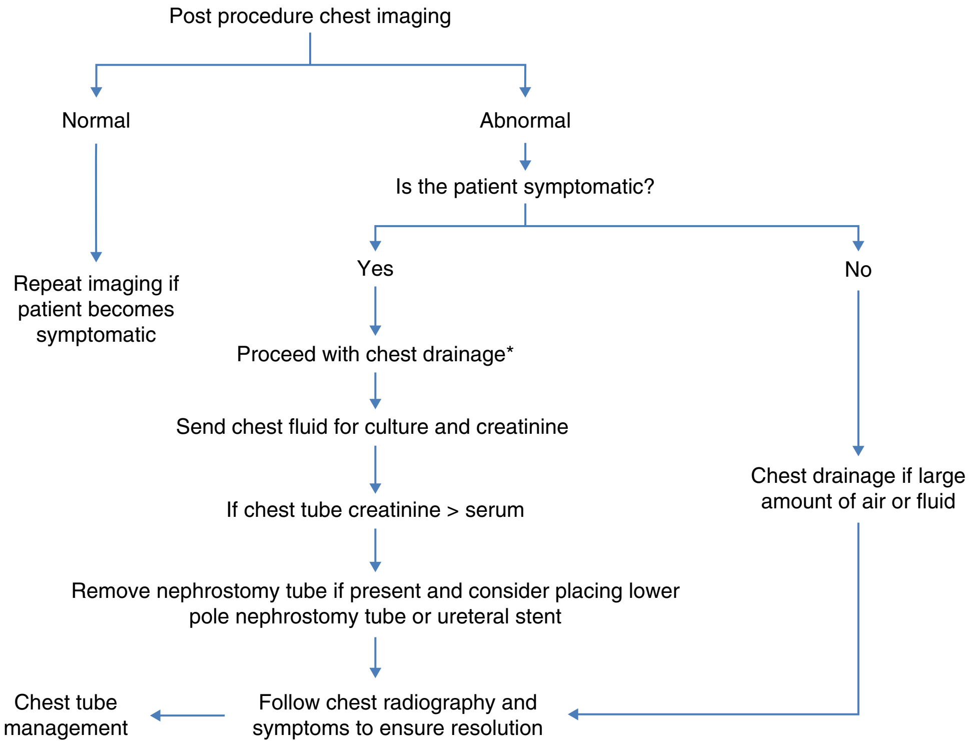
Post procedure chest imaging
Normal
Abnormal
Is the patient symptomatic?
Yes
No
Repeat imaging if patient becomes symptomatic
Proceed with chest drainage*
Send chest fluid for culture and creatinine
If chest tube creatinine > serum
Remove nephrostomy tube if present and consider placing lower pole nephrostomy tube or ureteral stent
Chest drainage if large amount of air or fluid
Follow chest radiography and symptoms to ensure resolution
Chest tube management

**Figure 34.6** Management algorithm for thoracic complications following percutaneous renal surgery. *If blood or pus is present, consider placing a larger bore chest tube. Consider early consultation with thoracic surgery. Chest tube removal: pneumothorax – consider trial of water seal for 6 hours to evaluate for recurrent pneumothorax; hydrothorax – can remove if chest tube drainage <300 ml per day.

typically placed to continuous suction at about 20 cm$H_2O$ and are flushed with small volumes of saline every 6 hours to minimize the risk of tube occlusion and ensure drainage. If clinical improvement is not seen after about 24 hours of drainage, imaging, such as CT or ultrasound, should be utilized to ensure appropriate placement. If the tube is in the correct location without improvement in the collection, consideration should be given to increasing the size of the chest tube [41]. Some urologists place their own drainage tubes, especially if this is done intraoperatively, while others refer this to an interventional radiologist, general surgeon, or a thoracic surgeon [39].

Once a chest tube is placed, the patient is followed clinically for resolution of symptoms. Serial chest radiography is often used as well to determine the duration of drainage and to ensure that the drainage modality is adequate.

## Hydrothoraces

Symptomatic or large hydrothoraces typically require chest tube drainage. The size of the chest tube and duration of drainage vary depending on the type and size of the hydrothorax. The role of aspiration alone in the management of hydrothoraces is poorly defined. If a small collection is diagnosed while the patient is under anesthesia, some favor aspiration alone. This offers the ability to differentiate the etiology of the hydrothorax. In addition, aspiration alone is less morbid to the patient than an indwelling chest tube. The concern with this approach is if the collection reaccumulates, the patient then needs to undergo a separate procedure. In addition, small collections can often be observed, meaning that some of the aspirations may not be required. The viscosity and visual assessment of fluid can be done on the initial aspiration during placement of the chest tube. If simple fluid or urine is detected, this may be adequately drained with smaller bore chest tubes. However, if pus is returned, a large-bore chest tube may be useful [40]. It is recommended that the chest tube aspirate be sent for creatinine and culture to aid in the diagnosis as mentioned earlier. If the culture demonstrates an infection or if there is clinical concern for infection, antibiotics should be initiated if they have not been already. The patient is followed for resolution of symptoms and serial chest radiographs are obtained to monitor resolution of the fluid collection. Once resolution has been documented, the chest tube may be removed.

## Empyemas

Empyemas can be difficult to treat and may not resolve with chest tube drainage alone as the purulent fluid can be quite thick. Furthermore, empyemas can become loculated, making them resistant to tube drainage. The use of fibrinolytics has been described for some time now in the treatment of empyemas with mixed results. The options for fibrinolytic therapy are: streptokinase, urokinase, tissue plasminogen activator (t-PA) or human recombinant deoxyribonuclease (DNase). Several small studies have shown benefits of using these agents, but larger studies and meta-analyses showed no statistical benefit for fibrinolytics over chest tube drainage alone [41, 42].

Surgical drainage is recommended in patients who fail chest tube drainage or for the primary treatment of patients with loculated or thick fluid on imaging [42, 43]. Surgical drainage can be accomplished via endoscopic approaches or open surgical drainage. Typically, minimally invasive endoscopic approaches can be used. In a small prospective randomized trial, early surgical drainage was associated with a higher treatment success rate, fewer days of chest tube drainage, and shorter hospital stay. Therefore, thoracic surgery consultation should be obtained early in the management of empyema [44].

Video-assisted thoracic surgery (VATS) may be used as a minimally invasive management of empyema or complicated hemothorax. VATS is similar to laparoscopy for the thoracic cavity. The patient is typically placed in the lateral decubitus position. A small incision is made between the ribs on the lateral aspect of the chest wall. Dissection is carried down through the subcutaneous layers and into the parietal pleural layer in order to enter the pleural space. Care is taken to avoid injury to the underlying lung during this process. The surgeon's finger is then used to free a space into which the trocar can be placed into the thoracic cavity. Occasionally the ipsilateral lung is deflated during the procedure using a dual-lumen endotracheal tube. This allows for an increase in working area in the thoracic cavity. A trocar is then inserted through the incision and a camera is used to inspect the surgical field. Because the chest wall is supported by the ribs, insufflation may not be required, although it is used by some surgeons. Other trocars can be placed under direct vision in the intercostal spaces in a manner similar to laparoscopy, or small incisions may be made and traditional surgical instruments can be inserted through the chest wall for use. A combination of suction and dissection is then used to remove the infected tissue while attempting to minimize injury to the lung tissue. A chest tube is placed at the end of the procedure to allow the lung to expand [45]. Open drainage is rarely required when minimally invasive approaches fail and typically requires consultation with a thoracic surgeon [41].

## Reactive effusions

Reactive effusions typically resolve spontaneously with time. If a nephrostomy tube has been left in place, this should be removed to eliminate the diaphragmatic irritation.

## Nephropleural fistulas

Nephropleural fistulas typically resolve with placement of chest tube and urinary drainage with a ureteral stent or a nephrostomy tube [27, 37]. If the patient has persistent drainage after placement of the ureteral stent, anticholinergics may be used to decrease bladder spasms or a Foley catheter may be placed to facilitate maximal drainage of the urinary system [26]. These typically resolve within 12 hours; however, prolonged periods of leakage can occur in 1.5–4.6% of patients [46]. If a Foley catheter was used to facilitate drainage, this can be removed once the drainage stops accumulating in the thoracic cavity [26].

The nephrostomy tube itself can be an exacerbating factor in hydrothoraces. If the nephrostomy tube traverses the pleura, urine can extravasate and course along the tube into the thoracic cavity. In this instance, removing the nephrostomy tube will aid in pleural closure and healing. If there is a concern for pleural violation at the time of surgery, placement of a lower pole nephrostomy tube can drain the kidney while allowing the pleural violation to heal [47].

## Hemothoraces

Hemothoraces are treated in a similar manner as other hydrothoraces. However, like empyemas, the fluid collection is typically quite thick and may require the use of a larger bore chest tube. Furthermore, the urologist must determine if the source of bleeding is ongoing. If there is evidence of continued, symptomatic bleeding, the urologist should consult regarding angioembolization of the bleeding.

## Pneumothoraces

Pneumothoraces may be observed when small and the patient is minimally symptomatic. If the patient is experiencing significant pleuritic pain, decreased oxygen saturations, shortness of breath, or has failure of the pneumothorax to resolve on chest radiography, a chest tube should be placed. The PCNL-associated pneumothorax is typically caused by air that is introduced at the time of the procedure. This etiology differs from a pneumothorax caused by injury to the lung itself or after thoracic surgery. In these instances, the air enters the pleura from the bronchial tree and continues to accumulate in the pleural space until the lung itself heals. However, direct injury to the lung is extremely rare in the case of PCNL. The chest tube is placed initially to provide wall suction until the pneumothorax resolves radiographically and the patient's symptoms improve. There is some debate whether a trial of water seal is necessary prior to removing the chest tube or if the chest tube may be removed while on suction. However, there is no clear consensus in the thoracic literature. The reason for performing a trial of water seal is to decrease the risk of recurrent pneumothorax after the chest tube is removed. The use of water seal may be of more importance when managing pneumothoraces versus other thoracic pathologies [48, 49]. Once the pneumothorax has resolved, the chest tube may be removed as previously described.

### Chest tube management

Chest tubes can typically be removed at the bedside depending on the comfort level of the patient. It maybe helpful to administer analgesics prior to tube removal, as the process can be painful. There is debate with no clear consensus as to whether the chest tube should be removed during inspiration or expiration. Prior to removing the chest tube, the securing suture should be cut and an occlusive dressing should be prepared. This is placed over the thoracostomy site prior to removing the chest tube. Once the dressing is in place, the tube is swiftly removed and the dressing secured in place with tape [40, 50].

The management of thoracic complications depends on the severity of the symptoms the patient is experiencing. Small pneumothoraces and hydrothoraces can generally be observed, especially if the patient is asymptomatic or minimally symptomatic. If the patient has a "large" pneumothorax or hydrothorax, this should be treated even if the patient is not experiencing significant symptoms. Aspiration may be considered for small hydrothoraces while a temporary chest tube is better suited for pneumothoraces and larger hydrothoraces. A larger bore chest tube is recommended to treat hemothoraces and empyemas. Hemothoraces and empyemas should be closely followed as they have a higher risk of developing into more complicated and loculated collections. It is prudent to involve the expertise of a thoracic surgeon in these cases to evaluate if the patient would benefit from early surgical evacuation.

## Prevention

Benjamin Franklin once remarked, "An ounce of prevention is worth a pound of cure." Performing percutaneous renal surgery carries with it certain risks, however, these should be minimized when possible. Careful patient selection and access planning is paramount in minimizing risks of thoracic complications. The most important aspect of minimizing complications is deciding when the benefits of upper pole access outweigh the risks associated with this. If it is decided that supracostal access is preferred, there are several techniques that can lower the incidence of clinically significant thoracic complications.

Needle access should be obtained in full expiration in order to decrease the amount of pleura and diaphragm that lies over the kidney [7, 23, 26]. If the 10th or 11th intercostal space is used for access, placement of the needle lateral to the midscapular line can help to minimize injury [7]. Another technique that has been used to is to place a needle or a small-caliber sheath into the lower aspect of the kidney in order to displace it inferiorly.

The use of a percutaneous access sheath throughout the entire procedure is recommended. This will serve to divert most of the urine and irrigation out of the body, which will minimize any accumulation in the chest. It is also important to ensure that the access sheath remains in the collecting system throughout the procedure. If the sheath is withdrawn from the collecting system, this may allow fluid to flow into the retroperitoneum and possibly the thoracic cavity [26]. Furthermore, the percutaneous access sheath serves to maintain a low intrarenal pressure. If this is not done, the intrarenal pressure can increase, causing extravasation of fluid which can accumulate in the thoracic cavity. Some had advocated for the use of a ureteral access sheath during PCNL. This can serve to further minimize the intrarenal pressures and minimize hydrothorax [51, 52].

Prompt removal of a nephrostomy tube is wise if there is concern about pleural violation as air and fluid can track along the tube into the pleural space. In addition, the presence of a tube will discourage the closure of the pleural defect.

## Conclusions

Percutaneous renal surgery is an effective modality with a relatively low rate of complications overall, yet thoracic injury accounts for a percentage of these complications. The endourologist must therefore be aware of the relevant anatomy, make careful selection with regard to access planning, and utilize techniques that minimize complications when performing percutaneous renal surgeries. When complications do arise, a prompt and accurate diagnosis will help the urologist to determine the appropriate management. Understanding the incidence, diagnosis, and management of these complications allows for better shared decision-making between the patient and the provider and for optimal care during the perioperative period.

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# 35

# Bowel and Other Organ Injuries with Percutaneous Nephrolithotomy

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## Overall complications

Complications of percutaneous nephrolithotomy (PCNL) are common and may occur in 12.5–20% of patients, but they typically are low grade with less than 4% of patients experiencing a Clavien grade III or higher [1–3]. Although rare, solid organ injuries associated with PCNL are among the most feared. While some may be managed conservatively (Clavien grade II), there is significant risk of subsequent intervention (Clavien III or higher) [1]. Although complications such as extravasation, fever, and transfusion are more common, solid organ injury (including colon, bowel, lung, liver and spleen) are fortunately rare, historically occurring in less than 1% of cases [4]. In a 2012 review, Seitz et al. found the overall incidence of organ injury (including liver, spleen, and bowel) to be 0.4%, while thoracic complications occurred in 1.5% of patients [5]. Although various risk factors for organ injury exist, the most unifying may be access through the 10th intercostal space and/or anterior to the posterior axillary line [5]. In this chapter we review the occurrence of organ injury during PCNL, including discussion of diagnosis and management.

## Colon injury

Colon perforation at the time of PCNL is uncommon, occurring in less than 1% of procedures [5–9]. In a review of the literature, Ozturk identified 36 colonic injuries among 9996 cases (0.36%) [7]. The colon is typically positioned anterior or anterolateral to the kidney, and in this orientation risk of injury occurs with extreme lateral access to the kidney, beyond the posterior axillary line. Thus, with normal anatomy, the risk of injury is low. However when abnormal anatomy is present, namely a retrorenal colon, the risk increases.

Anatomic studies have found that a retrorenal colon exists in between 0.6% and 2% of patients, and is more common on the left side (Figure 35.1) [10–14]. This risk may be markedly higher in patients with abnormal anatomy, such as severe spinal scoliosis, where retrorenal colon was identified in up to 25% of patients [15]. Additional risk factors may include chronic constipation and bowel distention, such as in elderly patients, previous surgery or neurologic impairment resulting in neurogenic bowel, prior renal surgery [14, 16], or horseshoe kidney and renal ectopia [9, 17]. Preoperative cross-sectional imaging will help identify high-risk patients and will allow the surgeon to plan their access in order to avoid colonic injury. For patients with severely altered anatomy with narrow windows of puncture, consideration should be given to CT-guided access in order to avoid colon injury.

Early diagnosis of colonic perforation is key to preventing more serious infectious complications. A nephrostogram during the case may demonstrate contrast within the colon, at which time drainage may be established. Postoperatively, the presence of diarrhea, hematochezia, or passage of gas or fecal material through the nephrostomy may all indicate injury. Intraoperative or postoperative imaging with nephrostogram or CT scan is recommended, at which time perforations may be seen. Delayed recognition may increase the risk for infection, including sepsis, and appropriate antibiotic coverage for urinary and colonic pathogens should be implemented.

Treatment of colonic perforation is usually conservative in the absence of peritoneal signs or sepsis [7, 8]. In 1985, LeRoy et al. reported their experience with

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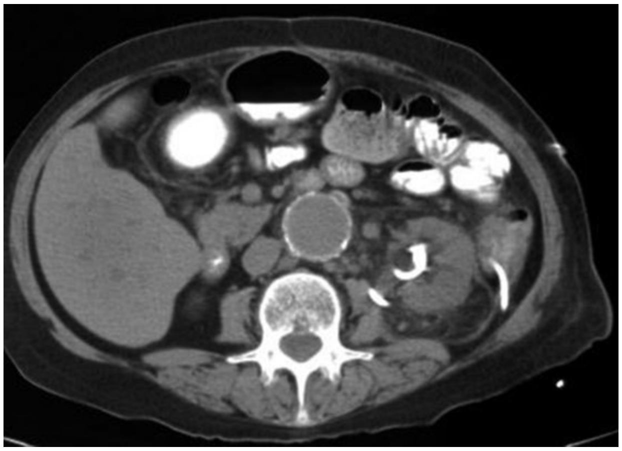

**Figure 35.1** CT scan showing colon injury at the time of left percutaneous nephrolithotomy.

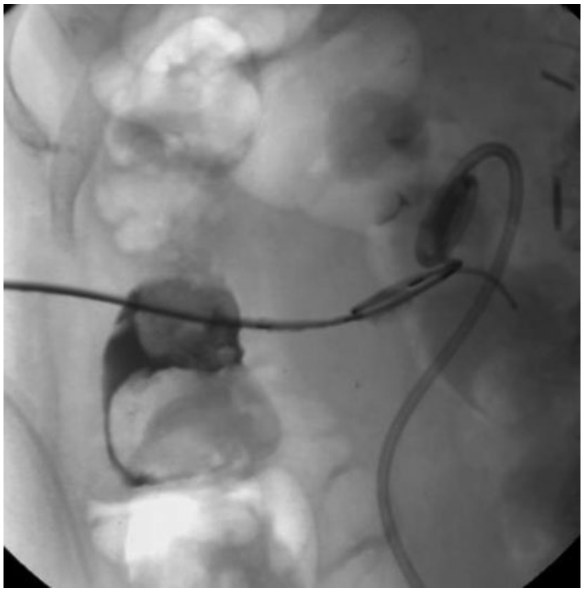

**Figure 35.2** Nephrostogram showing colon injury at the time of left percutaneous nephrolithotomy.

successful conservative management of two patients with colon injury during PCNL [12]. Of the 36 cases identified by Ozturk, a majority were managed conservatively [7]. Conservative management is accomplished by withdrawing the nephrostomy into the colon to serve as colostomy drainage and placing a double-J stent (Figure 35.2). A catheter should be placed into the bladder to create a low-pressure system. Patients should be covered with broad-spectrum antibiotics, and placed on a low-residue diet or alternately on total parenteral nutrition. After 5–7 days, if a colostogram or retrograde pyelogram fails to demonstrate communication between the colon and kidney, the colostomy is withdrawn into the retroperitoneum to serve as a drain. If a barium enema 2–3 days later demonstrates closure of the colon, the retroperitoneal drain can be removed by day 7–10. Patients who develop signs of sepsis or persistent nephron–colonic or colocutaneous fistula should be considered for surgical exploration with diverting colostomy.

## Other bowel injury

Due to the proximity of the second and third portions of the duodenum to the right kidney, injury may occur at the time of PCNL. However such injuries are very rare, with only nine reports of small bowel injury in the literature, including six jejunal and three duodenal injuries [7]. Eight injuries occurred at the time of right-sided PCNL, and one jejunal injury occurred at the time of left PCNL. With the duodenum lying anterior and medial to the kidney, retroperitoneal access should be able to avoid this potentially devastating complication. However, the duodenum may be injured during right PCNL if the renal pelvis is perforated during access or dilation when a needle or instrument is advanced too far. Jejunal injuries may occur in similar fashion. Careful visualization using fluoroscopy at the time of access and dilation may mitigate this risk.

Injury to the small bowel should be suspected if bowel mucosa or bowel contents are visualized along the guidewire or nephrostomy tract. It may also be identified on nephrostogram either intraoperatively or postoperatively. A large injury, signs of sepsis, or peritonitis typically necessitate surgical exploration with open surgical repair. Small perforations in a stable patient without evidence of sepsis or peritonitis may be observed. Of the nine available cases in the literature, seven proceeded to exploratory laparotomy while two were managed conservatively [7]. Conservatively managed patients should have confirmation of a well-draining nephrostomy tube and be placed on bowel rest with nasogastric suction and institution of total parenteral nutrition to allow closure. Follow-up interrogation with nephrostogram and upper gastrointestinal study may be performed 10–14 days after surgery to ensure closure. For example, Al-Assiri et al. report their experience managing a jejunal injury at the time of left PCNL, where an intraoperative connection to the jejunum was found on nephrostogram [18]. The patient had a Malecot catheter placed into the bowel lumen and a double-J stent was placed. The patient was put on total parenteral nutrition with bowel rest, and injection of contrast confirmed closure of the tract between the jejunum and kidney by day 7. After three weeks, the Malecot was removed without need for exploration. In this way, early identification of bowel injury allowed for more conservative approaches, as prompt drainage and initiation of bowel rest may minimize damage. Delayed recognition or large injuries to the small bowel typically necessitate surgical exploration and may be associated with more serious morbidity. However, although conservative measures may be appropriate for some patients, a majority of these rare injuries will require surgical exploration for repair.

## Gallbladder injury

Gallbladder injury during PCNL is a rare but serious complication, with eight reported cases in the literature, all requiring surgical exploration and cholecystectomy [7]. Of these, one case was identified intraoperatively when the gallbladder opacified with contrast, and the others presented with biliary peritonitis. Injury to the gallbladder should be suspected if a greenish discharge is found along the access or if a patient develops signs of peritonitis following a right-sided procedure, in which case a CT scan would be the imaging of choice. Timely diagnosis is important, as biliary leakage may result in profound peritonitis, infection, and scarring with adhesions. All injuries require exploration with cholecystectomy to avoid severe sequelae of this rare complication.

## Lung and pleural injury

Diagnosis and management of thoracic complications of PCNL are discussed in Chapter 34, but a few salient points are worth mentioning here. Hydrothorax and pneumothorax are primarily associated with supracostal access. A CT-based anatomic study by Hopper and Yakes concluded that risk existed for pleural injury with access between the 11th and 12th rib when puncture was performed, even during maximal expiration, with a transpleural puncture occurring 29% of the time on the right and 14% of the time on the left [19]. When puncture was performed between the 11th and 12th rib during inspiration, the pleura would be transversed in most patients. Access above the 10th rib was estimated to result in pleura or lung injury in all patients regardless of inspiration or expiration. These anatomic assessments appear to provide a reasonable estimate, as Munver et al. reviewed their series assessing the risk of injury with supracostal access and found that among 72 patients undergoing access above the 12th rib, the tract was transthoracic but extrapleural [20]. Access above the 11th rib, however, resulted in 19% incidence of hydro- or pneumothorax. Such risk may be decreased by careful inspection of a preoperative CT scan and avoidance of supracostal access where possible. Among patients undergoing supracostal access, surgeons should consider intraoperative or postoperative chest X-ray to assess for thoracic complications.

## Liver and spleen injury

Because of the close proximity of the right kidney to the liver and the left kidney to the spleen, a theoretical risk of injury occurs at the time of PCNL. However such injuries are rare. A 2014 review of organ injury at the time of PCNL identified 11 reports of splenic injury and 1 report of liver injury [7]. A CT-based analysis of the risk of organ injury during supracostal approach found a theoretical risk of splenic injury, which increased the higher the puncture [19]. While there was minimal risk of splenic injury with punctures above the 12th rib done on expiration, this risk rose to 33% for punctures above the 11th rib on inspiration [19]. Such access should be avoided whenever possible and if it is needed, the surgeon should consider CT-guided access. Careful inspection of cross-sectional imaging should precede PCNL so that the surgeon is aware of at-risk structures relevant to their access approach of choice.

Splenic injury should be suspected in the setting of profound hemorrhage, hemodynamic instability or pain out of proportion to the surgery occurring with a left-sided access. However, the presentation may be difficult to diagnose due to the low incidence. CT scan is the imaging of choice (Figure 35.3), but may not always be obtained immediately as patients with excessive bleeding are often sent for angiography in order to perform selective embolization. Of the reported splenic injuries, three were explored with two undergoing splenectomy, and

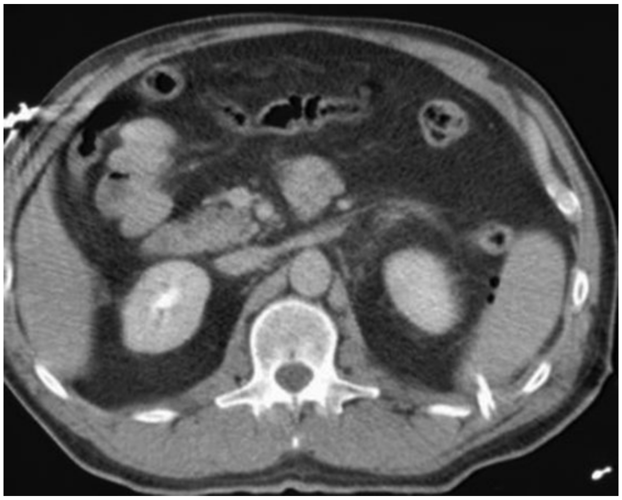

**Figure 35.3** CT scan showing splenic injury at the time of left percutaneous nephrolithotomy.

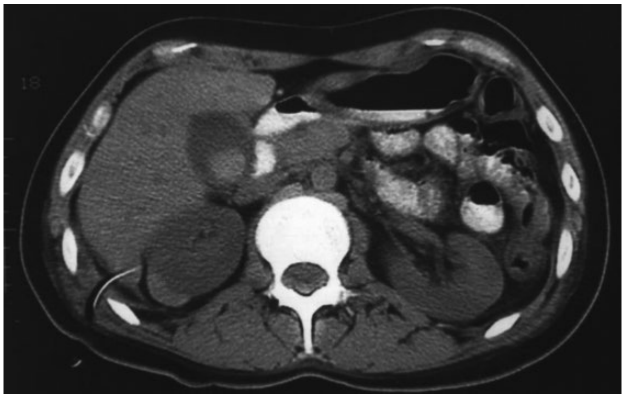

**Figure 35.4** CT scan showing liver injury at the time of right percutaneous nephrolithotomy.

eight were managed conservatively. In the truly unstable patient, exploration and splenectomy may be lifesaving. However, there are multiple reports of successful conservative management of splenic injuries. Thomas et al. report the use of a collagen–thrombin hemostatic sealant down the nephrostomy tract following delayed removal of the nephrostomy tube four days after surgery [21]. In another novel approach, Desai et al. injected Gelfoam pledgets along the nephrostomy tract and placed a ureteral stent, after which the patient had an uneventful recovery [22]. While there is no standard management for splenic injury, conservative options in the stable patient may include close observation, delayed removal of the nephrostomy tube, and novel coagulants down the tract. However unstable patients, or patients who become unstable during a trial of conservative measures, should be prepped for emergent splenectomy.

Liver injury at the time of PCNL is rare, with only one reported case in the literature [7]. Study of anatomic relationships on CT scan predicted minimal risk to the liver with access above the 12th rib, but a 14% risk was found in tracts above the 11th rib [19]. Hepatomegaly may place the patient at risk, particularly if the access takes a more lateral orientation (Figure 35.4), but can usually be avoided with careful inspection of a preoperative CT scan. Fortunately, most liver injuries can be observed and surgical exploration is rare. Conservative measures may include delayed removal of a nephrostomy tube, ureteral stenting to avoid fistula, and use of coagulants along the tract.

## Conclusions

Organ injury at the time of PCNL is an uncommon complication, occurring in less than 1% of patients. However it is important that patient informed consent includes discussion of adjacent organ injury. Among these, colonic injury may be the most common. At-risk anatomy, particularly a retrorenal colon, may be identified on preoperative imaging and access planned accordingly to minimize the risk of injury. Fortunately, a majority of colon injuries may be managed conservatively with stenting, withdrawal of the nephrostomy into the colon, and bowel rest. In contrast to colonic injury, small bowel injury is less common and more severe. Although cases of conservative management have been described in the literature, the majority require surgical exploration. Similarly, gallbladder injury is rare, with only eight reported cases, all of which required exploration with cholecystectomy.

Splenic injury may be seen at the time of surgery, or may result in hemorrhage leading to splenectomy. Several reports of conservative management with delayed nephrostomy removal and injection of coagulants down the tract have been described to be successful. However, surgeons should have a low threshold for exploration and splenectomy when needed. Liver injury occurring at the time of right-sided PCNL can typically be managed conservatively and surgical exploration is rarely needed.

Although solid organ injuries are uncommon during PCNL, the risk can be minimized with meticulous inspection of preoperative imaging and careful planning of access. For patients with challenging anatomy, CT-guided access may be considered to minimize risk. Prompt identification and management of solid organ injuries may call for more conservative management, but when these rare complications occur surgeons should be prepared for surgical exploration when necessary.

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# 36

# Exit Strategies After Percutaneous Nephrolithotomy

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## Introduction

Percutaneous nephrolithotomy (PCNL) is the gold standard treatment for staghorn stones, large renal stones, and complex renal calculi [1–4]. Since its description and introduction over 30 years ago, there has been continual improvement in PCNL surgery [5]. Technological enhancements and technical advances now mean that the puncture is more accurate and safer than ever, stone clearance is maximal, and the complication rate is low and acceptable [6]. Attention has now turned to decreasing postoperative pain, preventing urine extravasation, and reducing the duration of hospital admission while maintaining excellent stone clearance rates.

Urinary drainage with a nephrostomy tube (NT) has been a part of PCNL surgery ever since Winfield et al. reported serious complications due to early NT removal [7]. Subsequent to this publication, NT placement at the end of PCNL surgery became doctrine and an integral part of postoperative urinary drainage. This occurred despite Wickham et al., several years earlier, publishing that “nephrostomy-free” PCNL was safe and associated with minimal complications in a much larger series [8].

Following this report, the practice was to leave a large-bore NT or re-entry catheter in the PCNL tract. Hunter et al. stated that the NT should only be 2–4 Fr smaller than the nephrostomy sheath, meaning that an NT of 26–28 Fr would be needed for a standard PCNL [9]. The rationale for this was that the large-bore NT would maintain drainage of the kidney, while preventing urinary extravasation and providing hemostasis through compression [10]. However, it soon became clear that NTs this large were not necessary and that smaller NTs would suffice instead of large-bore variants.

As a result, a large collection of drainage tubes was developed to meet the demands of post-PCNL NT drainage. These range from large-bore NTs, such as Councill tip, re-entry Malecot catheters, and Circle tubes, to smaller bore tubes, such as the Coop loop NT, pigtail NT, and the range of nephroureterostomy catheters (NUC). Ultimately, it become apparent that the placement of these tubes at the end of the procedure could actually have a negative impact in the postoperative period, possibly increasing pain, analgesia use, and hospital stay [11–16]. This, coupled with the fact that the main function of NT is only to maintain urinary drainage and does little to prevent bleeding or urine leak, led to the reintroduction of NT-free PCNL surgery [17].

NT-free PCNL surgery has now been termed tubeless or totally tubeless PCNL, depending on whether internal ureteric drainage is utilized. Tubeless refers to NT-free PCNL surgery, where instead of a NT drain, a ureteral catheter or double-J (JJ) stent is placed internally for renal drainage with or without a urethral catheter. Thus ureteric catheters and JJ stents have also been added to the endourologist’s options for post-PCNL drainage. Totally tubeless PCNL surgery is truly tubeless, and at the end of the procedure no NT or internal drainage is utilized. The use of hemostatic agents in the PCNL tract of tubeless and totally tubeless PCNL surgery has been recently described as a potential way to reduce bleeding and may become more regularly utilized following PCNL surgery.

It is the goal of this chapter to examine the rationale behind NT tube placement in PCNL surgery and to review the exit strategies available for this procedure. We review the evidence for large-bore NT, small-bore NT, tubeless PCNL, and totally tubeless PCNL. We also look

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at the modifications to each procedure, such as JJ stents with tethers and the placement of hemostatic agents in the PCNL tract.

## Large-bore or small-bore nephrostomy

A large-bore NT is generally regarded as of size ≥18 Fr. Councill tip, Circle loops, and re-entry Malecot catheters are some of the most common large-bore NTs available. Small-bore NTs are ≤18 Fr, and several different varieties also are obtainable [18]. These include Cope loop NT, pigtail NT, and the nephroureterostomy catheter (NUC). All NTs have certain important characteristics, especially perforations or openings to allow drainage. There should also be a self-retaining loop or device to keep the tube in place, as well as an effluent channel to allow urinary drainage out and a tap to which to connect a drainage bag. An example of a small-bore NT is shown in Figure 36.1.

Other important intrinsic features of a NT are its retention strength and flow properties. These are its ability to resist accidental removal and its urinary drainage rate. In a recent study, Canales et al. found the Cope loop NT to be superior to pigtail NT and both Councill tip and Malecot catheters. They found that the Cope loop NT had better flow and stronger retention strength during *in vitro* testing compared to other devices [19]. Accidental removal is a preventable complication of all NT drains. All devices need an additional method to secure the device in place to prevent unintentional removal, such as a drain secure dressing or suture. An NT drain secure device is shown in Figure 36.2.

In the early years of PCNL surgery, it was common practice to use large and very large NT drains, sometimes only 2 Fr smaller than the tract [9]. It was thought that these large tubes would allow optimal drainage, and prevent urine leak and bleeding. However large-bore tubes also result in increased pain, and hence the use of smaller drainage tubes was explored [11, 12]. In almost

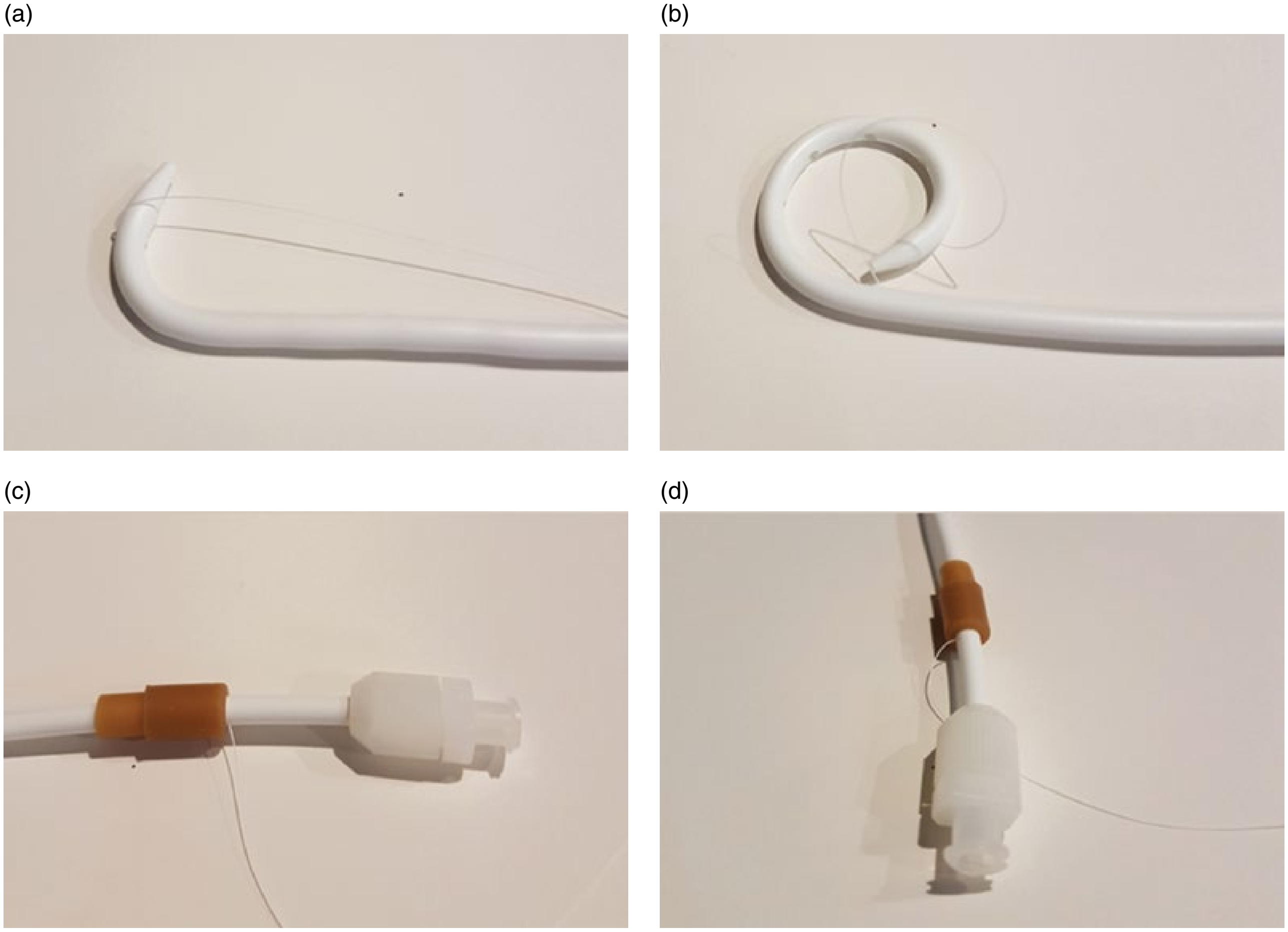

**Figure 36.1** Key characteristics of a nephrostomy tube. (a) Perforations to allow internal drainage. (b) Self-retaining loop. (c) Method to lock loop. (d) Effluent channel and connector for drainage bag.

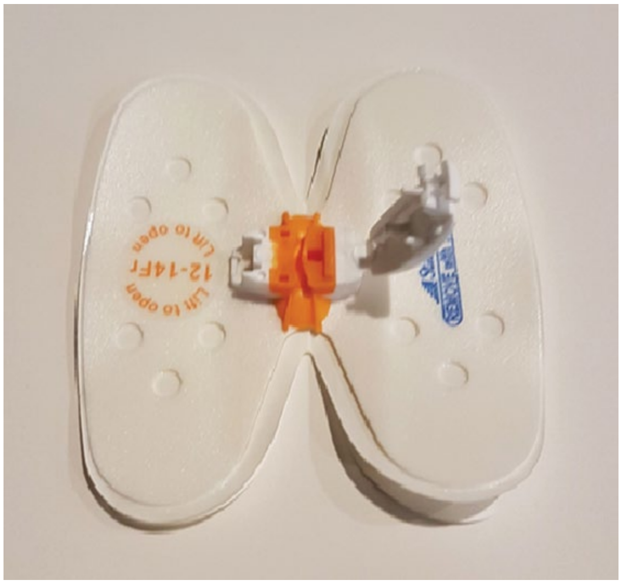

**Figure 36.2** Device to secure nephrostomy in place.

every report, small-bore NTs appeared to be superior in some aspects to large-bore drains. A prospective trial, a worldwide analysis of current PCNL practice, three randomized control trials, and a meta-analysis have confirmed this observation.

Maheshwari et al. undertook a study of PCNL in 40 consecutive patients, in which alternate patients were managed with a 28 Fr NT tube or a 9 Fr pigtail NT. They demonstrated that the small-bore NT was statistically associated with reduced postoperative pain, shortened duration of urinary leak, and a reduced period of hospital admission [20]. Similar findings were reported in four subsequent randomized trials. In these trials, a total of 211 patients were randomized to receive a large-bore NT or a small-bore NT. In all cases, the small-bore NT was assocated with less postoperative pain compared to the large-bore NT [14, 21–23].

Shen et al. performed an meta-analysis of large-bore NT versus small-bore NT. Nine studies, with a total of 547 patients, were included in their analysis. Post-PCNL drainage was differentiated into no NT tube, small-bore NT, middle-sized NT, and large NT. They concluded that no NT and small-bore NT were superior to middle and large-bore NT with regard to postoperative pian, analgesic requirements, and hospital stay [24], thus confirming the findings of the previous studies.

The Clinical Research Office of the Endourological Society (CROES) prospectively collected data from consecutive patients treated with PCNL over a 1-year period at 96 participating centers worldwide. Data were collected on 3968 patients. The goal of the study was to examine the postoperative outcomes and relate these to NT size. For this study, small-bore NT was considered to be ≤18 Fr and large-bore NT >18 Fr. They reported that large-bore NT had a significantly lower rate of hemoglobin reduction, overall complications, and a trend toward a lower rate of fever compared to small-bore NT. In addition, they found that large-bore NTs were statistically associated with a longer postoperative hospital stay [18]. All studies comparing large-bore to small-bore PCNL NTs are summarized in Table 36.1.

NUCs have been used in PCNL surgery as an alternative to large- and small-bore NTs. NUCs are similar to a NTs, but comprise a much longer tube and have a second curl at the distal end. The distal end is placed in the bladder or ileal conduit and the proximal end exits the nephrostomy tract. When tension is applied to the strings, a curl occurs at the tip to aid retention in the bladder or conduit. A second curl will occur more proximally to

**Table 36.1** Studies reporting larger bore nephrostomy compared to small-bore nephrostomy.

| Author | Year | *N* | Study type | Large bore | Small bore | Conclusions |
|---|---|---|---|---|---|---|
| Maheshwari [20] | 2000 | 40 | Prospective | 28 Fr NT | 9 Fr pigtail NT | Small-bore NT associated with reduced pain, reduced urinary leak, and reduced hospital stay |
| Pietrow [21] | 2003 | 30 | Randomized | 22 Fr Councill tip | 10 Fr pigtail NT | Small-bore NT associated with reduced pain |
| Desai [14] | 2004 | 30 | Randomized | 20 Fr NT | 9 Fr NT | Large-bore NT had most pain |
| Kim [22] | 2005 | 106 | Randomized | Malecot or 20 Fr NT | 8.5 Fr or 10 Fr NT | Small-bore NT provided greater patient comfort |
| De Sio [23] | 2011 | 45 | Randomized | 22 Fr NT | 12 Fr NT | Can safely be used instead of a large-size NT |
| Cormio L [18] | 2013 | 3968 | Consecutive | >18 Fr NT | ≤18 Fr NT | Large-bore NT associated with reduced bleeding and fewer overall complications |
| Shen [24] | 2012 | 547 | Meta-analysis | 16–24 Fr NT | None or 8–9 Fr NT | NT-free and small-bore NT similar |

*N*, total number of patients; NT, nephrostomy tube.

drain the renal pelvis. The NUC thus allows both internal and external drainage of urine. Canales et al. reported that a 6 Fr NUC minimized postoperative intravenous narcotic use, and expedited both recovery and discharge in 99 consecutive patients who underwent PCNL [25].

Kader et al. in a consecutive series of 30 patients reported that NUC use diminished postoperative pain while maintaining ureteral patency and nephrostomy access, and was also associated with decreased hospital stay [26]. In contrast, in a single-blind, prospective randomized trial of 188 patients, Weiland et al. compared an 8.3 Fr pigtail NT to an 8.2 Fr NUC and concluded that the pigtail NT resulted in greater ease of placement and less pain than the NUC drain [27]. This is not unexpected due to the size of the NUC and the difficulty in placing a device that requires both a distal curl and curl in the renal pelvis.

## Tubeless PCNL

Early PCNL innovators often performed "nephrostomy-free" surgery. In 1984, Wickham et al. published the results of 100 patients who underwent "nephrostomy-free" PCNL in which no internal or external drainage was used. They determined that nephrostomy-free PCNL was safe and associated with a shorter hospital stay than a PCNL with an external drain. Some patients in this study were discharged from hospital within 24 hours [8].

However, in 1986 Winfield reported that two patients developed serious complications due to premature removal of the NT after the extraction of simple upper-tract calculi. Both of these patients experienced significant hemorrhage requiring blood transfusion and urinary leakage requiring internal stenting. Both patients had a prolonged hospital admission [7]. Their conclusion was that NT drainage is unquestionably necessary in the early postoperative period to prevent such complications. This quickly became doctrine and consequently became the standard of practice for PCNL worldwide.

Over time it became evident that an NT was not absolutely necessary and hence the possibility of "nephrostomy-free" PCNL was revisited. However, it was 11 years after Winfield's report that Bellman et al. coined the phrase "tubeless PCNL." In their study of 50 consecutive patients, 30 patients were given JJ stents and Councill tip catheters (which were removed within 3 hours of surgery) and 20 patients received JJ stents only. These patients were compared to 50 age-, sex-, and procedure-matched patients who received an NT [17]. Bellman et al. found that the tubeless PCNL was a safe procedure, contrary to what was believed. In addition, they determined that the procedure offers various advantages over routine placement of an NT. These include reduced hospital stay, lower analgesia requirements, less postoperative pain, and quicker time to return to normal activities. In addition, a tubeless PCNL was shown to cost less than a standard PCNL with an NT.

Tubeless PCNL is shown in Figure 36.3.

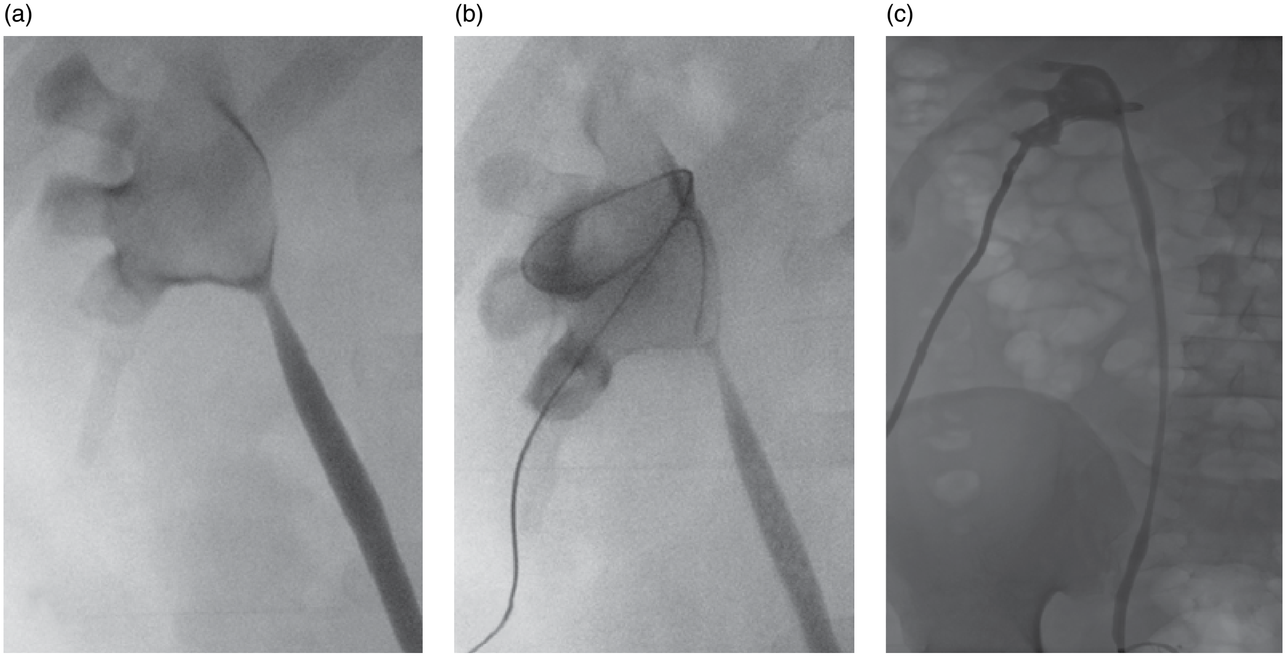

**Figure 36.3** Tubeless PCNL. (a) A large staghorn calculus. (b) Puncture was achieved through the lower pole calyx in supine position. (c) Antegrade placement of double-J stent for tubeless PCNL.

## Nephrostomy tube-free PCNL compared to standard PCNL with nephrostomy tube

Over the next two decades, 19 studies involving 1438 patients were published comparing NT-free PCNL to standard PCNL with NT placement. Sixteen of these studies compared NT placement to JJ stent, while three studies compared NT to externalized ureteric catheters. Nine of these studies evaluated the duration of hospital admission of NT-free PCNL compared to standard PCNL with an NT. Eight (88%) reported that NT-free PCNL led to shortened hospital admission [11, 12, 14, 15, 28–31]. Only one study (12%), a retrospective analysis found NT-free PCNL to be equivalent to standard PCNL with regard to hospital stay [32].

Eleven of these studies reported on postoperative pain and analgesic requirement, and nine (81%) trials showed that NT-free PCNL is associated with reduced postoperative pain and analgesia requirements compared to standard PCNL with NT placement [11–15, 28–30, 33]. Only two (18%) trials, found that postoperative pain and analgesia was equivalent between NT-free PCNL and cases with NT placement [31, 32]. Three trials specifically looked at urine leak and extravasation post-PCNL. Two trials reported that urine leak was less with NT-free PCNL [14, 33]. The other trial reported equal rates of urine leak for both NT-free and standard PCNL [32]. From these data, it can be concluded that NT-free PCNL is at least equivalent if not superior to standard PCNL with regard to admission duration, postoperative pain, and urine leak.

Since the original report by Bellman et al. many trials have compared the complication rates post tubeless PCNL and standard PCNL. Only six studies (31%), reported a higher rate of complications with tubeless PCNL [12, 31, 34–37]. The rate of complications in these studies ranged from 7.9% to 14% [35, 37]. However, this rate is well below a complication rate of 21.5% for PCNL, as reported in the CROES series [38]. It must be noted that the majority of these studies reported that tubeless PCNL is a safe procedure. Tubeless PCNL was found to be safe even in obese patients [36] and even if it is performed as an outpatient procedure [39]. Studies comparing tubeless PCNL to standard PCNL with an NT are summarized in Table 36.2.

Several authors have performed meta-analyses comparing tubeless to standard PCNL with an NT. First, Yuan et al. reported that tubeless PCNL was an effective and safe procedure for treatment of renal stones in selected patients. They concluded that tubeless PCNL was associated with a shorter hospital stay, less analgesic requirements, less urine leakage, and similar complication rates to standard PCNL [43]. Borges et al. reported that tubeless PCNL is a safe and effective procedure with a stone clearance rate comparable to that of standard PCNL. Tubeless PCNL was also associated with a shorter hospital stay and less postoperative urinary leakage. Pain reduction and reduction of analgesic requirements were also demonstrated [44].

Amer et al. found that the levels of pain recorded, analgesic requirements, duration of inpatient stay, and convalescence time were all significantly reduced in the tubeless PCNL [45]. Wang et al. found tubeless PCNL to be a good option in noncomplicated cases, with the advantages of reduced hospital stay and little need for postoperative analgesia [46]. Shen et al., in their meta-analysis, compared tubeless PCNL to small-bore NT, middle-sized NT, and large-bore NT. Similarly, they found tubeless PCNL and small-bore NT are similar in all measurements and possibly superior compared to middle- and large-bore NTs [24]. Overall, the meta-analyses showed that tubeless PCNL was significantly associated with less pain, leak, and shortened hospital stay. A summary of the meta-analysis findings is presented in Table 36.3.

## Tubeless PCNL compared to PCNL with a small-bore nephrostomy

Several studies have examined tubeless PCNL in comparison to small-bore NT placement. In three studies it was confirmed that tubeless PCNL was associated with reduced pain and shorter hospital admissions with similar rates of complications when in comparison to small-bore NT use [12, 14, 47]. This served to confirm the advantages of tubeless PCNL over standard PCNL with NT in select patients. The relevant data of these manuscripts are summarized in Table 36.4.

Small-bore nephrostomy is shown in Figure 36.4.

Patient selection is a key component for success with tubeless PCNL patients, as confirmed by numerous studies and meta-analyses [32, 41, 43, 46]. Patients ideally suitable for a tubeless PCNL should meet several criteria. These include:

- The planned surgery should be a straightforward and uncomplicated PCNL.
- Minimal bleeding must have been encountered.
- The calculus must be a noninfection stone.
- There should be absence of collecting system perforation.
- The urinary tract anatomy must be normal.
- Complete stone clearance should have been achieved.

If a patient has had any of the above potentially complicating factors then a tubeless procedure should be avoided. A tubeless PCNL decision-making aid is summarized in Table 36.5.

**Table 36.2** Studies comparing nephrostomy use and stent drainage.

| Author | Year | *N* | Study type | Drainage | Pain | Urine leak | Hospital stay | Complications |
|---|---|---|---|---|---|---|---|---|
| Bellman [17] | 1997 | 50 | Consecutive | JJ stent and Councill tube vs. JJ stent only | Reduced | – | Shorter | Similar |
| Delnay [11] | 1998 | 33 | Consecutive | JJ stent | Reduced | – | Shorter | Similar |
| Feng [12] | 2001 | 8 | Consecutive | JJ stent | Reduced | – | Shorter | 2 patients blood transfusion |
| Limb [34] | 2002 | 112 | Consecutive | JJ stent | – | – | – | 1 transfusion<br>3 patients complications |
| Yew [13] | 2003 | 4 | Consecutive | 7/3 Fr tail-stent | Reduced | – | – | Similar |
| Desai [14] | 2004 | 30 | Randomized | JJ stent | Reduced | Less | Shorter | Similar |
| Yang [36] | 2004 | 133 | Consecutive | JJ stent | – | – | – | 2 episodes hematuria<br>1 needed embolization |
| Singh [15] | 2008 | 60 | Randomized | 20 Fr nephrostomy vs. JJ stent | Reduced | – | Shorter | Similar |
| Singh [40] | 2008 | 30 | Randomized | JJ stent | – | – | – | Similar |
| Agrawal [33] | 2008 | 202 | Randomized | JJ stent vs. nephrostomy | Reduced | Less | – | Similar |
| Giusti [28] | 2009 | 99 | Consecutive | 6 Fr JJ stent | Reduced | – | Shorter | Similar |
| Beiko [39] | 2010 | 3 | Consecutive | 6 Fr JJ stent | – | – | – | Similar |
| Sofer [35] | 2010 | 200 | Consecutive | 7Fr JJ stent | – | – | – | Complication rate 14% |
| Garofalo [29] | 2013 | 114 | Consecutive | JJ stent | Reduced | – | Shorter | Similar |
| Isac [30] | 2014 | 83 | Retrospective | 5 Fr JJ stent | Reduced | – | Shorter | Similar |
| Lee [41] | 2014 | 29 | Prospective | JJ stent | – | – | – | Similar |
| Abbot [32] | 2016 | 38 | Retrospective | JJ stent | Same | Equal | Equal | Similar |
| Lojanapiwat [42] | 2001 | 37 | Consecutive | Ureteric catheter | – | – | – | Similar |
| Karami [37] | 2007 | 201 | Consecutive | Ureteric catheter | – | – | – | 10.9% transfusion, 7.9% UTI |
| Mishra [31] | 2010 | 22 | Randomized | 6 Fr ureteric catheter | Same | – | Shorter | More complications with tubeless PCNL |

*N*, total number of patients; NT, nephrostomy tube; JJ, double-J; UTI, urinary tract infection.

**Table 36.3** Meta-analysis of tubeless PCNL compared to standard PCNL with nephrostomy tube.

| Author | Year | *N* | No. of studies | Pain | Urine leak | Hospital stay | Caveat |
|---|---|---|---|---|---|---|---|
| Yuan [43] | 2011 | 776 | 14 | Reduced | Less | Shorter | Selected patients |
| Borges [44] | 2010 | 621 | 10 | Reduced | Less | Shorter | – |
| Amer [45] | 2012 | – | 24 | Reduced | – | Shorter | – |
| Wang [46] | 2012 | 1365 | 7 | Reduced | – | Shorter | Noncomplicated cases |
| Shen [24] | 2012 | 547 | 9 | Reduced | – | Shorter | – |

*N*, total number of patients..

**Table 36.4** Tubeless PCNL versus PCNL with small-bore nephrostomy.

| Author | Year | *N* | Study type | Method of drainage | Pain | Hospital stay | Complications |
|---|---|---|---|---|---|---|---|
| Feng [12] | 2001 | 27 | Consecutive | JJ stent or small-bore nephrostomy | Reduced | Shorter | 2 patients required blood transfusion |
| Desai [14] | 2004 | 30 | Randomized | 20 Fr NT, 9 Fr NT, or JJ stent | – | – | Same |
| Shah [47] | 2008 | 65 | Randomized | 8 Fr nephrostomy vs. JJ stent | Reduced | Shorted | Same |

*N*, Total number of patients; NT, nephrostomy tube; JJ, double-J.

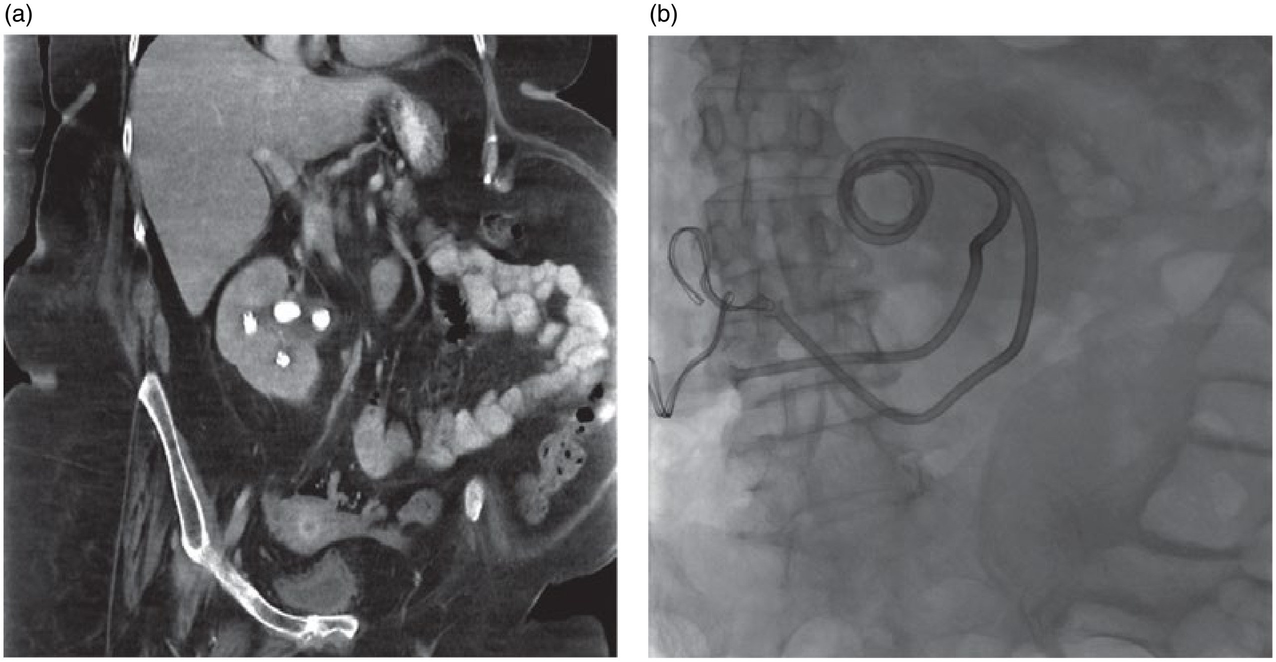

Figure 36.4 Double small-bore nephrostomy placement. This patient presented with severe urosepsis and septic shock. An emergency nephrostomy tube was placed. An interval PCNL was carried out via the emergency nephrostomy tract and through a second tract. Two small-bore nephrostomies were placed at the end of the procedure.

## Tubeless PCNL Compared to Early Tube Removal

Some authors also have argued that the key disadvantage of a tubeless PCNL is that it eliminates the ability to do an interval nephroscopy for management of any residual stone fragments. Two studies have evaluated the results of removing a small-bore NT on the first postoperative day when stone clearance has been confirmed, and have compared this to tubeless PCNL [31, 48]. According to these small randomized studies of a total of 77 patients, early NT tube removal results in levels of analgesic

**Table 36.5** Patient selection factors for tubeless PCNL.

| Tubeless OK | Leave nephrostomy tube |
|---|---|
| Straightforward PCNL | Complicated PCNL |
| No bleeding | Significant bleeding |
| No infection | Infection |
| No collection system perforation | Collection system perforation |
| Normal urinary tract | Abnormal urinary tract |
| Compete clearance | Incomplete clearance |

requirement, decrease in hemoglobin, and hospital stay similar to those seen with tubeless PCNL. These data suggest that early NT removal is an equivalent option to tubeless PCNL, which also preserves the ability to do a repeat PCNL. Data relevant to this comparison are summarized in Table 36.6.

## Tubeless PCNL versus modifications to JJ stent placement

A potential downside to tubeless PCNL is the need for cystoscopy to remove the internal JJ stent, and also the potential for stent-related pain and symptoms. To avoid these difficulties, variations of tubeless PCNL have been examined and described. Choi et al. [49] and Yew and Bellman [13] reported tubeless PCNL with placement of a JJ stent with a distal tether exiting the urethra. This tether was then used to pull the stent out at the chosen time. Choi et al., in a randomized controlled trial of small-bore NT versus tubeless PCNL with the JJ stent tether exiting the urethra, noted that tubeless and small-bore NT cause similar postoperative discomfort, with indwelling stents appearing to quicken return to normal activities [49]. Yew and Bellman noted that using this technique pain scores were low and stent symptoms appeared minimal [13].

Unintentional removal of the JJ stent by the patient pulling on the tether has been reported as a disadvantage to this technique [49]. To prevent this, several studies have also examined JJ stent placement with a tether attached to the proximal end of the JJ stent and the tether exiting the nephrostomy tract [50, 51]. This allows the stent to be removed directly from the flank without the need for cystoscopy and reduces the risk of the patient inadvertently extracting the stent. This method also has the additional advantage of allowing for a second-look PCNL if needed, thus removing the key disadvantage of tubeless PCNL. The JJ stent can be pulled to the level of the skin and a guidewire may be placed through it and down the ureter to the bladder in order to re-establish access. In addition to these advantages, Shpall et al. found that utilization of the tether to remove the ureteral stent via the flank after tubeless PCNL is safe and a cost-effective improvement on the standard tubeless form of PCNL [50].

Externalized ureteric catheters have been used as alternatives to JJ stents. Several authors found such use of ureteric catheters to be safe, effective, economical, and associated with reduced analgesia requirements even in patients with moderate stone burden [37, 42, 52]. The obvious disadvantage of using a ureteric catheter is that it is difficult to keep this catheter in for a long period of time, thus negating the benefits of a tubeless procedure. Indeed, Mouracade et al. reported that 15 patients in their series required JJ stent placement after the removal of the ureteric catheter [52].

Nephrostomy and double-J stent placement are shown in Figure 36.5.

## Totally tubeless PCNL

Wickham et al. were the first to report totally tubeless PCNL, but termed it nephrostomy-free PCNL [8]. However, Winfield's unsuccessful trial of totally tubeless PCNL led to the practice being abandoned [7]. Nearly two decades passed before the totally tubeless technique was attempted again. Over the last decade, 14 different trials have re-examined totally tubeless PCNL and confirmed its place as a surgical option for endourologists [37, 53–65].

Three of these studies were retrospective, and they identified that totally tubeless PCNL had complication rates similar to those of PCNL with NT. These studies concluded that totally tubeless PCNL is a safe procedure and is associated with reduced hospital stay and analgesic requirements [54, 63, 64]. Only in one study did one

**Table 36.6** Studies comparing tubeless PCNL to PCNL with early tube removal.

| Author | Year | *N* | Study type | Drainage | Pain | Urine leak | Hospital stay |
|---|---|---|---|---|---|---|---|
| Misha [31] | 2010 | 22 | Prospective | Early NT removal or ureteric catheter | Equal | – | Equal |
| El-Nahas [48] | 2012 | 55 | Prospective | Early NT removal or ureteric catheter | Equal | – | Equal |

*N*, total number of patients; NT, nephrostomy tube.

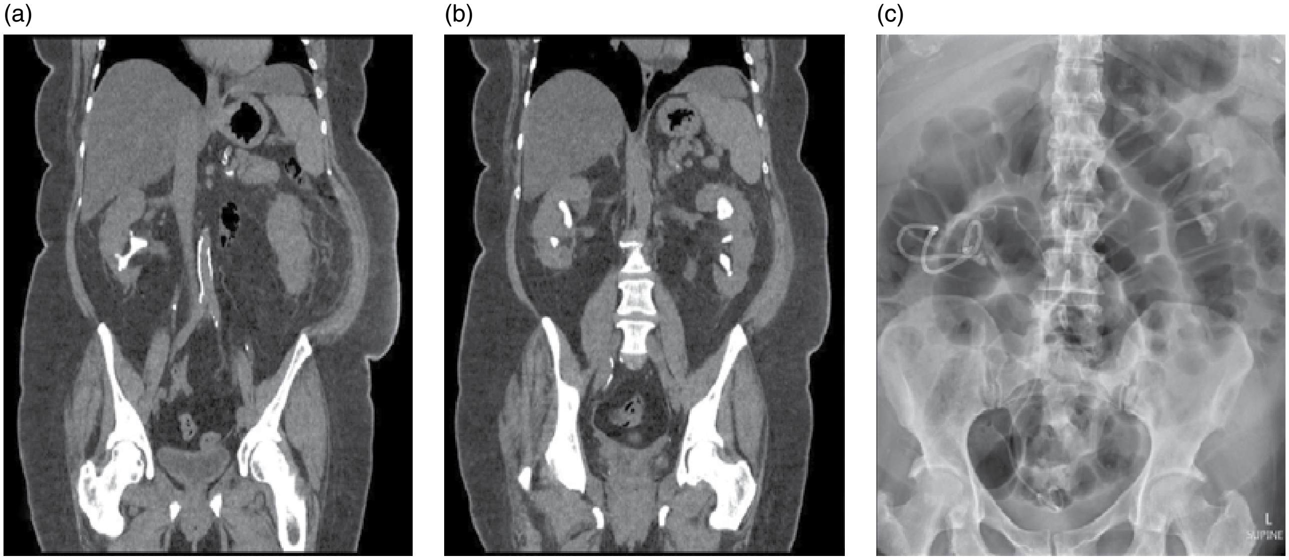

**Figure 36.5** Nephrostomy and double-J stent. (a, b) Bilateral staghorn stones. Right prone PCNL was performed. Complete stone clearance was achieved and a nephrostomy and double-J stent were placed for drainage. Nephrostomy was removed early within 24 hours. (c) The double-J stent was placed to allow for easy retrograde access for interval flexible ureteroscopy for further stone clearance.

patient require a JJ stent placement [54]. Three trials examined totally tubeless PCNL in selected patients only. These studies found totally tubeless PCNL to be safe, but associated with some complications. A sepsis rate of 5%, a major sepsis rate of 1% and a readmission rate of 1% was reported [55, 62].

Studies of consecutive patients who underwent totally tubeless PCNL again later demonstrated this procedure to be safe, and median hospital stays of 1.5–3.1 days were reported [37, 53, 65]. Five randomized control trials of totally tubeless PCNL and standard PCNL with NT have been reported. A total of 251 patients were included in these studies. All studies concluded that totally tubeless PCNL is a safe procedure, and is associated with reduced hospital stay and analgesic requirements in comparison to standard PCNL.

Furthermore, it has been reported that complication rates are similar for both totally tubeless PCNL and standard PCNL [56, 57, 59, 60]. Interestingly, Aghamir et al. reported that tubeless PCNL was even safe even in upper pole punctures [59]. Even more remarkably, Beiko et al. reported that totally tubeless PCNL could be performed as an outpatient procedure [58]. The trials reporting totally tubeless PCNL are summarized in Table 36.7.

## Hemostasis agents in tubeless PCNL tract

Several techniques have been tested to reduce the bleeding from the PCNL tract in tubeless and totally tubeless PCNL tracts. Techniques examined include diathermy of visible bleeding vessels, insertion of oxidized cellulose into the nephrostomy tract, use of fibrin sealant in the tract, putting gelatin sealant into the tract, and use of autologous fibrin glue. Jou et al. [66], Mouracade et al. [52], and Aron et al. [67] reported using diathermy to coagulate bleeding in intrarenal vessels and bleeding vessels in the tract [66, 67]. They found this procedure to be simple to do and safe as a hemostatic adjunct. However, these studies failed to prove any difference in bleeding complication rates between groups.

Aghamir et al. placed oxidized cellulose into the PCNL tract. They found that it did not decrease the complication rate and did not affect bleeding or urine leak rate [68]. Several authors have also examined the use of fibrin sealants in the PCNL tract [69–72]. Noller et al. [69] and Mikhail et al. [72] found fibrin sealants to be safe and feasible, while Gudeman et al. found it to be associated with shorter hospital stays and low complication rate [71]. However, the latter publication did report that two patients had bleeding complications and a further two patients had a urine leak with the use of the fibrin sealant [71].

Similarly, Shah et al. noted that fibrin sealant use is associated with less analgesic requirement and a shorter hospital stay [70]. The use of autologous fibrin glue in the PCNL tract was examined by Ziaee et al. [73]. In a randomized control trial they found that the use of such autologous fibrin glue had no effect on complication rate and that autologous fibrin glue played no significant role in improving results.

Gelatin matrix hemostatic sealant and thrombin-soaked absorptive gelatin sealants have also been used with some success in tubeless PCNL [40, 74, 75].

**Table 36.7** Studies evaluating totally tubeless PCNL.

| Author | Year | *N* | Study type | Pain | Urine leak | Hospital stay (days) | Complications | Observations |
|---|---|---|---|---|---|---|---|---|
| Wickham [8] | 1984 | 100 | Consecutive | – | – | 2 | 22% bleeding<br>10% infection | – |
| Winfield [7] | 1986 | 2 | Consecutive | – | – | 9 | 100% | Totally tubeless PCNL should be avoided |
| Karami [37] | 2004 | 30 | Consecutive | – | – | 1.5 | 3.3% UTI | Totally tubeless PCNL safe |
| Aghamir [53] | 2004 | 43 | Consecutive | – | – | 1.6 | Same | Totally tubeless PCNL safe |
| Gupta [54] | 2005 | 96 | Retrospective | – | – | 1.8 | 1 patient required transfusion and JJ stent placement | Cost-effectiveness |
| Crook [55] | 2006 | 100 | Select cases only | – | – | 2.9 | Sepsis rate 5%, major sepsis rate 1%. Readmission rate 1% | Safe procedure |
| Kara [56] | 2010 | 60 | Randomized | Reduced | Shorter | 1.5 | Same | Safe procedure |
| Istanbulluoglu [57] | 2009 | 45 | Randomized | Reduced | Shorter | 2.1 | 4.5% rate | – |
| Beiko [58] | 2009 | 1 | Select cases only | | | 4 h | Same | Can be performed as outpatient procedure |
| Istanbulluoglu [59] | 2010 | 43 | Randomized | Reduced | Shorter | 2.12 | Same | – |
| Chang [60] | 2011 | 68 | Randomized | Reduced | Shorter | – | Same | – |
| Aghamir [61] | 2011 | 35 | Randomized | Reduced | Shorter | 1.49 | Same | Safe for upper pole puncture |
| Yun [62] | 2012 | 27 | Select cases only | Reduced | Shorter | 3.92 | 4 patients had UTI<br>4 patients transfused | – |
| Nalbant [63] | 2012 | 85 | Retrospective | Reduced | Shorter | 1.6 | Same | – |
| Choi [64] | 2014 | | Retrospective | Reduced | Shorter | 1.72 | Same | – |
| Aghamir [65] | 2016 | 103 | Consecutive | | | 3.1 | Same | – |

*N*, total number of patients; NT, nephrostomy tube; JJ, double-J; UTI, urinary tract infection.

**Table 36.8** Studies evaluating hemostatic agents in tubeless and totally tubeless PCNL.

| Author | Year | *N* | Study type | Hemostasis | Complications | Observations |
|---|---|---|---|---|---|---|
| Gudeman [71] | 2012 | 107 | Retrospective | Fibrin sealant | 2 patients bleeding, 1 patient had urine leak | Associated with shorter hospital stays, and lower complication rates |
| Noller [69] | 2004 | 8 | Consecutive | Fibrin sealant | Same | Tubeless PCNL using fibrin sealant appears to be safe and feasible |
| Shah [70] | 2006 | 70 | Consecutive | Fibrin sealant | Same | Fibrin glue was safe and was associated with less analgesic requirement and a shorter hospital stay |
| Mikhail [72] | 2003 | 43 | Retrospective | Fibrin sealant | Same | Fibrin glue is safe |
| Jou [66] | 2004 | 51 | Consecutive | Diathermy | Same | Cauterization of tract bleeding points may make this PCNL a more secure procedure |
| Aron [67] | 2004 | 40 | Consecutive | Diathermy | Same | Fulguration of visible intrarenal and tract bleeders is a simple procedure |
| Singh [40] | 2008 | 50 | Consecutive | Gelatin sealant | Same | Hospital stay, urinary extravasation, and analgesia were significantly lower |
| Nagele [74] | 2006 | 11 | Prospective | Gelatin sealant | Same | Closing the tract of the mini PCNL with gelatin matrix hemostatic sealant is a safe procedure |
| Lee [75] | 2004 | 2 | Prospective | Gelatin sealant | Same | May be of value in preventing bleeding after PCNL |
| Ziaee [73] | 2013 | 43 | Randomized | Autologous fibrin glue | Same | Autologous fibrin glue did not improve results |
| Aghamir [68] | 2006 | 22 | Randomized | Oxidized cellulose | Same | Did not affect bleeding or urine leak rate |

*N*, total number of patients.

Lee et al. found that gelatin sealant may be of value in preventing bleeding after PCNL [75]. Nagele et al. reported that closing the tract of the mini PCNL with gelatin matrix hemostatic sealant was a safe and complication-free adjunct to this procedure [74]. Singh et al. noted that hospital stay, urinary extravasation, and analgesia requirement were significantly lower with the use of a gelatin sealant [40]. Data concerning the use of hemostatic agents in PCNL are summarized in Table 36.8.

## Conclusion

The choice of postprocedure drainage after PCNL has been demonstrated to impact on the postoperative course of any patient undergoing this procedure. Small-bore NT usage has distinct advantages over large-bore NT with regard to postoperative pain and hospital stay. Patients without a NT after a PCNL have less pain, a shorter stay in hospital, use less analgesia, and are not at increased risk of bleeding complications or urine extravasation compared to those that receive an NT, particularly a large-bore NT. Similarly, totally tubeless PCNL has also been shown to be safe and effective in selected cases with outcomes similar to those in tubeless PCNL. In all instances of tubeless PCNL, however, the potential for a second-look PCNL via an established tract is unavailable.

It is clear that patient selection is critically important in consideration of suitability for a tubeless procedure to be undertaken. Any patients with infection stones, complex staghorn stones, an abnormal urinary tract, significant bleeding, or the need for a second-look procedure should have a small-bore NT placed at the end of the procedure. A JJ stent with the tether exiting the nephrostomy tract is an alternative option. For straightforward PCNL cases, a JJ stent may be placed and the PCNL can be simply closed with a suture or steri-strip. Hemostatic agents such as fibrin glue or gelatin-based agents may be placed in the tract to improve hemostasis if desired. If the surgeon wishes to remove the need for a cystoscopy to remove the JJ stent, the tether can be left in place, exiting the urethra so that the stent can be removed easily once stone-free status has been confirmed. In all instances consideration of the individual circumstances of the patient and their stone burden is required to guide the endourologist to the optimal exit strategy after PCNL.

See accompanying Videos 36.1 and 36.2.

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## 37

# Problems with Residual Stones

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## Introduction

Recent epidemiologic studies show that the prevalence of nephrolithiasis is rising. In the United States, nearly 9% of the population will be diagnosed with a stone in their lifetime [1], with comparable increases in prevalence seen in European and Asian countries [2]. Accordingly, cost estimates for the diagnosis and treatment of stone disease in the United States are projected to increase substantially, from US$3.79 billion/year in 2007 to US$5.03 billion/year in 2030 [3]. Because of this, efforts to improve the efficiency of stone care are imperative.

Although nearly all patients with stones requiring treatment are now managed initially by noninvasive or minimally invasive means, and open surgery has all but disappeared [4], the need for secondary procedures to remove persistent stones or residual fragments (RFs) has increased. In this chapter, we review the outcomes of patients left with RFs after minimally invasive stone interventions, including shock-wave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PCNL).

## Shock-wave Lithotripsy

Although the introduction of SWL in 1980 by Chaussy et al. revolutionized the management of stone disease [5], it also brought with it a new management challenge – what to do with fragmented stones that fail to pass spontaneously. Although early reports documented high SWL treatment success rates, 20–30% of patients were left with ≤4–5 mm RFs [6, 7]. The term “clinically insignificant residual fragments” (CIRFs) was coined to denote small fragments that were expected to ultimately pass spontaneously and were considered a benign consequence of stone fragmentation. Indeed, Moon and Kim reported stone-free rates (SFRs) of 33%, 73%, and 93% at 1, 3, and 6 months, based on kidney–ureter–bladder (KUB) radiographs post-SWL among 248 patients with small RFs, validating the assumption that most small fragments eventually pass [8]. These authors concluded that practitioners should wait six months after SWL before offering repeat or secondary treatment.

Buchholz and associates also found a high rate of fragment clearance after SWL [9]. Among 55 patients with <5 mm RFs, 88% were stone free at a mean of 2.5 years after SWL. Likewise, Osman et al. found that 79% of 173 patients with ≤4 mm RFs after SWL cleared their RF within six months of SWL [10]. However, other studies have been less optimistic about fragment clearance. El-Nahas et al. used computed tomography (CT) to follow 154 patients left with ≤5 mm RFs at over three months after SWL and found that only 13% of patients had cleared their fragments at a mean of 31 months [11].

Streem et al. were the first to recognize that not all small RFs after SWL remain inert [12]. They identified 160 patients treated with SWL who were left with ≤4 mm RFs and found that 43% experienced a symptomatic event and/or required surgical intervention at a mean of 26 months following treatment. By Kaplan–Meier analysis, the 5-year probability of becoming symptomatic or requiring surgery was 71% and the probability of stone growth was 20%, indicating that RFs can have significant consequences.

Since the report by Streem et al., other investigators have likewise reported on the natural history of RFs after SWL and found that they can be a significant source of morbidity. Khaitan et al. prospectively followed

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75 patients with ≤4 mm RFs identified on abdominal radiographs obtained three months after SWL and found that at a mean follow-up of 15 months, 24% of patients cleared their fragments. However, among the 57 patients who retained their RFs, 72% demonstrated growth of the fragments, 61% experienced pain, and 42% required surgical intervention [13]. Osman et al. reviewed a series of 173 patients with RFs post-SWL and found that 21.4% of patients in whom there was growth of the fragments required surgical intervention at a mean of 4.9 years [10]. El-Nahas et al. followed 154 patients with RFs for a mean of 31 months, and noted that nearly half (48.7%) required surgical intervention or needed pain medication due to progression or movement of the RFs [11]. Finally, Candau et al. reviewed 83 patients with ≤4 mm RFs identified on three-month post-SWL imaging and found that at a medium follow-up of 40.6 months, 37% of patients demonstrated an increase in stone size by nephrotomogram imaging, and 58% of those patients underwent secondary treatment [14].

In contrast, Buchholz et al. followed 44 patients with ≤5 mm RFs after SWL for a mean of 33 months and found that only 12.5% of patients retained those fragments at the end of the period of observation and no patients experienced pain with stone passage [9]. Furthermore, only 2.1% of patients showed an increase in stone size.

Factors associated with an adverse outcome as a consequence of small RFs has been investigated. Although Candau et al. failed to identify any variables associated with clinically significant outcomes [14], other investigators reported that larger fragment size and/or greater stone burden correlated with worse outcomes [10, 11, 13]. In addition, RF location likely plays a role, as renal pelvic fragments tend to pass spontaneously [13], whereas calyceal, particularly lower pole, stones have lower clearance rates [10, 13]. Sahin et al. identified 80 patients with RFs after SWL and divided them into those with ≤2 mm (*n* = 30), 2– ≤ 4 mm RFs (*n* = 21), and >4 mm RFs (*n* = 35) [15]. Fragment clearance occurred in 100% of patients with ≤2 mm RFs, 76% of patients with 2– ≤ 4 mm RFs and 52% of patients with >4 mm RFs within three months. Moreover, emergency department (ED) visits were required in 19% and 51% of patients with 2– ≤ 4 mm and >4 mm RFs, respectively, compared to no ED visits in patients with ≤2 mm RFs. Accordingly, quality of life assessment using the SF-36 survey demonstrated that larger RF size was associated with significantly lower scores at one month and three months following SWL.

Considering the totality of these studies, growth of RFs after SWL occurred in 29% of patients, 25% of patients became symptomatic as a result of their RFs, and 33% of patients with RFs required intervention (Table 37.1). However, there are several limitations in comparing these natural history studies. Differences in imaging modalities result in differences in the sensitivity of detecting RFs. Furthermore, the definition of small RF after SWL is variable and has included ≤4 mm [12–14] and ≤5 mm [9–11]. Regardless, the literature has been reasonably consistent in identifying adverse outcomes in more than a quarter of patients with RFs after SWL.

## Ureteroscopy

Historically, series of URS for intrarenal calculi have demonstrated high SFR, ranging from 77 to 91% [16–18]. With further improvement in URS technology, progressively larger renal calculi have been addressed, with reported SFRs of approximately 85% in series of patients with >2 cm stones [19, 20]. However, these early URS series relied on abdominal radiography and/or ultrasonography to assess stone-free status, imaging modalities known to be inferior to CT for detecting RFs. Furthermore, the fate of RFs after URS was not typically assessed.

In a multicenter randomized controlled trial (RCT) comparing URS and SWL for the treatment of patients with ≤1 cm lower pole stones, Pearle et al. used three-month CT to determine SFRs and found sobering outcomes for both modalities: 35% for SWL and 50% for URS [21]. More contemporary series have likewise validated lower SFRs for URS than previously reported. Portis et al. prospectively evaluated 69 patients undergoing URS for 5–15 mm renal or proximal ureteral calculi who were imaged with CT one month post procedure [22]. Among 58 patients who completed follow-up, the mean CT SFR was 53.6%. Furthermore, at mean follow-up of 1.4 years, 5.2% of patients underwent repeat endoscopic intervention. Macejko et al. reviewed 92 patients who underwent 119 ureteroscopic procedures for renal or ureteral calculi and reported an SFR by CT of 50.4% [23]. When stratified by stone location, the SFR for stones in the kidney only was 34.8% compared with 80% for stones located in the ureter only. Rippel et al. also reviewed 265 URS procedures among 248 patients who were imaged with CT postoperatively and found an SFR of 62% [24]. On multivariate analysis, they determined that only pretreatment stone diameters of 6–10 mm (OR 2.03, 95% confidence interval (CI) 1.07–3.84, $P = 0.03$) and >10 mm (OR 3.74, 95% CI 1.57–8.94) were independent predictors of RFs.

The low SFR after URS revealed by CT in these studies underscores the need to understand the fate of these RFs. Several investigators have evaluated the natural history of RFs after URS. Rebuck et al. reviewed 330 URS procedures among 307 patients and identified 46 patients with 51 renal units containing ≤4 mm RFs [25]. Restricting

**Table 37.1** Outcomes of residual fragments after shock wave lithotripsy.

| Author (year) | No. of patients | RF size (mm) | Mean follow-up | Imaging | Asymptomatic | Passed | Stone growth | Symptomatic | Intervention |
|---|---|---|---|---|---|---|---|---|---|
| Streem (1996) [12] | 160 | ≤4 | 23 months | KUB/US | 56.9% (91/160) | 23.8% (38/160) | 18.1% (29/160) | 25.6% (44/160) | 27.5% (41/160) |
| Buchholz (1997) [9] | 44 (94 RF) | ≤5 | 2.5 years (median) | KUB | 12.5% | 87.5% | 2.1% (2/94) | 0.0% (0/94) | 0.0% (0/94) |
| Candau (2000) [14] | 83 | ≤4 | 40.6 months (median) | KUB | – | 33.0% (27/83) | 37.0% (31/83) | – | 22.0% (18/83) |
| Khaitan (2002) [13] | 75 | ≤4 | 15 months | KUB/IVP/US | 17.3% (13/75) | 24.0% (18/75) | 54.7% (41/75) | 46.7% (35/75) | 32.0% (24/75) |
| Osman (2005) [10] | 173 | ≤4 | 4.9 years | IVP/RGP/US | – | 78.6% (136/173) | 21.4% (37/173) | – | 43.9% (76/173) |
| El-Nahas (2006) [11] | 154 | ≤5 | 31.3 months | CT | – | 13.6% (21/154) | 33.8% (52/154) | 14.9% (23/154) | 33.8% (52/154) |
| Total | 689 | – | – | – | 44.3%* | 37.3%* | 29.4%* | 25.4%* | 33.2%* |

[a] Excludes Bucholz et al. because denominator indicated RFs instead of patient/renal units.

RF, residual fragment; KUB, kidney–ureter–bladder; US, ultrasound; IVP, intravenous pyelogram; RGP, retrograde pyelogram.

their analysis to only those with calcium-based stones, these investigators determined the outcome of these patients out to a mean follow-up of 18.9 months. They found that 22% of patients passed their fragments, 59% remained asymptomatic with retained fragments, and 20% experienced a stone-related event (SRE) (ED visit, hospitalization, or intervention) at a mean of 27 months post operatively. In addition, they noted that asymptomatic stones tended to demonstrate minimal growth (from 2.7 mm at three months to 3.0 mm at 33 months), while patients who experienced an SRE demonstrated growth of RFs from 2.5 mm at three months to 6.3 mm at 27 months, suggesting perhaps that stone growth portends increased risk of an SRE.

Ozgor et al. also followed 44 patients with ≤5 mm RFs detected on CT within three months of URS with annual CT imaging [26]. At a mean of 30.5 months follow-up, 66% of patients either passed their RFs or remained asymptomatic with no stone progression. However, stone growth was detected in 11% of patients, 23% experienced symptoms, and surgical intervention was required in 25%.

Portis et al. used need for repeat surgery as the primary outcome parameter in a retrospective review of 226 URS procedures in 217 patients for one or more renal or ureteral calculi for which no individual stone exceeded 15 mm in size [27]. SFR (by CT in 71% of renal units) at one month following stent removal was 53%. At a median follow-up of 4.1 years, 8.7% of patients ($n = 19$) underwent repeat surgery, including 14 URS and 5 PCNL procedures. By Kaplan–Meier analysis, the repeat surgery rate at 1 and 5 years was 5.8% (95% CI 3.4–9.8) and 8.6% (95% CI 5.6–13.1), respectively. The need for repeat surgery correlated strongly with the size of the RF ($P < 0.001$). When outcomes were stratified by RF size, need for repeat surgery at 1 and 5 years was 2.3% and 3.5%, respectively, for patients with no RFs; 20.8% at both 1 and 5 years for patients with RFs of >2– ≤ 4 mm; and 30.1% and 46.2%, respectively, for patients with RFs of >4 mm. For patients with ≤2 mm RFs, 1- and 5-year cumulative repeat surgery rates were low at 1.6% and 2.5%, respectively, but higher at 8.5% at both 1 and 5 years for patients with ≤4 mm RFs. Consequently, although patients with RFs ≤2 mm in size rarely required repeat surgery, those with RFs >2 mm were at substantially greater risk.

The largest series to date evaluating the fate of small RFs after URS is a multicenter retrospective review from Chew et al., representing the Endourology Disease Group for Excellence (EDGE) consortium [28]. This group identified 232 patients who underwent URS at one of six centers and were left with RFs of any size. At a mean follow-up of 16.8 months, 44% of patients experienced an SRE, defined as stone growth, stone passage, need for reintervention, or complication, and 29% underwent surgical intervention. When outcomes were stratified by RF size, they found that stone passage rates were comparable between those with RFs ≤4 mm and those with RFs >4 mm (26–27%). However, larger fragments were more likely than smaller fragments to demonstrate stone growth (59% vs. 28%, respectively, $P < 0.001$), to require intervention (38% vs. 18%, respectively, $P = 0.01$) and to be associated with complications (59% vs. 22%, respectively, $P = 0.039$).

Overall, taking into account three natural history series comprising 322 patients, 38% of patients experienced pain or an SRE and 26% of patients required surgical intervention (Table 37.2). Multivariable analyses have demonstrated that stone growth and the occurrence of symptomatic events after URS are associated with non-lower pole calyceal location [25], preoperative stone burden [24, 26] and hypocitraturia [26].

The increasing evidence of adverse outcomes associated with RF after URS has coincided with a contemporary debate over URS technique, namely “dusting” versus “basket extraction.” While “dusting” represents “complete” stone fragmentation to allow spontaneous passage of fragments over time, “basket extraction” implies an active retrieval process aimed at leaving the patient stone free at the end of the procedure. The EDGE consortium prospectively evaluated patients undergoing URS with either a “dusting” or “basketing” strategy and found a higher SFR by KUB/ultrasound in the “basket extraction” group than in the “dusting” group (86% vs. 59%), without any difference in readmission, reintervention, or symptomatic events at three-month follow-up [29]. Of note, the short follow-up currently limits any meaningful conclusions regarding the ultimate fate of RFs after URS, but longer prospective follow-up from this trial should ultimately add evidence to the RF debate.

## Percutaneous nephrolithotomy

Among the minimally invasive procedures for stone removal, PCNL is the most efficacious modality and the one that is typically used to treat large and/or complex renal calculi. Multi-institutional reporting through the Clinical Research Office of the Endourological Society (CROES) has demonstrated an overall SFR for PCNL of 76% [30]. However, with only 14% of these results based on CT imaging, SFRs are likely underestimated and RFs after PCNL are likely more prevalent than previously thought. Indeed, Pearle et al. prospectively evaluated 36 patients/41 renal units undergoing PCNL for >3 cm renal calculi who were imaged with CT on postoperative day 1 and identified RFs in 80.5% of renal units despite careful

**Table 37.2** Outcomes of residual fragments after ureteroscopy.

| Author (year) | No. of patients | RF size (mm) | Mean follow-up (months) | Imaging | Asymptomatic | Passed | Stone growth | Stone-related event/symptomatic | Intervention |
|---|---|---|---|---|---|---|---|---|---|
| Rebuck (2011) [25] | 46 | ≤4 | 18.9 | CT | 58.7% (27/46) | 21.7% (10/46) | – | 19.6% (9/46) | 13% (6/46) |
| Ozgor (2014) [26] | 44 | <5 | 30.5 | KUB/US, annual CT | – | – | 11.4% (5/44) | 22.7% (10/44) | 25.0% (11/44) |
| Chew (2016) [28] | 232 | all | 16.8 | KUB or CT | 56.0% (131/232) | 26–27% | – | 44.0% (101/232) | 28.9% (67/232) |
|  |  | ≤4 |  |  | – | – | 28.0% | 27.8% | 18.0% |
|  |  | >4 |  |  | – | – | – | 59.2% | 38.0% |
| Total | 322 |  | – | – | 56.4%[a] | 25.7%[a] | 11.4%[b] | 37.6%[a] | 26.1%[a] |

[a] Includes all RF regardless of size from Chew et al. [28].

[b] Excludes Chew et al. [28] because denominator not known.

RF, residual fragment; KUB, kidney–ureter–bladder; US, ultrasound.

flexible nephroscopy at the time of initial PCNL [31]. With second-look flexible nephroscopy (SLFN), however, an SFR of 90% was ultimately achieved. Osman et al. also prospectively evaluated 98 patients/100 renal units who were imaged with CT within 48 hours post PCNL and found RFs in 62% of patients [32]. These studies underscore the high prevalence of RFs after initial PCNL and highlight the potential for long-term sequelae if CT is not utilized to assess stone-free status and secondary flexible nephroscopy is not performed when RFs are detected. Table 37.3 lists clinically relevant series reporting outcomes of RF after PCNL.

Several investigators reviewed their series of PCNL to determine the outcomes of patients with RFs. Raman et al. reviewed 527 patients who underwent PCNL and identified 42 patients with RFs (median size 2 mm) who were observed for a minimum of six months [33]. At a mean follow-up of 32 months, 43% of patients experienced an SRE (defined as stone growth or need for ED visit and/or hospital admission) and 61% of those patients (26% overall) required surgical intervention. Multivariate logistic regression analysis revealed that maximum RF size >2 mm (HR 3.9, 95% CI 1.3–11.5, $P = 0.01$) and location in the renal pelvis or ureter (HR 4.4, 95% CI 1.0–13.5, $P = 0.01$) were independent predictors of an SRE. On Kaplan–Meier analysis, 1- and 3-year probability of freedom from an SRE was 87% and 65%, respectively, for RFs ≤2 mm and 56% and 33%, respectively, for RFs >2 mm in size.

Ganpule et al. identified 187 patients with RFs after PCNL (mean RF size 38.6 $\text{mm}^2$) and found that 45% of RFs passed spontaneously, most within three months [34]. No RF >100 $\text{mm}^2$ cleared without intervention, and RF size correlated inversely with spontaneous passage rates. On the other hand, Altunrende et al. found that among 38 patients with ≤4 mm RFs after PCNL and a minimum follow-up of 24 months (mean 28.4 months), only 8% spontaneously passed their fragments [35]. Additionally, although no patient required surgical intervention, 26% experienced symptoms (pain or hematuria), and 21% demonstrated growth of the RFs.

Osman et al. also reviewed the outcomes of 75 patients with ≤5 mm RFs after PCNL (mean RF size 4.7 mm) [36]. At a mean follow-up of 36 months, a third of patients had apparently passed their RFs spontaneously (presumably asymptomatically), 29% retained stable, asymptomatic RFs, a third demonstrated growth of the RFs, and 4% had an RF pass into the ureter. All of the 25 patients demonstrating growth of RFs and the three patients presenting with ureteral stones underwent surgical intervention. On multivariate analysis, only RF size >3 mm correlated with stone growth or symptomatic passage into the ureter (OR 1.882, 95% CI 0.919–3.854, $P = 0.05$).

Olvera-Posada et al. identified 44 patients with RFs (median size 5.5 mm) among 202 patients who underwent CT imaging post PCNL and had at least 12 months of follow-up [37]. At a mean follow-up of 57.9 months, 45.5% of patients remained asymptomatic while 54.5% of patients became symptomatic (pain or UTI) and 72.7% of patients underwent surgical intervention (electively or urgently). Overall, 84% of patients demonstrated growth of RFs at last follow-up. By Kaplan–Meier analysis, the 1- and 5-year probability of remaining intervention-free with the RFs was 91% and 29%, respectively. Furthermore, the likelihood of requiring intervention was significantly greater in patients with RFs >4 mm compared to those with RFs ≤4 mm. Of note, the likelihood of a symptomatic event was unrelated to RF size.

Predictors of an SRE in multivariable models included RF size >2 mm [33], >3 mm [36], >4 mm [37], stone location in the renal pelvis [33] or ureter [33], or no associated factors [37]. Larger stone size has consistently been shown to predict need for retreatment [33, 37, 38], but stone composition (notably struvite/apatite) may additionally correlate [37, 38]. Raman et al. showed that patients with RFs >2 mm had a 53% retreatment rate compared to 8% in those with RFs ≤2 mm [33]. In the longest follow-up study evaluating retreatment after PCNL, Portis et al. reviewed 150 patients undergoing 160 PCNL procedures to determine need for repeat surgical intervention [38]. At a median follow-up of 5.4 years, after controlling for stone composition, renal units with RFs were found to be 7.87 times more likely to require retreatment than those rendered stone free (95% CI 2.21–28.0, $P = 0.001$). By Kaplan–Meier survival analysis, cumulative retreatment rates at 7 years were 4.1% in those with no RF (95% CI 0–8.7), 33.3% in those with RF ≤4 mm (95% CI 6.1–60.5) and 29.8% in those with RF >4 mm (95% CI 12.1–47.5). Furthermore, non-calcium-containing RFs had a greater likelihood of requiring retreatment compared to calcium-containing RFs (56% vs. 23%, respectively).

Overall, among these series, stone growth occurred in 45%, symptoms developed in 42%, and surgical intervention was needed in 43% of patients (Table 37.3). Because of this, there is compelling evidence to support SLFN after PCNL to retrieve RFs. However, SLFN is costly and associated with additional morbidity, hospital length of stay, and cost. Raman et al. performed a cost effectiveness analysis to compare the cost of SLFN with the cost of expectant management in patients with RFs, taking into account the cost of the additional procedure and hospital length of stay for SLNF and the cost of additional ED visits and need for retreatment arising from observation of RFs [39]. Based on rates of RFs and need for surgical intervention obtained from the literature, the cost of observing RFs ≤4 mm was estimated at US$1743

**Table 37.3** Outcomes of residual fragments after percutaneous nephrolithotomy.

| Author (year) | No. of patients | RF size | Mean follow-up | Stone composition | Asymptomatic | Passed | Stone growth | Symptomatic | Intervention |
|---|---|---|---|---|---|---|---|---|---|
| Raman (2009) [33] | 42 | Median 2 mm (range 1–12 mm) | 41 months | 48% CaOx mono<br>26% hydroxyap<br>12% brushite<br>10% CaOx di<br>5% cystine | – | – | – | 43.0% (18/42) | 26.0% (11/42) |
| Altunrende (2011) [35] | 38 | ≤4 mm | 28.4 months (median) | 81% CaOx mono<br>5% uric acid<br>13% struvite | – | 7.9% (3/38) | 21.1% (8/38) | 26.3% (10/38) | – |
| Osman (2013) [36] | 75 | Mean 4.7 mm (range 2–5 mm) | 36.2 months (median) | – | 29.4% (22/75) | 33.3% (25/75) | 33.3% (25/75) | – | 34.7% (26/75) |
| Olvera-Posada (2016) [37] | 44 | Median 5.5 mm (IQR 3.25–8 mm) | 57.9 months | 39% CaOx mono<br>7% CaOx di<br>27% uric acid<br>14% CaPhos<br>9% struvite | 6.8% (3/44) | 9.1% (4/44) | 84.0% | 54.5% (24/44) | 72.7% (32/44) |
| Total | 199 | – | – | – | 21.0% | 20.4% | 44.6% | 42.0% | 42.8% |

RF, residual fragment; IQR, interquartile range.

and the cost of observing RFs >4 mm was US$4674. With a cost of SLFN in 2009 of US$2475, the model predicted that SLFN was cost-advantageous for RFs >4 mm, not cost-beneficial for ≤2 mm RFs, and only marginally cost-advantageous for RFs 3–4 mm in size [39]. Therefore, using the outcomes defined by prior work, SLFN should be strongly considered when RFs >2 mm remain after PCNL.

## Residual fragments in the pediatric population

Few studies have evaluated the outcomes of RFs after minimally invasive and noninvasive stone procedures in children. With evidence suggesting a growing prevalence of nephrolithiasis in children [40] and the longer time period of observation in this population, knowledge of the potential adverse effects of RFs is all the more important when selecting a treatment modality.

In the only series to evaluate the outcomes of RFs after SWL in children, Afshar et al. reviewed 26 children (mean age 7 years) with ≤5 mm RFs followed for a mean of 46 months [41]. Only 15% of RFs passed spontaneously, while 35% of patients experienced a symptomatic episode and 35% demonstrated stone growth. Of note, the only significant predictors of adverse outcomes in this population were the presence of a metabolic disorder and growth of RFs.

Dincel et al. reviewed the outcomes of 85 children (mean age 9 years) with ≤4 mm RFs after PCNL and found a rate of spontaneous passage of 26%, growth of RFs in 21%, and need for secondary intervention in 29% of patients at a mean follow-up of 22 months [42]. Likewise, El-Assmy et al. identified 61 children (mean age 6 years) with RFs (median size 4 mm, range 2–5 mm) after PCNL who had a mean follow-up of 18 months, and found comparable rates of spontaneous passage (26%), stone growth (25%), and need for intervention (23%) [43]. The only predictor of reintervention in this series was a history of stone disease.

## Medical therapy

Historically, dissolution therapy, particularly for stones composed of struvite and uric acid, was utilized after open stone surgery if RFs remained [44, 45]. With technological advances in endoscopic management of stones and better patient selection for SWL, such interventions are now only of historical interest. However, *in vitro* studies have demonstrated that even normal urine parameters can induce growth of RFs after intervention [46], and inhibitors of crystallization, such as phytate and citrate, can impede this process [47, 48]. Because of this, the ability to medically manage RFs after intervention is a promising area of study.

Cicerello et al. investigated the use of potassium citrate in patients with <5 mm sterile calcium or struvite RFs after SWL. Among 70 patients randomized to receive either alkali citrate or placebo, the authors found that citrate therapy significantly increased 12-month stone clearance rates over placebo (74% vs. 32% clearance, respectively, for sterile calcium stones and 86% vs. 40% clearance, respectively, for infection stones) and decreased stone growth [49]. Fine et al. also found that targeted medical therapy improved stone clearance in patients with RFs after SWL. At a mean follow-up of 36 months, the remission rate in 36 patients treated medically was significantly higher than in 13 patients not on medical therapy (63.9% vs. 23.1%, $P < 0.05$) [50]. In a similar retrospective study after PCNL, Kang et al. reviewed 40 patients with RFs and found a significantly higher remission rate (77% vs. 21%, respectively) and a lower stone formation rate (0.02 vs. 1.0 stones/patient/year) in patients treated with medical therapy compared with those on no medical therapy [51].

Soygur et al. investigated the role of potassium citrate therapy in promoting clearance of RFs after SWL [52]. Among 34 calcium oxalate stone formers with <5 mm RFs four weeks after SWL randomized to potassium citrate or placebo, stone remission rates at 12 months were higher in the potassium citrate group (44.5%) than in the placebo group (12.5%). Likewise, Lojanapiwat et al. randomized 76 patients who underwent SWL or PCNL to potassium–sodium citrate or placebo [53]. At 12 months follow-up, among the 37 patients who had <4 mm RFs, 30.8% of patients on potassium–sodium citrate compared to 9.1% on placebo were stone-free (RR 1.38, 95% CI 0.96–1.98). Furthermore, the RFs increased in size or new stones recurred in 54.5% of patients in the control group versus 7.7% of patients in the potassium–sodium citrate group (RR 0.3, 95% CI 0.08–1.0).

Other investigators assessed the role of hydrochlorothiazide, a known hypocalciuric agent, in promoting fragment clearance or reducing stone growth. Arrabal-Martin et al. randomized 100 patients with RF after SWL to hydrochlorothiazide or placebo [54]. At a mean follow-up of 36 months, overall fragment expulsion was higher in the hydrochlorothiazide group than in the placebo group (72 vs. 36%), even in the setting of a higher rate of secondary SWL in the placebo group (42 vs. 18%, respectively). Additionally, 58% of RFs in the placebo arm demonstrated stone growth compared to only 18% in the hydrochlorothiazide arm. In a subset of patients with hypercalciuria, the differences were even more pronounced.

These studies highlight the potential benefit of adjunctive medical therapy in promoting clearance and reducing the growth rate of RFs. Unfortunately, medical therapy cannot prevent the symptoms or the unpredictability associated with passage of these fragments.

## Conclusion

An abundance of literature suggests that regardless of the modality, RFs can be problematic after any surgical intervention. The likelihood of adverse outcomes seems to correlate with stone size, although the optimal size cutpoint for safe observation of RFs after surgery is unclear but likely lies somewhere around 2 mm. Because of this, the goal for every stone procedure should be to maximize stone clearance so as to limit regrowth, symptomatic events, and need for unplanned secondary intervention, all of which are associated with significant cost and decrement in quality of life. In patients with metabolic derangements or infectious etiologies, this recommendation is potentially even more important, and adjunct medical therapies should be considered.

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# SECTION 3

# Ureteroscopy

## Part 1 General Principles

# 38

# Ureteral Anatomy

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## Introduction

The ureters are muscular tubes located in the retroperitoneum that deliver urine from the bilateral kidneys to the urinary bladder in the pelvis. They originate as extensions of the renal pelvis and average 22–30 cm in length and 1.5–6.0 mm in diameter in adults [1]. They are divided by convention into three sections: proximal, middle, and distal (Figure 38.1). Alternatively, they can be divided into abdominal, pelvic, and intramural portions. The proximal ureter begins at the renal pelvis at about L2 and ends at the level of the proximal sacrum. The middle ureter refers to the ureter from the proximal sacrum to the distal edge of the sacrum. The distal ureter is the portion of the ureter that runs from the distal edge of the sacrum and ends at the ureteral orifice.

## Embryology

During fetal development, three urinary systems with increasing complexity and function appear: the pronephros, the mesonephros, and the metanephros. The pronephros is a rudimentary group of cells with limited excretory function that appears in the cervical region during the fourth week of development which completely regresses by the end of that week [2, 3]. During the fourth week as the pronephros begins to regress, the mesonephros, which is derived from intermediate mesoderm, appears bilaterally on either side of what will be the spine [4]. The developing gonadal structures are just medial to the mesonephros, and the two developing organs together make up the urogenital ridge. At this point, further development of the mesonephros results in formation of the excretory tubules, capillaries, glomeruli, and Bowman's capsule. A collecting system called the wolffian or mesonephric duct also forms. However, the mesonephros regresses like the pronephros.

The definitive urinary system is not formed until the permanent kidneys develop from the metanephric mesoderm in the fifth week [5]. The ureters and collecting system are derived from the ureteric bud, which grows from the wolffian duct. The wolffian duct otherwise regresses; however, in males, its remnants also contribute to structures of the genital system. Molecular signaling between the abutting ureteric bud and metanephric tissue results in development of the collecting system from the ureteric bud, specifically, the ureters, renal pelvis, calyces, and collecting tubules. The metanephric tissues become the glomeruli and nephrons.

At around 18 days, the ureter undergoes elongation, which results in redundancy and the formation of pleats that straighten as the ureter continues its elongation. As the ureter elongates it loses its lumen in the mid portion during days 37–40. Recanalization originates in the mid portion and extends cephalad and caudal to the ureteropelvic junction and ureterovesical junction, respectively. Hydrostatic pressure of secreted urine from the mesonephros is thought to contribute to recanalization. At nine weeks of development the metanephros, which will become the mature kidney, starts to produce urine. As this fetal urine drains into the bladder, patency of the ureter is maintained.

## Anatomical course

The gentle sigmoid curve that the ureters take begins at the ureteropelvic junction (UPJ). They begin posterior to the renal vessels close to the renal hilum, lateral to the transverse processes of the lumbar vertebrae. The right ureter starts posterior to the second part of the duodenum

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

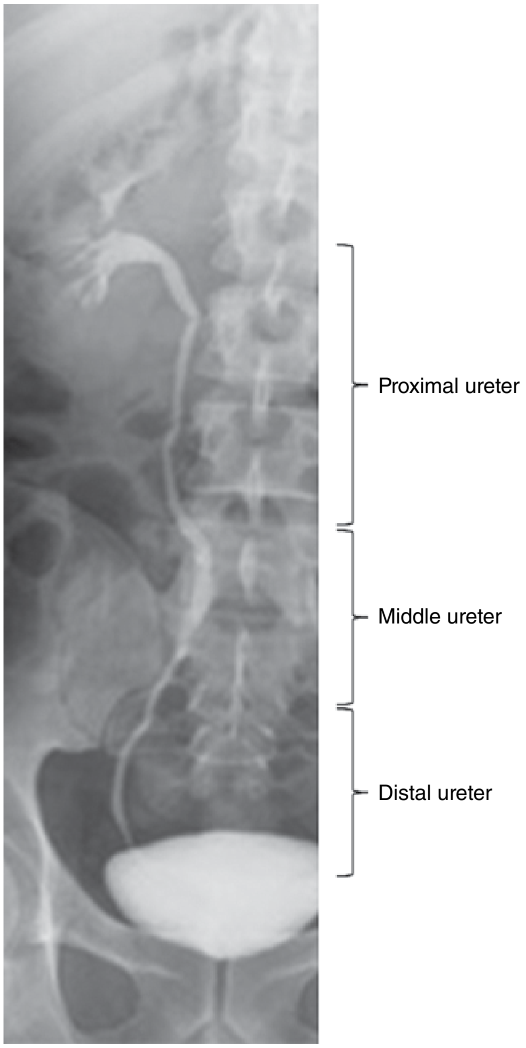

**Figure 38.1** Normal intravenous pyelogram demonstrating course of ureter from kidney to bladder.

and descends posterior to the ascending colon, cecum, appendix, and terminal ileum [1, 6]. The branches of the superior mesenteric artery and vein lie anterior to the right ureter. Both ureters lie just anterior to the psoas muscles, pass over the genitofemoral nerve, and under the gonadal vessels. The left ureter is attached to the mesocolon and passes under the sigmoid colon and its vessels, and travels behind the intersigmoid fossa. The left ureter also passes behind the inferior mesenteric artery in close proximity. The peritoneum covers the ureters anteriorly until they enter the pelvis.

As the ureters enter the pelvis, they also travel across the common iliac vessels and its branches. At the level of the ischial spine, the ureters lose their peritoneal layer and become completely retroperitoneal. The ureters further descend medially toward the bladder and pass anteriorly to the obturator neurovascular structures and posterior to the obliterated umbilical artery. In the male, the ureters pass behind the ductus deferens. In the female, the ureters pass under the ovarian and uterine vessels. In both genders, the ureters enter the bladder wall at an oblique angle at the ureterovesical junction (UVJ).

The caliber of the ureteral lumen varies along its course with average ranging from 1.8 to 3.0 mm [7]. There are three main areas of anatomical narrowing important during endoscopic procedures: at the UPJ, at the pelvic brim at the iliac vessels, and at the UVJ, with the UVJ being the narrowest of the three.

## Histology

The ureter can be separated into three histologic layers: mucosal layer, muscular layer, and adventitial layer. The innermost layer in the mucosa begins with the urothelium (transitional epithelium), which lines the lumen and is atop the lamina propria. The lumen of the decompressed ureter has a stellate (Figure 38.2) configuration that becomes progressively circular as it becomes distended with urine during peristalsis [8]. The lamina propria, composed of collagen fibers and fibrocytes, houses the microscopic vascular supply of the wall of the ureter and unmyelinated nerves. The muscular layer carries bundles of smooth muscle fibers that control peristalsis. These bundles of muscles are arranged longitudinally into subtle layers. The prominence of each muscle layer depends on the segment of ureter. In the abdomen the muscle layers are extremely thin and almost nonexistent on light microscopy [9]. In the pelvis, two layers of muscles have been identified:

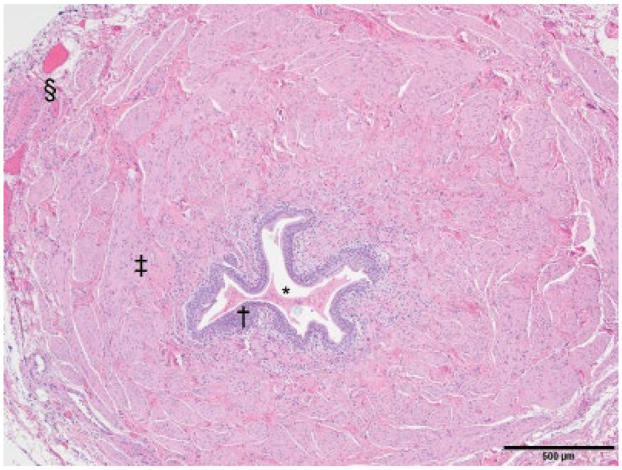

**Figure 38.2** Cross section of ureter under light microscopy demonstrating the lumen (*), mucosal layer (†), muscular layer (‡), and adventitial layer (§).

the outer circular layer and an inner longitudinal layer [10]. Additionally, as the ureter enters the bladder, the inner longitudinal layer becomes even more prominent and is thought to eventually contribute to the muscles fibers in the floor of the bladder to form the trigone. The adventitial layer, also called the ureteric sheath, carries two vascular networks that supply the ureteric wall. The inner network has perforating arteries that are continuous with the vascular network of the mucosal layer. The outer network contains vessels that run longitudinally along the course of the ureter. The adventitial layers also consist of collagen, fibrocytes, nerves, and muscle cells. All three layers contain unmyelinated nerve fibers.

## Blood supply

Vascular supply to the ureters varies along its course. It relies on an anastomotic network of vessels in the adventitia, which is the richest in the proximal and distal segments. Although the vast majority of the blood supply to the ureters is provided by the abdominal aorta, renal, gonadal, common iliac, and internal iliac arteries, there is considerable variation to the contribution of vessels of origin for the remaining blood supply [11]. The upper third of the ureter is supplied mostly by branches of the renal artery with contributions from the gonadal and colic arteries. The vascularization of the mid third of the ureter is variable, with contributions from the aorta, iliac, and gonadal arteries. In some patients the mid ureter is supplied primarily by peritoneal vessels. The distal ureter receives its main arterial supply from the internal iliac, superior vesical, and inferior vesical artery. Additional ureteral vascular supply may be provided by branches from the renal capsular arteries, adrenal arteries, umbilical artery, aortic branches, uterine artery, and the middle rectal artery. These small arterial branches, which may be quite long in relation to their caliber, subdivide in ascending and descending branches and coalesce into the periureteric arterial plexus within the adventitia. The supplying dominant branches enter the ureter differently at various segments. In the abdomen, arterial branches supplying the ureter enter anteriorly and medially. In the pelvis, the arterial supply enters posteriorly and laterally. This is important when considering incisions into the ureter if ischemia and development of strictures are to be avoided.

The venous drainage of the ureters begins in the lamina propria and extends into the adventitia. This venous plexus drains proximally via the renal and gonadal veins and distally into the vesical venous plexus and uterine veins in females and gonadal veins.

## Lymphatics

Lymphatic drainage of the ureter is dependent on the ureteral segment. The proximal ureter is drained by the ipsilateral renal lymphatics. In other words, they are drained by the aortic lymph nodes surrounding the gonadal artery. The middle ureter on the right is drained by the right paracaval and interaortocaval lymph nodes. The left middle ureter is drained by the left paraaortic lymph nodes. The pelvic ureters bilaterally are drained by the common iliac, the internal iliac, and external iliac lymph nodes.

## Innervation

The innervation of the ureters can also be divided into proximal, middle, and distal. The proximal nerve supply begins in the renal and aortic plexuses. The middle ureter is supplied by the superior hypogastric plexus, and the pelvic plexus provides innervation to the distal ureter. Visceral pain fibers are referred from the proximal ureter to L2 spinal nerve mostly, but they can also be carried to T11, T12, and L1 by the thoracic and lumbar splanchnic nerves that are part of the sympathetic nervous system. Stimulation of these sensory nerves (usually due to acute dilation of the ureter) results in referred pain to the dermatomes of T12–L2, namely the back and sides of the abdomen, the scrotum (males) or labia majora (females) and superior part of the anterior thigh. Peristaltic waves for ureteral contraction are controlled by pacemaking cells in the minor calyces and renal pelvis and are not dependent on autonomic stimuli [4]. Each minor calyx possesses these pacemaker cells, which can initiate a sustained contraction. These contractions are propagated away from the renal pyramid and toward the renal pelvis [12]. The duration of the contractile wave is dependent on the amount of urine being transported. With low urine flow rates the calyceal generated peristalsis may fail to precipitate generation of a pelviureteric peristalsis. With high urine flow rates, each contractile wave that reaches the pelviureteric junction is sustained and results in generation of a ureteral peristaltic wave and thus distal propulsion of urine toward the bladder. Specifically, the ureteric muscular coat is stimulated by the stretch of muscle fibers due to urine and thus peristalsis occurs [13]. The ureter makes an average three peristaltic contractions in a minute. There is debate on whether or not autonomic ganglia are present in the ureteric wall along its entire course as they have only have been identified in the very distal ureter [14, 15].

On a molecular level, activation of various S alpha-1-adrenoceptors 1A and 1D as well as muscarinic receptors have been found to cause ureteral contractions and have thus been the target of pharmaceutical manipulation [13, 16]. Efferent and afferent innervation from cholinergic, adrenergic, nonadrenergic, and noncholinergic receptors have also been identified, though the roles of the latter are not all completely understood [17]. Distribution of these different receptors is not evenly distributed throughout the course of the ureter, with the lower ureter being more densely populated than the upper ureter.

## Radiologic anatomy

Radiological imaging is important for planning endoscopic procedures as they provide a personalized anatomical guide that is specific to each individual patient. While excretory urography can provide a wealth of information about the ureter, new technological advances, namely computed tomography, have given our radiologic colleagues the ability to generate three-dimensional images of the urogenital system, which can provide opportunities for improved endourologic, laparoscopic, robotic, or open surgical planning.

The right kidney is situated 1–2 cm below the left kidney due to the liver. The renal pelvis and its relationship with the renal parenchyma can affect the configuration of the ureter at the UPJ. The renal pelvis, situated at the level of L2, can be intrarenal, extrarenal, or both. The ureter can exit the renal pelvis abruptly or with a gentle tapering where the beginning of the ureter and the end of the renal pelvis cannot be identified. The abdominal ureter descends from the renal pelvis vertically and begins to curve medially at the level of L5. Asymmetric medial deviation of the ureters at this level is considered a normal variant, and is often seen in young African American males [18]. However, deviation medial to the pedicles is considered abnormal. Likewise, lateral deviation of the ureters greater than 1.5 cm from the transverse processes is abnormal (Figures 38.3a,b).

From a lateral perspective, the ureters travel posterior to the anterior margin of the vertebral bodies. At the level of L4, they travel anteriorly past this margin, and at the level of L5, the ureters lie completely anterior to the vertebral bodies.

In addition to the normal anatomical narrowing of the ureters described earlier, there are several instances where narrowing can appear on excretory urography; thus it is important to distinguish imaging artifacts from true pathology. For example, normal peristaltic activity of the ureters can mimic a ureteral stricture. Comparing successive images temporally from the radiographic study usually results in normal visualization of the ureteral segment in question. At the levels of L3 and L5, an anterior oblique extrinsic narrowing is likely due to the gonadal vessels crossing the ureters. Similarly, narrowing of the ureteral lumen as it enters the pelvis is usually

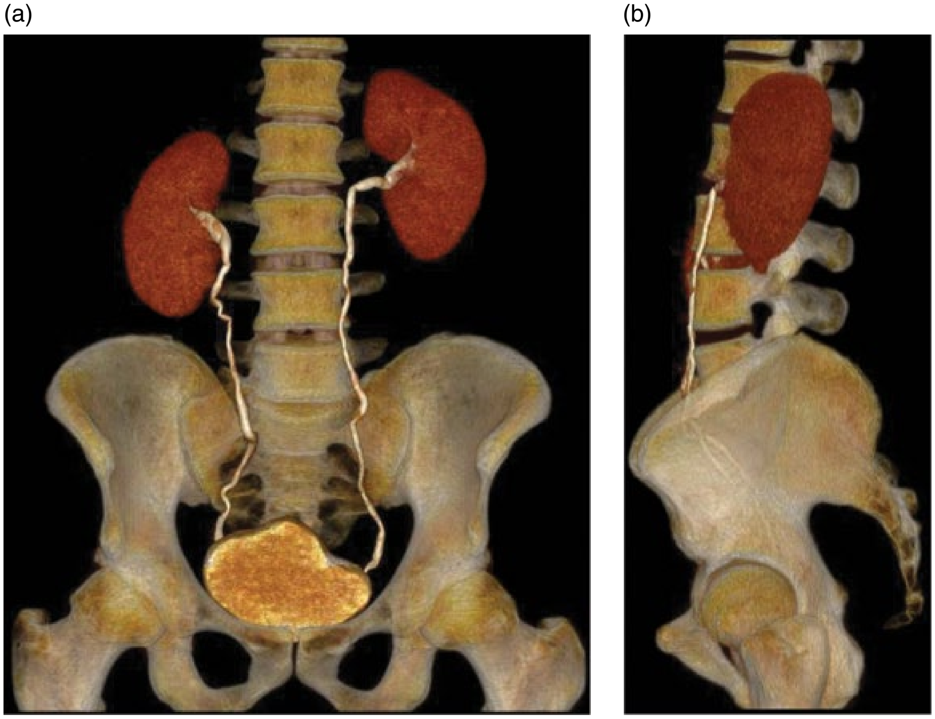

Figure 38.3 Three-dimensional imaging reconstruction of ureters using CT urography. (a) Anterior–posterior view, (b) lateral view.

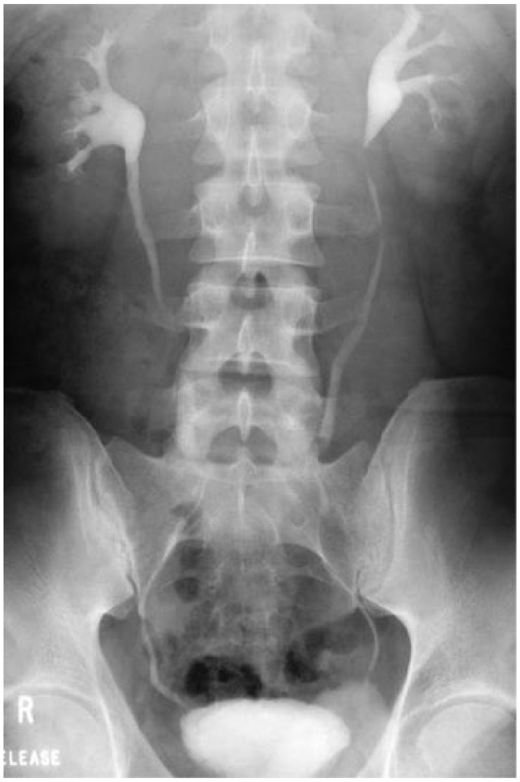

**Figure 38.4** Intravenous pyelogram of a patient with retroperitoneal fibrosis. Note the medial ureteral deviation typically seen at the L4–5 region.

secondary to extrinsic compression by the iliac vessels. Furthermore, kinks can appear in the abdominal ureters near the UPJ when inspirations cause kidney excursion, especially in patients with some redundancy of the ureter [19]. With bladder obstruction secondary to an enlarged prostate, ureters can truly be kinked at the distal end due to anterior displacement of the intramural ureter. This is identified as a "J hook" on urography [20].

Other pathologies can also be identified with urography. Asymmetric medial displacement of the intramural ureters can be caused by bladder diverticula, internal iliac aneurysms, and enlarged pelvic lymph nodes. Symmetric displacement of the intramural ureters medially (Figure 38.4) suggests retroperitoneal fibrosis [19]. An intraluminal mass can result in a filling defect known as the "goblet sign" and while most common with urothelial neoplasms, this proximal dilation can also be seen in benign processes such as ureteral fibroepithelial polyps.

## Endoscopic anatomy

When inspecting the bladder endoscopically the ureteral orifices at the UVJ are approximately 5 cm apart with the bladder full and about 2.5 cm in a decompressed bladder [6]. The ureteral orifices make up the lateral proximal border of the trigone and are located along the interureteric ridge (Mercier's bar), which is often more prominent in males than females. The superficial vessels coursing along the trigone point in the direction of the ureteral orifices and can assist the endoscopist in localizing and identifying the ureteral orifice.

The configuration of the ureteral orifice is classified into four structures based on visual appearance: grade 0 (volcano or cone shaped), grade 1 (stadium shaped), grade 2 (horse shoe shaped), and grade 3 (golf hole shaped) [21]. Grade 0 is most common and is considered normal while the other shapes are abnormal variations. The higher the grade of orifice configuration, the greater the likelihood to be displaced laterally and to be associated with vesicoureteral reflux (VUR) [22, 23].

The ureteral orifice normally effaces and compresses as the bladder fills, which is one of the mechanisms proposed in the prevention of reflux. Emptying the bladder in some instances can also assist in identifying the ureteral orifice and obviate the need for dilation prior to upper tract instrumentation.

Traumatic instrumentation or incision of the ureteral orifice can result in permanent reflux. Atraumatic dilation either with a catheter or balloon appears to not result in permanent reflux [24]. However, dilation of the ureteral orifices alone in some instances may be insufficient for passage of a ureteroscope to the upper tract due to an intrinsically narrow ureter. It is estimated that inability to pass the ureteroscope occurs in about 9% of cases [25]. There is ongoing controversy about the best method for access to the ureter and upper tract in this situation focusing on passive dilation with deployment of a ureteral stent and active dilation with use of a ureteric access sheath or balloon dilator [25–28]. Passive dilation with placement of a stent is arguably safer in terms of ureteral injury but requires a second attempt at ureteroscopy at a later time. Second attempts are mostly successful and seems to be based on the duration of stent [26]. Though active dilation with a balloon dilator or use of a ureteral access sheath can provide immediate access to the ureter, they are more traumatic to the ureteral walls, leading to local tissue ischemia and reperfusion injury that can result in scarring and strictures. The degree of ureteral wall injury when employing a ureteral access sheath for upper tract manipulation has been classified into five grades based on endoscopic findings: grade 0 (no lesion or mucosal petechiae), grade 1 (mucosal erosion without smooth muscle injury), grade 2 (injury to mucosa and smooth muscle with preservation of adventitium), grade 3 (injury to mucosa, smooth muscle, and perforation of adventitium), and grade 4 (total avulsion of ureter) [29]. High-grade injuries (grades 2, 3, and 4) were seven times more likely not to have had stenting prior to the use of the ureteral access sheath.

## Normal variations, congenital anomalies, and surgical alterations in ureteral anatomy

Congenital anomalies of the kidneys and ureters are relatively common and comprise about 20–30% of all congenital anomalies [30, 31].

### Deviation

Bilateral medial deviation of the pelvic ureters is considered a normal variant but can also result from retroperitoneal fibrosis, postsurgical changes, or pelvic lipomatosis. In retroperitoneal fibrosis, the upper collecting system is also dilated. When unilateral medial deviation of the ureter is present, it is more common on the right side and also more common in females due to uterine tilt to the left.

### Retrocaval ureter

In some circumstances, the right ureter can even deviate more medially and descend posterior to the inferior vena cava and then cross back the midline anteriorly to finish its course entering the pelvis over the iliac vessels. This variation is called retrocaval or circumcaval ureter.

### Ureteropelvic junction stenosis

UPJ stenosis is the abnormal narrowing at the site of the UPJ that potentially causes ipsilateral hydronephrosis and decreased renal function. The cause of the narrowing at the UPJ can be classified into intrinsic or extrinsic. Lack of adequate muscle fibers and increase in collagen fibers is one hypothesis of an intrinsic cause of UPJ stenosis. Failure of recanalization of the UPJ during development is another hypothesis [32]. Still yet another hypothesis focuses on extra tissue within the UPJ, causing a one-way valve picture resulting in difficulty draining urine. Other possible etiologies of UPJ stenosis may be persistence of valves during elongation of the ureter during fetal development. Extrinsic causes of UPJ stenosis or obstruction include crossing vessels, bands, kinks, high insertion of the ureter, or acute angulation.

### Agenesis

Renal agenesis occurs if the metanephric diverticulum fails to penetrate the metanephrogenic blastema. The result is that the collecting system does not induce the formation of nephrons.

### Duplicated systems

Normally, the ureters develop embryologically from a single ureteric bud. If there are two ureteric buds on one side during development, it is possible for any part of the collecting system to be duplicated. The collecting system can be duplicated both partially and completely. Partial or complete duplication is the most common ureteral anomaly with an overall incidence of 0.6–0.8% [31, 33, 34]. The Weigert–Meyer rule states that in a completely duplicated system, the ureteral orifice of the upper pole moiety empties into the bladder in a position that is medial and inferior to the ureteral orifice of the lower pole moiety (Figure 38.5).

Bifid ureters result from incomplete division of the metanephric diverticulum and ureteric bud during development, resulting in a bifid kidney. Complete division of the metanephric diverticulum results in a supernumerary kidney. The ureters draining the orthotopic kidney and the supernumerary kidney can be completely separate or be partially duplicated as a bifid ureter.

### Ectopic ureters and ureteral orifices

During fetal development, the ureteric bud is derived from the wolffian duct and normally separates from each other. The ureteric bud migrates cephalad while the wolffian duct migrates caudally. If the ureteric bud does not separate from the wolffian duct, then it can be pulled to migrate caudally as well. This is the reason that ectopic

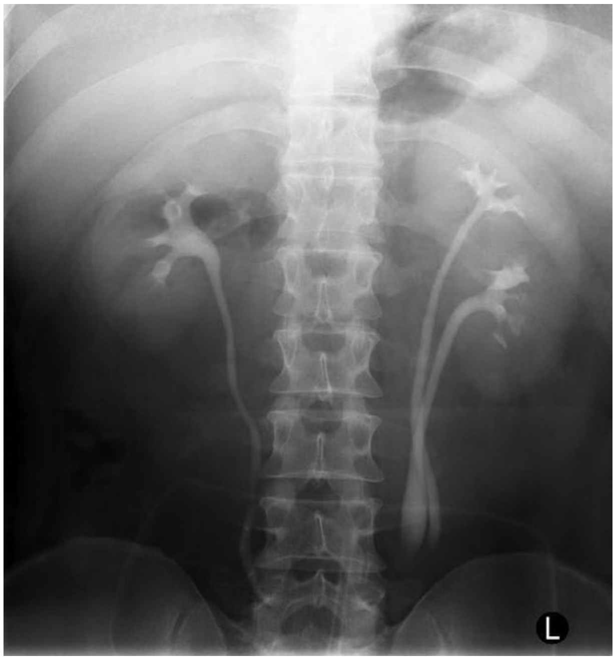

**Figure 38.5** Intravenous pyelogram demonstrating left duplicated collecting system and ureters.

ureters are more commonly caudally ectopic. These ectopic ureters can empty into the lower bladder, urethra, vestibule, or vagina in females and posterior urethra, seminal vesicle, vas deferens, or ejaculatory duct in males.

### Ureterocele

A ureterocele is an abnormal sacculation of the intramural ureter that is often caused by a congenital stenotic ureteral orifice, producing upstream dilatation [22]. Access to a ureter with a ureterocele may require dilation of the orifice. Ureteroceles are associated with duplicated systems and typically are associated with the ureter of the upper pole moiety [35]. Since complete duplication is seen more commonly in females, ureteroceles are concomitantly more common in females compared to males. It is not uncommon for patients to develop a urinary stone in a ureterocele, which may require an incision for removal (Figure 38.6a,b).

### Ureters of neobladders and conduits

As there are no anatomical landmarks in neobladders or urinary conduits, identifying the ureteral orifices of these ureters can be a challenge. Use of flexible ureteroscope for retrograde ureteroscopy is both easier and safer given unclear anatomy and potential to injure structures [36]. If possible, placement of antegrade guidewires percutaneously can address these issues.

### Reimplanted and reconstructed ureters

Reimplantation of a ureter is most often performed in children for VUR. There are various techniques for reimplantation with some reimplanting the ureter in its orthotopic position while others not (Figure 38.7).

### Ureters of malpositioned or fused kidneys

In normal development, the kidneys migrate cephalad from the pelvis into their retroperitoneum positions. They begin with the pelvis anteriorly and calyces posteriorly; as the kidneys ascend, they rotate 30° so that the pelvis faces medially. If kidneys fail to ascend, they remain in the pelvis and are often malrotated. Their ureters exit more laterally and are highly inserted; they can also be tortuous.

Fused kidneys may be located anywhere along the path of normal ascent of the kidney. The most common renal fusion anomaly is a horseshoe kidney. A horseshoe kidney has abnormal fusion of the lower poles of the two renal units resulting in an isthmus of functioning or nonfunctional renal parenchyma. This renal isthmus limits the kidney's fetal ascent of the horseshoe kidney at the level of the inferior mesenteric artery. In addition to abnormal ascent, the fusion prohibits the proper rotation of the kidneys, typically resulting in a high and lateral insertion of the ureter at the level of the UPJ.

Fused kidneys occur due to abnormal fusion of the metanephric blastema during embryogenesis and can also result in abnormal ascent of the kidneys. Crossed fused renal ectopia refers to an anomaly where the kidneys are fused and located on the same side of the midline. The estimated incidence is around 1 out of 1000 births [37]. There is a recognized male predilection with a 2:1 male to female ratio. More than 90% of crossed renal ectopia results in fusion and failure of the kidneys to reach their appropriate positions at the level of L2 in the eighth week of fetal life.

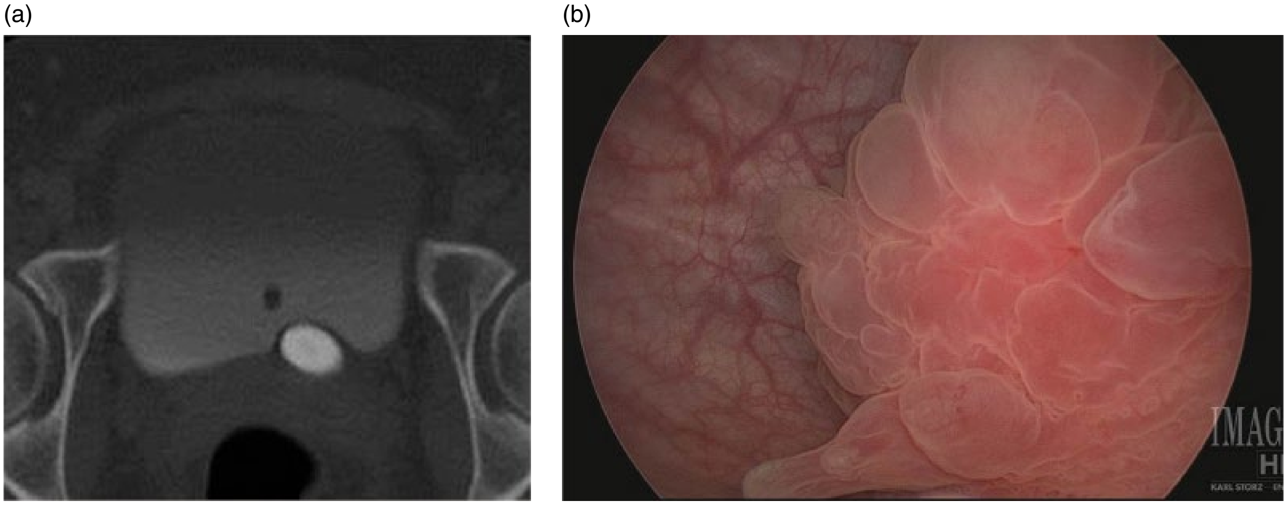

**Figure 38.6** (a) CT image of left ureteral stone in a simple ureterocele. (b) Endoscopic view of an inflamed left ureterocele. The ureteral orifice was identified and required an incision to remove the stone.

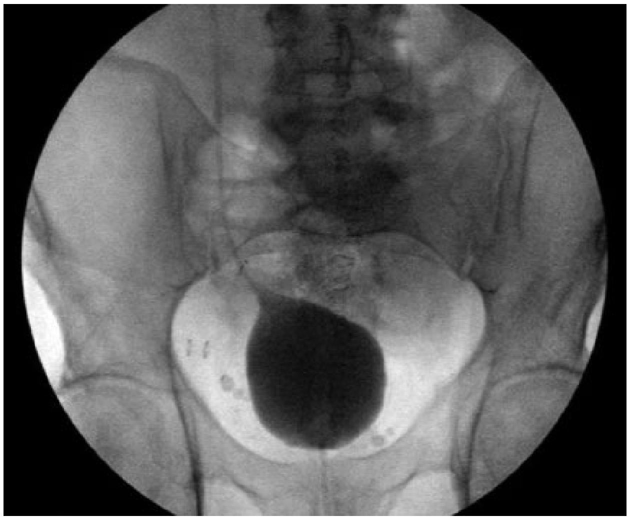

**Figure 38.7** Ureteral reimplant to the bladder dome.

Some evidence supports that an abnormally situated umbilical artery prevents normal cephalad migration. Another theory is that the ureteric bud crosses to the opposite side and induces nephron formation in the contralateral metanephric blastema. The result is a single renal mass with two collecting systems being located on one side of the abdomen. There are several subtypes of crossed renal ectopia based on the appearance of the fusion abnormality: inferior crossed fusion, sigmoid kidney, lump kidney, disc kidney, L-shaped kidney, and the superiorly crossed fused (Figure 38.8) [37]. Left-to-right ectopy is thought to be three times more common. Of note, the trigone retains its anatomic integrity with the involved ureter draining the ectopic renal unit into the correct corresponding contralateral ureteral orifice.

## Key points and conclusions

Intimate knowledge of the ureter and its associated structures remains critical in endourology. Advancements in endoscopy and imaging have facilitated numerous procedures for urologists. Three-dimensional reconstitutions in particular can help map urogenital systems that have undergone complex reconstruction. However, even without these adjuncts, understanding of the normal ureteral course can help make endoscopic procedures proceed without complications and help identify true abnormalities versus normal variants.

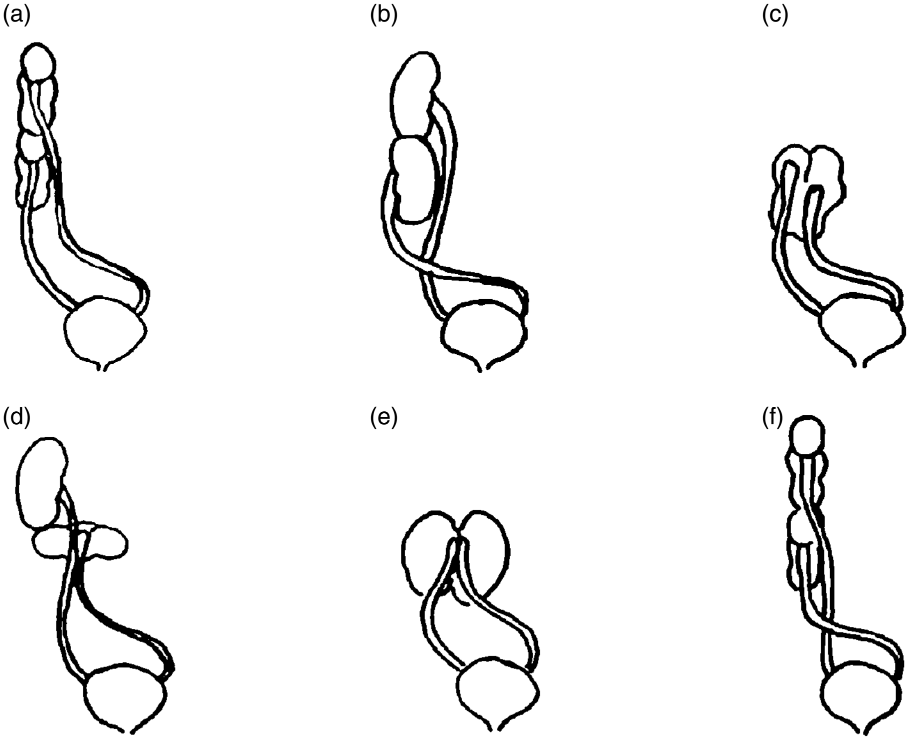

**Figure 38.8** Diagrammatic representation of classification of crossed fused renal ectopia [37]. (a) Unilateral fused kidney (inferior ectopia). (b) Sigmoid or S-shaped kidney. (c) Lump kidney. (d) L-shaped kidney. (e) Disk kidney. (f) Unilateral fused kidney (superior ectopia). *Source*: Solanki S, Bhatnagar V, Gupta AK et al. Crossed fused renal ectopia: challenges in diagnosis and management. *J Indian Assoc Pediatr Surg* 2013;18(1):7–10. Reproduced with permission of the Indian Association of Pediatric Surgeons.

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# 39

# Rigid Ureteroscopes

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## Introduction

The natural progression from open surgery to minimally invasive procedures is a testament to the technological evolution that has brought about the modern day ureteroscope. Young performed the first recorded ureteroscopy in 1912 using a 9.5 Fr pediatric cystoscope [1]. Since then, advancements in endoscopic design and the use of fiber-optic technology has led to smaller scopes with improved maneuverability, allowing for not only rigid and semirigid ureteroscopes, but also flexible ureteroscopes. The latest generation of ureteroscopes now provides high-definition digital images of the ureter and intrarenal collecting system, allowing procedures to be carried out safely, with high success rates and minimal morbidity in adults and children.

To appreciate how rigid and semirigid ureteroscopes have evolved through time, this chapter will portray a summary of key technical developments, starting with the first endoscope, the effect of changes in instrumentation, and progressing through to the latest digital technology. A description of key features of ureteroscopes is then given, discussing their similarities and differences and potential future trends for their further development.

## Rigid and semirigid ureteroscopes

### Rigid ureteroscopes

**Historical perspective**

The history of the endoscope dates back to 1853 [2–4] and has developed considerably to the present day ureteroscopes (Table 39.1). The traditional components required to carry out a rigid endoscopic procedure are the telescope with working channels for irrigation and instrumentation, a light source, optics to convey the image, and a camera system to capture the image. This has been revolutionized by the use of fibroptic technology; however, with the increasing speed of technological evolution, fiber-optics will one day make way for the digital era.

The forerunner of the endoscope can be traced back to 1806 with the construction of the light-guiding instrument or “Lichtleiter” by Phillip Bozzini for direct inspection of internal organs [5]. This scope was basic in design, consisting of a direct vision hollow tube through which candlelight was transmitted by a mirror. The French surgeon Antoine Jean Desormeaux further developed the Lichtleiter, producing the “endoscope” in 1853 using a system of mirrors and lens, and a kerosene flame to provide light to examine the urethra and bladder (Figure 39.1). Gustave Trouvé further upgraded indirect illumination by candlelight to electrical illumination using glowing heated platinum wires at the tip of the instrument in 1873 [5]. The filaments were later replaced by Edison’s incandescent lightbulb. The Nitze-Leiter cystoscope, a rudimentary version of the modern cystoscope, was constructed in 1879 and incorporated a simple lens system into the viewing tube [5].

Fiber-optic lighting technology was introduced in the 1960s, replacing the incandescent bulb and revolutionizing the manufacture of rigid endoscopes. The design was based on the principle of total internal reflection: when light travels in a transparent medium such as glass, internal reflection of the light occurs at the interface between the medium and its surroundings, as demonstrated by John Tyndall in 1854 [6]. This physical property of internal reflection allows the “bending” of

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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 39.1** Landmark evolutionary steps in the development of the rigid endoscope.

| Year | Pioneer | Rigid endoscope and technologic advances |
|---|---|---|
| 1806 | Phillip Bozzini | German doctor who introduced the "Lichtleiter" or light-guiding instrument |
| 1853 | Antoine Jean Desormeaux | French surgeon who first introduced the "endoscope." Often considered as the father of endoscopy |
| 1873 | Gustave Trouvé | French inventor who moved the light source from outside to the inner tip of the endoscope and developed the "polyscope" |
| 1879 | Maximilian Nitze and Joseph Leiter | German urologist (Nitze) and Viennese electro-optician (Leiter) credited with the invention of the modern cystoscope |
| 1960s | Several contributors | Various people introduced the use of fiber-optic cable, enabling transmission of light from an external source |
| 1960s | Harold Hopkins | British physicist who filed a patent for the "rod–lens" system that was later adopted by Karl Storz in 1965 |

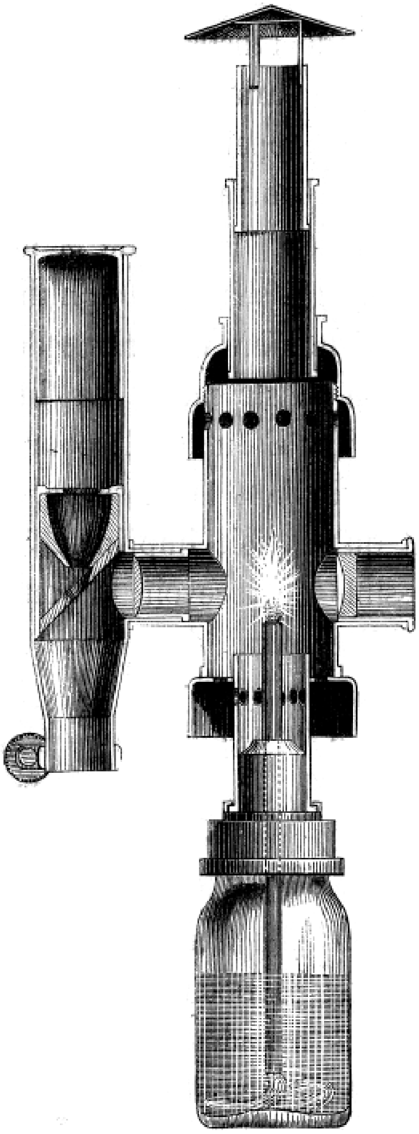

**Figure 39.1** Antoine Jean Desormeaux modified the "Lichtleiter" to produce the "endoscope." *Source:* A.J. Desormeaux, *De l'endoscope*. 1865. Reproduced courtesy of Wellcome Library, London, UK.

light within flexible glass. Thus, light travelling inside a small-diameter flexible glass fiber surrounded by cladding of lower refractory index can be transmitted over a long distance with minimal degradation. The benefit of modern fiber-optic lighting is greater illumination by cooler light, ultimately making it safer. An additional benefit is that the scopes can be made with a smaller profile shaft, allowing more room within the shaft for the addition of an irrigation and instrument channel. The fiber-optic cable is often attached via a light post to the endoscope, but may alternatively be built into the design of the scope.

The innovative work of the British physicist Harold Hopkins led to the next major breakthrough in rigid endoscopic design with the introduction of the rod–lens system in the 1960s [7]. Until then, the shaft of the scope consisted of a hollow tube with a series of thin relay lenses separated by long air spaces. The relay lenses had to remain in precise alignment and any displacement of the lens resulted in a significant loss of image transmission. There was also a significant loss of light transmission with this system. Hopkins replaced the thin relay lenses within the shaft of the endoscope with long, contoured glass rods acting as the transmission medium, while the thin pockets interspersed between the glass rods acted as lenses. With the telescope primarily being made of glass, which has a higher refractive index than air, light transmission could be increased ninefold over previous lens systems, with the additional benefit of reduced image distortion and a wider viewing angle. The outer diameter of the endoscope shaft could also be reduced, paving the way for the development of the rigid ureteroscope and the introduction of working channels. The old lens system was notorious for its lack of durability and the Hopkins rod–lens system produced a significant improvement in this area. There were a few apparent weaknesses in the rod–lens design: any deviation in the use of the cystoscope from being used in straight lines, as can occur with the application of torque to the shaft, could lead to misalignment of the rod–lens setup and the permanent disappearance of up to half the image. The problem manifests itself as a half-moon or crescent-shaped defect when viewing through the scope eyepiece. This design flaw would be seen to be disadvantageous in the passage of the endoscope through the natural undulations of the ureter. A further consideration for ureteroscopic design centers on the diameter of the lens that dictates the size, or degree of magnification, of the image; the reduced diameter of the ureteroscope would inadvertently have a smaller image than the larger cystoscope.

## Endoscopic evolution

Young undertook the first recorded ureteroscopy in 1912, and it took another 65 years before Goodman [8] and Lyon et al. [9] ventured into the ureter, performing distal ureteroscopy in both male and female patients (Table 39.2). Goodman reported using an 11 Fr pediatric rod–lens cystoscope to inspect the distal ureter in three adults [8]. In one of these patients, a distal ureteral tumor was fulgurated, marking the first ureteroscopically treated tumor. Lyon et al. reported ureteroscopy in five adults using sound dilators for ureteral dilation before passing an 11 Fr pediatric cystoscope [9]. However, most of these early ureteroscopy patients were women. Lyon et al. reported in 1979 the use of specially designed ureteral dilators attached to the tip of a flexible probe. They were able to dilate the orifice to 16 Fr, permitting insertion of a standard-length 13 Fr cystoscope for distal ureteroscopy in men. These early investigators demonstrated the ease and safety of rigid ureteroscopy for the distal ureter in both sexes.

The first rigid ureteroscope specifically designed for ureteric use was produced in 1979 by Richard Wolf Medical Instruments and was used by Lyon et al. [10]. Modeled on a pediatric cystoscope, this 13 Fr instrument had a working length of 23 cm and sheath sizes of 14.5 and 16 Fr; a 16 Fr resectoscope sheath was also available. The 13 Fr sheath was used only for inspection, but the larger sheaths allowed simultaneous passage of a ureteral catheter or basket for stone manipulation and removal. For the first time, ureteral calculi were visualized, engaged in a basket, and removed [10, 11]. A longer ureteroscope that could reach the renal pelvis was developed by Enriqué Pérez-Castro in collaboration with Karl Storz Endoscopy in 1980 [12]. Its 39 cm length allowed inspection of the renal pelvis for the first time.

Further ureteroscopic modification was not due to advances in scope technology, rather the introduction of and progression in instrumentation. The launch of ureteroscopic ultrasonic lithotripsy for the treatment of urolithiasis led to modifications in ureteroscopic configuration. Initially, the probes were hollow and 8 Fr in diameter, requiring removal of the telescope and blind stone lithotripsy. These were replaced by smaller solid probes (1.5–2.0 mm) that could pass through the working channels but that were too rigid to negotiate the angles of the instrument working ports. This led to the development of the offset eyepiece which allowed the direct passage of the probe through a straight working channel under direct vision. Rigid ureteroscopes were later designed with an interchangeable offset eyepiece and standard telescope, allowing easier passage of the scope. Due to difficulties and complications from inserting rigid rod–lens type ureteroscopes with diameters approaching 14.5–15 Fr, it became apparent that smaller ureteroscopes were needed. With the availability of smaller working instruments, Huffman described a compact ureteroscope that was 8.5 Fr in diameter and had a working channel of 3.5 Fr [13]. The rod–lens telescope was integrated into the ureteroscope, which helped decrease the outer diameter while maintaining a good-sized working channel.

## General properties

The rigid ureteroscope has not deviated significantly from the original pediatric cystoscope used to inspect the ureter. Any development has centered on the

**Table 39.2** Landmark evolutionary steps in the development of the rigid ureteroscope.

| Year | Pioneer | Rigid ureteroscope technological advances |
|---|---|---|
| 1977 | TM Goodman and Edward Lyon | Provided the first reported series of distal ureteroscopically performed cases |
| 1979 | Richard Wolf | Credited with the design and construction of the first rigid ureteroscope |
| 1980 | Enriqué Pérez-Castro | Developed the “long” ureteroscope in collaboration with Karl Storz Endoscopy |
| 1980 | ACMI | The Rigiflex was the first ureteroscope to adopt the use of fiber-optics to allow the “gooseneck” eyepiece |
| 1989 | Huffman | Produced the 8.5 Fr “compact ureteroscope” with a 3.5 Fr working channel. The rod–lens was integrated into the ureteroscope |

improvement in the light source, the introduction of the rod–lens optics system, the launch of a single working channel, and changes in the overall ureteroscope dimensions. That said, over the years the ureteroscope has become narrow enough to ensure easier ureteric access and long enough to venture into the renal pelvis, and has a working channel to allow instrumentation for intervention and diagnostic purposes.

#### Optics, angle, field of view, and eyepiece

The rod–lens systems has provided excellent optical quality over the years, but scopes incorporating this design tend to have larger diameters and are prone to damage following angulation of the ureteroscope. The “angle of view” in an endoscope can vary from 0°, providing a straight view of the structure in question, to 70°, which allows inspection of tissues at an oblique angle from the straight axis. These rod–lens ureteroscopes were either interchangeable (from 0 to 70° angle of view) or integrated within the ureteroscope itself. The 70° lens was primarily used to inspect the renal pelvis and calyces, although these lenses are now virtually obsolete with the development of flexible ureterorenoscopes. The few current rod–lens ureteroscopes have integrated telescopes because of their smaller size advantage, and the angle of view through the objective lens is fixed at 0–5°. The advantage of a slight angulation on the direct vision lens is easier and quicker visualization of working instruments being passed out of the tip, reducing the potential for inadvertent iatrogenic injury to normal urothelium. The “field of view” is often quoted for ureteroscopes and is the entire view seen by the eye when it is trained in any particular direction. For endoscopes, this can vary from 60° to 90°, depending on the type of instrument.

Ureteroscopes had a standard eyepiece design, which sees the ocular lens drawn in a straight line through the shaft of the scope (Figure 39.2). When rigid ultrasound probes were first introduced for ureteroscopic lithotripsy, an offset ocular configuration was trialed that allowed for direct access to the instrumentation port, allowing easy entry and removal of rigid accessories without impairing the view of the scope.

#### Dimensions and sheath tip

From the earliest days of ureteroscopic evolution, the diameter of the rigid scope has come down from 16 Fr to 8.5 Fr, while the length of the scope ranges from 25 to 54 cm, allowing the ureter and renal pelvis to be accessed. Early ureteroscopes had beaked tips emulating early cystoscopes, which could result in ploughing of the ureteral epithelium. This was replaced with the current beveled tip designs to provide safer and easier advancement into the ureter (Figure 39.3).

#### Working channel

The single channel in most rigid ureteroscopes varied in size from 3.5 to 5 Fr, a range dictated by the size of the largest of instruments available at the time. The working channel was triangular in cross-section and allowed irrigation to continue around the sides of any deployed instrument within. Ureteroresectoscopes incorporated manually working elements much like standard transurethral resectoscopes. Working elements included resecting loops, cold and hot knife blades, and fulguration electrodes.

## Semirigid ureteroscopes

#### Endoscopic evolution

Developed in the early 1980s, the Rigiflex ureteroscope by ACMI had a straightened eyepiece for introducing the scope into the ureter and later offset to admit the ultrasonic lithotripter. The ACMI HTO-5 was unique in being the first ureteroscope to incorporate fiber-optic imaging technology to produce the flexible “gooseneck” eyepiece. Although the scope had a 12.7 Fr diameter shaft and a 5 Fr single working channel, comparable rod–lens ureteroscopes of the time with a 5 Fr channel were 14.5–15 Fr in size.

Ureterorenoscopy with a rigid scope still had inherent problems with the rod–lens optics due to the tortuous nature of the ureter and the caliber and working length of the instrument, which gave impaired vision. With the growing demand for rigid ureteroscopes in the 1980s, the further use of fiber-optic technology enabled further miniaturization of the shaft diameter along with reduction in size of the working channels. The “miniscope” or semirigid ureteroscope combined smaller working channels and fiber-optics, allowing both illumination and image incorporated into a metal sheath. The optical system was reduced in size compared with the rod–lens design, leading to its primary advantage, an overall reduction in the outside diameter of the scope, but not at the expense of reducing the size of the working channels.

Although the rigid rod–lens system provided excellent optical quality, an additional advantage of the miniscope was that the fiber-optic bundles within the metal shaft could be flexed significantly without distortion of the image and the appearance of a dark crescent-shaped area that can occur with excessive torque applied to the rod–lens telescope. Such flexibility allows easier passage of the scope through the intramural ureter and then anteriorly over the iliac vessels with great maneuverability to negotiate narrowed or strictured ureters. Other advantages of the miniscope included easier access, reduced requirement for ureteric dilation, and decreased ureteric injury.

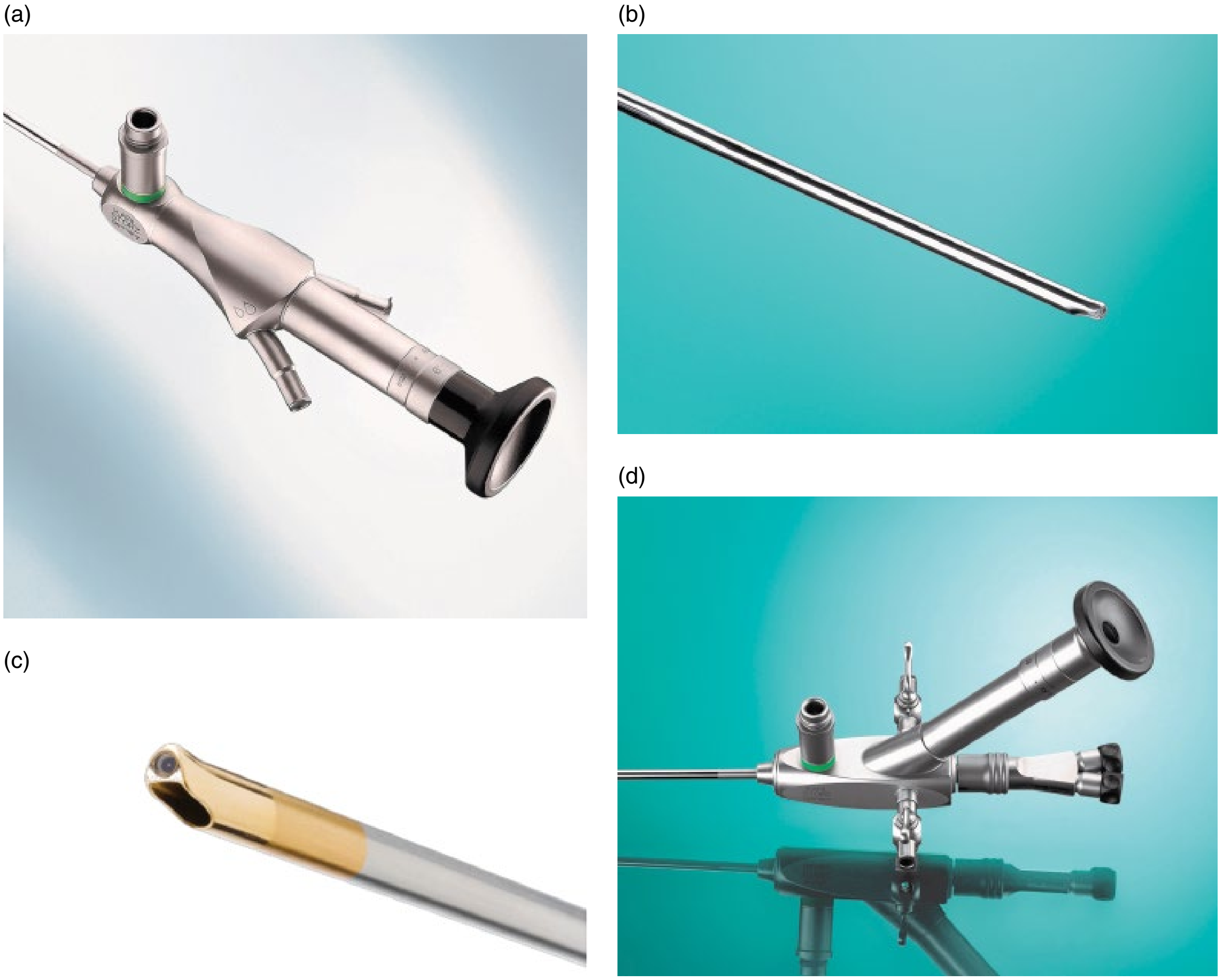

**Figure 39.2** The Storz (a, b) and Olympus (c, d) series demonstrates the available eyepiece designs. These facilitate both easy insertion under direct vision with the (a,c) standard design, as well as the ability to use the straight rigid accessories in comfort with the (b, d) oblique offset designs. *Source:* (a, b) Karl Storz GmbH & Co. KG, Germany. (c, d) Olympus Medical, UK. Reproduced with permission of Karl Storz GmbH (a, b) and Olympus UK (c, d).

The first available "miniscope" was Candela Laser Corporation's semirigid ureteroscope, as described by Dretler and Cho in 1989 [14]. It was the first to incorporate two independent working channels, one for an accessory and one for flow, each of 2.1 Fr size. It was the success of this 41 cm instrument with a 7.2 Fr distal section that established it as the benchmark instrument of its time and prompted other US manufacturers to develop competitive instruments of similar design, such as the MR-6 ureteroscope from ACMI. The MR-6 proved to be much more durable than the Candela scope and quickly gained supremacy [15]. It had a sub-7 Fr distal section with larger throughput capacity of one 2.3 Fr and one 3.4 Fr device in separate channels. The final distal shape was determined by enclosing the smallest size optical system the engineers could conceive at the time, along with the two separate throughput channels in a triangular-shaped outer tube, giving a 6.9 Fr distal section. For the image system, by designing a conventional glass objective coupled to a 0.5 mm diameter fused quartz fiber bundle, more individual pixels of optical information were provided than the etched glass fiber bundle in either the Candela or the HTO-5 scopes. It came in a short 33 cm length version to allow access to the distal ureter and up to the ureteropelvic junction (UPJ) of females. The MR-6L was 41 cm long and was intended for use primarily in males and obese patients. Over the past decade, mini-ureterosopes or semirigid ureteroscopes have been refined in terms of materials, ergonomic layout, fiber-optics, and camera systems,

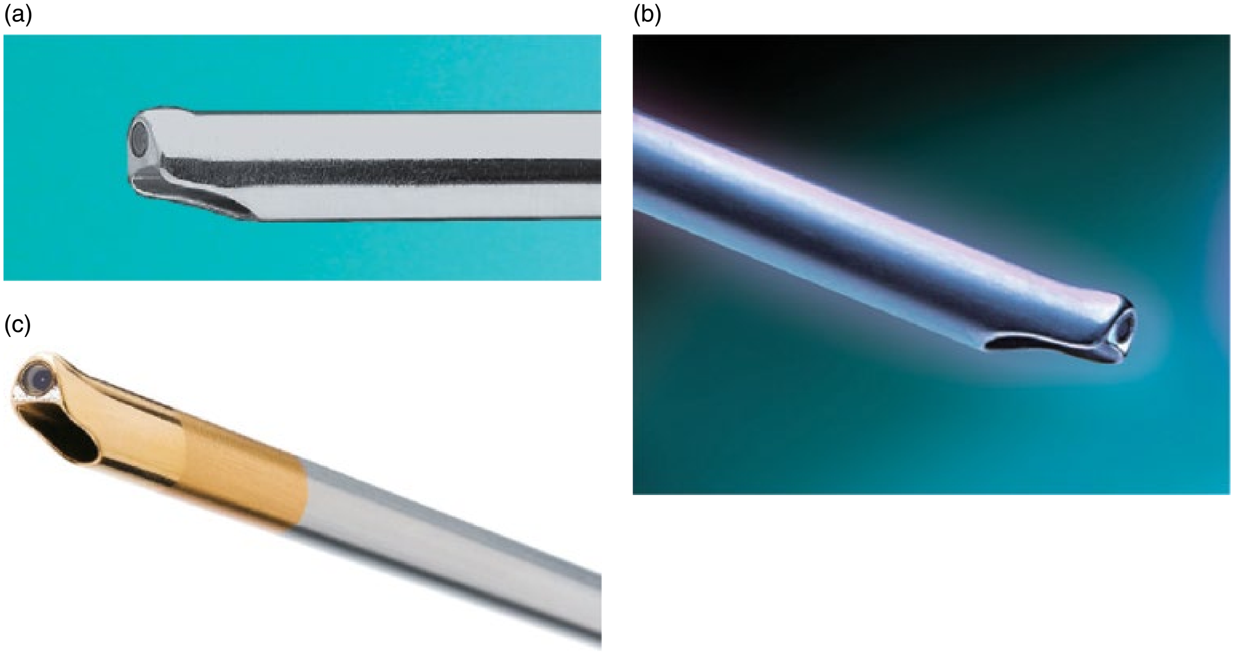

**Figure 39.3** Ureteroscope atraumatic distal tip. The tips generally come beaked, beveled, or flat, as each manufacturer argues a case for easier atraumatic negotiation of the ureteric orifice. *Source:* Karl Storz GmbH & Co. KG, Germany and Olympus Medical, UK. Reproduced with permission of Karl Storz GmbH and Olympus, UK.

though there have been no significant steps forward in scope evolution. They remain the most commonly used type of ureteroscope [16].

### Optics and eyepiece

In practice, the rod–lens ureteroscope offers quality images, but allows only limited vertical deviation on advancement and is suited in ureters that require only minimal change in direction. The introduction of fiber-optic bundles within a rigid shaft has enabled navigation through the more challenging tortuous ureter without leading to optical malfunction. Although earlier fiber-optic image bundles were disadvantaged by a characteristic graining effect, the pixel density in most current semirigid ureteroscopes has now increased beyond 30 000, such that the images are large and bright and are much closer in quality and size to those of the traditional rod–lens system. Newer fiber-packing techniques and advanced camera systems have led to further improvement. Fiber-optic systems now provide light and image transmission through most current semirigid ureteroscopes.

As discussed earlier, offset eyepieces became necessary when rigid ultrasound probes were developed for ureteroscopic lithotripsy. These probes, as well as larger, more rigid working instruments, required a straight working channel for passage through the scope. Offset eyepieces can either be fixed or moveable and can be either angled or offset, although always straight and parallel to the ureteroscope shaft. The angle of view is usually 0–5°.

### Dimensions and sheath tip

It is important for ureteroscopic design and procedural success that the scope is narrow and flexible enough to deal with the changing caliber of the ureter, with areas of natural lumen reduction at the UPJ, iliac vessels (12 Fr), and vesicoureteric junction (3–10 Fr), along with potential pathologic narrowing. Instrument manufacturers have made attempts to reduce the trauma of insertion by modifying shaft design. The mini-ureteroscope shaft has a graduated stepped design, starting with a distal tip diameter as small as 6.9 Fr [15], rising up to 13 Fr in the larger scopes. This ensures maximal proximal strength of the scope while providing a gradual dilation of the ureter as the scope is advanced. The continued reduction in ureteroscope diameter has led to a reduction in the number of ureteral strictures seen and an increased success rate for the procedure [17]. Furthermore, the profile of the semirigid ureteroscope beveled tip is designed to ensure minimal iatrogenic damage to the ureteric orifice and urothelium while maximizing the successful passage of the ureteroscope into the ureter (see Figure 39.3). The semirigid ureteroscope is generally manufactured in two lengths. A “short” ureteroscope of just over 30 cm can be used to access up to the level of the mid ureter in males and renal pelvis in females. To reach the renal pelvis in a male requires a “long” ureteroscope of 40 cm or more.

#### Working channel

Advances in construction of the miniscope led to the option of either a larger diameter single working channel with one large space for both irrigation and instrumentation to run through, or two separate working channels allowing separate instrumentation and irrigation. A larger single channel permits the use of larger instruments and possible removal of small stone fragments or biopsy specimens through the sheath, and dual instrumentation depending on the limits of each channel port. Two separate channels allow the operator to work through one channel without impeding irrigation flow through the other. The diameters of the two separate working channels range from 2.1 to 5.4 Fr, but are usually 3.4 Fr, allowing the introduction of a more rigid 3 Fr instrument and 2.4 Fr for irrigation or a second accessory. The channels are either triangular or oval in cross-section, which allows irrigation to continue around the sides despite the placement of an accessory instrument.

The introduction of holmium laser lithotripsy for the treatment of upper urinary tract stone disease in 1996 [18] was a revolutionary leap forward in endoscopic stone treatment, and is now the bedrock of contact lithotripsy in most departments. With fiber diameter measuring only 200 and 365 μm, this has virtually abolished the requirement for anything larger than a 3.4 Fr channel, allowing smaller outer diameter ureteroscopes to be used with better flow and therefore better vision. The narrow lasers also allow them to be used simultaneously with another accessory down a working channel, while still maintaining some flow.

#### Camera and video systems

Image transmission has evolved in line with changes seen with the semirigid ureteroscopes. Although images are occasionally viewed directly from the eyepiece due to technical problems or, rarely, the surgeon's preference, it has been conventional for some years to use indirect imaging on a television monitor using a video system. The video camera and monitor-based endoscopes allows binocular vision that is projected onto a large television monitor; this is ergonomically easier for the urologist and also can be enjoyed by the theater team. The high-resolution image output has also reduced the discrepancy between the better images obtained with the larger endoscopes compared with those previously seen with the ureteroscope.

Analog images produced by transmission down fiberoptic bundles continue to be the main pathway to deliver views of the subject matter to the camera in the majority of semirigid ureteroscopes. The drive to engineer semirigid ureteroscopes with digital distal sensor chip technology to produce high-quality digital images has not yet taken off to the same degree as seen with the flexible scopes. This is partly due to the high density of fiber-optic bundles that can be incorporated into the semirigid ureteroscope, which are more resistant to image degradation when compared to those found in the flexible ureterorenoscope. Olympus produce the only digital semirigid ureteroscope, called the EndoEye video ureteroscope (also known as the Oes Pro Video), which has a distal charge-coupled device (CCD) video chip (see Table 39.3).

#### Irrigation

An effective irrigation system is important to optimize the chance of access into the ureteric orifice and provide good visibility during either rigid or flexible ureteroscopy. The simplest arrangement involves gravity irrigation, which has to contend with the small diameter and long length of the ureteroscope, causing a reduction in flow. Other configurations are available that generate a greater pressure and therefore flow, with the pneumatic sleeve applied around the bag of fluid being the most common semi-automated setup. Devices requiring operator/assistant input to supply increased flow on demand include attaching two 60 ml syringes via a Y-connector to inject irrigation as needed, and the Peditrol irrigation device that delivers a bolus via a foot pedal [19]. Automated infusion systems offering continuous saline irrigation, such as the Ureteromat, also exist which require no input from the endoscopist. The more recent continuous-flow ureterorenoscope (10.5 Fr) promises to provide a 100 times higher flow capacity while preserving the intrarenal pressure compared with conventional ureteroscopy *ex vivo* [20].

## Current ureteroscopes

Rigid ureteroscopes are available in many of the designs previously described. The characteristics of the latest designs of currently available semirigid ureteroscopes are given in Table 39.3.

### Care, maintenance, and technical failure

An important consideration when weighing up the purchase of a new ureteroscope is its longevity, and there is often a balance to be sought between optimal duration of scope life and its efficacy. Although less of a problem with the semirigid ureteroscope in comparison with its flexible counterpart, applying excessive torque causing deflections over 5 cm can lead to significant image distortion and scope failure. The majority of ureteroscopic failures are attributed to iatrogenic causes, including improper handling at the time of instrumentation and problems during the sterilizing process [21]. Regardless of the type and make of ureteroscope, the frequency of

**Table 39.3** Specifications of currently available semirigid ureteroscopes.

| Model | Eyepiece | Field of view (degrees) | Diameter (Fr) | Length (mm) | Sheath construction | Tip style | Angle of view (degrees) | Working channels | Channel size (Fr) |
|---|---|---|---|---|---|---|---|---|---|
| **Olympus Gyrus – ACMI** | | | | | | | | | |
| MR-6A Bagley | Straight | 65 ± 5 | 6.9–10.2 | 330 | Stepwise | Beveled | 5 | 2 | 3.4 + 2.3 |
| MR-6LA Bagley | Straight | 65 ± 5 | 6.9–10.2 | 330, 410 | Stepwise | Beveled | 5 | 2 | 3.4 + 2.3 |
| MRO-733A | Angled | 61 | 7.7–10.8 | 330 | Stepless | Beveled cutaway | 5 | 1 | 5.4 |
| MRO-742A | Angled | 61 | 7.0–11.2 | 420 | Stepless | Beveled cutaway | 5 | 1 | 5.4 |
| **Olympus** | | | | | | | | | |
| OES Pro Single | Straight | 90 | 6.4–7.8 | 330, 430 | Stepless | Beaked | 7 | 1 | 4.2 |
| | Angled | 90 | 6.4–7.8 | 330, 430 | Stepless | Beaked | 7 | 1 | 4.2 |
| | Angled | 95 | 8.6–9.8 | 430 | Stepless | Beaked | 7 | 1 | 6.4 |
| | Flexible | 90 | 6.4–7.8 | 430 | Stepless | Beaked | 7 | 1 | 4.2 |
| | Flexible | 90 | 8.6–9.8 | 430 | Stepless | Beaked | 7 | 1 | 4.2 |
| OES 4000 Double | Straight | 90 | 7.5 | 430 | Flat | None | 7 | 2 | 3.4 + 2.4 |
| | Angled | 90 | 7.5 | 330, 430 | Flat | None | 7 | 2 | 3.4 + 2.4 |
| EndoEYE Video | Angled | 95 | 8.5 | 430 | Flat | Beaked | 7 | 1 | 4.2 |
| **Karl Storz** | | | | | | | | | |
| 27000 LK/KK | Angled | – | 6.5–9.9 | 340, 430 | Stepwise | Beaked | 6 | 1 | 4.8 |
| 27001 LK/KK | Angled | – | 7.0–12 | 340, 430 | Stepwise | Beaked | 6 | 1 | 5.0 |
| 27002LK/KK | Angled | – | 8.0–12 | 340, 430 | Stepwise | Beaked | 6 | 1 | 5.0 |
| 27003 LK | Angled | – | 9.0–12 | 340, 430 | Stepwise | Beaked | 6 | 2 | 3.0 |
| 27010 LK/KK | Straight | – | 7.0–9.9 | 340, 430 | Stepwise | Flat | 6 | 2 | 3.4 |
| 27011 K/L | Straight | – | 7.0–13.5 | 340, 430 | Stepwise | Beaked | 6 | 1 | 5.0 |
| 27012 K/L | Straight | – | 8.0–13.5 | 340, 430 | Stepwise | Beaked | 6 | 1 | 6.0 |
| 27013 LK | Straight | - | 7.0–13.5 | 340, 430 | Stepwise | Flat | 6 | 1 | 5.0 |
| 27014 K/L | Remote | – | 9.0–15.0 | 340, 430 | Stepwise | Beaked | 6 | 1 | 5.0 |
| **Stryker** | | | | | | | | | |
| SRU-6X | Standard | – | 6.9–10 | 430, 330 | Stepless | Flat | 6 | 2 | 3.4 + 2.5 |
| **Richard Wolf** | | | | | | | | | |
| 8702 (.517, .518) | Straight | 90 | 6.0–7.5 | 330, 430 | Stepless | Beaked | 5 | 1 | 4.0 |
| 8703 (.517, .518) | Straight | 95 | 8.0–9.8 | 330, 430 | Stepless | Beaked | 12 | 1 | 5.0 |
| 8708 (.517, .518) | Straight | 90 | 6.5–8.5 | 330, 430 | Stepless | Beaked | 5 | 2 | 4.2 and 2.55 |
| 8702 (.523, .524) | Oblique | 90 | 6.0–7.5 | 315, 430 | Stepless | Beaked | 5 | 1 | 4.0 |
| 8703 (.523, .524) | Oblique | 95 | 8.0–9.8 | 315, 430 | Stepless | Beaked | 12 | 1 | 5.0 |
| 8704 (.523, .524) | Oblique | 95 | 8.5–11.5 | 315, 430 | Stepless | Beaked | 12 | 1 | 6.0 |
| 8701 (.533, .534) | Lateral | 95 | 4.5–6.5 | 315, 430 | Stepless | Beaked | 5 | 1 | 3.0 |
| 8702 (.533, .534) | Lateral | 90 | 6.0–7.5 | 315, 430 | Stepless | Beaked | 5 | 1 | 4.0 |
| 8703 (.533, .534) | Lateral | 95 | 8.0–9.8 | 315, 430 | Stepless | Beaked | 12 | 1 | 5.0 |
| 8708 (.533, .534) | Lateral | 90 | 6.5–8.5 | 315, 430 | Stepless | Beaked | 5 | 2 | 4.2 and 2.55 |

repair increases with decreasing ureteroscope diameter and increasing length of instrument [22]. Previously, with stepped shaft design of the rigid ureteroscope, bend stress was concentrated at solder points. Newer tapered shafts were produced to reduce this problem, making them more durable and less traumatic. Other notable risk factors for predicting the number of uses expected from a ureteroscope are its age and whether the ureteroscope has undergone comprehensive repair as a result of prior damage [21]. For optimal scope life, it is important that optimal care is taken in looking after the instrument and cleaning procedures are carried out with strict adherence to company instructions.

## Future trends

The digital video endoscope is now here to stay and the endless possibilities using this technology are just starting to be realized. With further improvements in materials and endoscope design, the ability of the endourologist of tomorrow to diagnose and treat pathologic conditions affecting the urinary tract will continue to improve. It will not be long before all major endoscope manufacturers produce a distal sensor ureteroscope, and the endoscope of the future, whether rigid or flexible, will contain no viewing lens component. Further progress in digital technology will ensure further reductions in shaft diameter and the addition of increased functions, including wireless transmission of images to high-definition PC monitors, and potentially portable ureterorenoscopes. It remains to be seen whether these changes will result in improved durability.

### Three-dimensional ureteroscopy

Current endoscopic systems provide an image output in two dimensions with stereoscopic or three-dimensional (3D) imaging existing only in the domain of robotic and, rarely, laparoscopic surgery. With miniaturization of the CCD chips and future reduction in the cost of this technology, positioning two of them in the distal tip of the scope would enable stereoscopic images to be created with true depth perception. The advantages of 3D imaging during ureteroscopic procedures however, have not been confirmed and the additional costs may not be offset if the benefits prove to be small.

### Virtual ureteroscopy

The use of virtual endoscopy for computer-driven reconstruction has been applied to multiple sites in the human body where there is a hollow viscus, including the renal collecting system and ureter [23, 24]. Although it is early days for this technology, this technique may prove to be useful as a noninvasive way of surveilling the urinary tract.

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# Flexible Ureteroscopes

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## History and evolution

The flexible ureteroscope is a versatile and ever-improving instrument utilized by many urologists. As the technology of flexible ureteroscopes improves, the indications for which it is used increase, pushing the boundaries of its capabilities and paving the way for further innovation. Due to cost concerns relating to the fragility of these endoscopes, manufacturers have recently endeavored to produce less expensive, disposable versions of these highly technologically advanced instruments [1–4]. In response to ergonomics and operator use concerns, manufacturers have also developed remote operator/robotic platforms for use with flexible ureteroscopes [5–7]. These latter ideas are now being clinically tested for feasibility and practicality.

The history of the evolution of flexible ureteroscopes involves many aspects of engineering, evolving technologies, and issues that relate to their practical clinical use. Although many of the technologies and earlier models of flexible ureteroscopes discussed herein are no longer in regular use in many parts of the world, an understanding of their working paradigms is critical to understanding proper and most effective use, possibilities and limitations, and risk for damage that can occur.

## Components

All flexible ureteroscopes require a number of key components. Similar to all rigid ureteroscopes, flexible ureteroscopes require a mechanism for optics, lighting, irrigation, and channels for passage of instruments, all of which need to be configured within a small-diameter shaft in order to traverse the narrow ureter. Flexible ureteroscopes also require an ability to manipulate the direction of the distal tip in order to negotiate the course of the ureter, renal pelvis, and calyces. Another requirement for these fragile instruments was demonstration of durability, including the ability to withstand repetitive extensive torqueing as well as sterilization and processing. As outlined in the ensuing discussion, it will become evident as to how modern flexible ureteroscopes have evolved, and continue to evolve, through sequential generations of design and function to optimize their function, control, and ability within the smallest diameter shaft allowable.

## Optics and illumination

To design a flexible ureteroscope that can fully navigate the ureter and its nonlinear and often tortuous anatomy, as well as the renal pelvis and its calyces, the ureteroscope must be flexible with an ability to bend extensively without significant compromise in function, have the ability to manipulate the direction of its distal tip by the operator, transmit sufficient light to the operative site, and transmit the image of the operative site to the operator in a highly reliable manner. The application of fiber-optics was critical to the development of a flexible ureteroscope, as fiber-optics enabled the transmission of imaging as well as the transmission of light across a medium that could bend, twist, and turn. Although current production of flexible ureteroscopes is focused on digital technology, fiber-optic ureteroscopes are still in use today and are an integral part of the history and understanding of their evolution.

Fiber-optic flexible ureteroscopes are made up of bundles of individual fibers in parallel sequence. The image

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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at the distal end of the fiber-optic is transmitted via the fiber to the proximal end with identical perception and orientation. The fibers make up a composite of the image on a whole and thus give a honeycomb appearance to the final image, also known as the Moiré effect, due to the arrangement of the bundle of fiber-optics (Figure 40.1). This final image is seen through an eyepiece and can be observed with the naked eye through a lens or transmitted to a television or computer screen via a camera. Fiber-optics are also used to transmit light from the proximal end of the scope to the distal end in a similar fashion, thus illuminating the working field. Due to the flexible nature of these bundles of fibers, the ureteroscope is able to bend and turn without altering the image or lighting quality. Nonetheless, the image quality of even the most modern fiber-optic ureteroscopes remains inferior when compared to the rod–lens system of rigid ureteroscopes [8]. To improve the quality of the image with a flexible ureteroscope, the number and diameter of the fiber-optics must be increased. However, this leads to an increase in diameter of the shaft of the ureteroscope, limiting its ability to access the upper urinary tract, its flexibility, and size of irrigation and working channels [9, 10].

The fiber-optics within ureteroscopes produce an image that is “grainy” with regard to clarity because of the Moiré effect. These fibers are also disposed to fracturing with wear and tear, and water can leak into the lens, compromising image quality (Figure 40.1) [11]. Thus, even though the inclusion of fiber-optics was critical in the development of flexible ureteroscopes, it also contained inherent engineering limitations.

## Digital flexible ureteroscopes

More recently, digital imaging systems have been introduced into the design of flexible ureteroscopes. Charge-coupled devices (CCD) and complementary metal-oxide semiconductor (CMOS) sensors were first used on the cameras mounted to the lenses of fiber-optic flexible ureteroscopes, aptly referred to as “chip-on-the-tip” technology, allowing transmission of images in digital format, leading to a crisper and cleaner image compared to analog video. Within the last few years, however, there has been significant miniaturization of this technology. Now the CCD and CMOS sensors are small and powerful enough to be placed at the distal tip of the flexible ureteroscope, obviating the need for any fiber-optics. Rather than using an external light source which is transmitted via fiber-optics, these ureteroscopes use light-emitting diodes present at the tip to provide a light source. The image transmitted through the distal lens is then processed either at the tip of the ureteroscope or within a remote device prior to being transmitted and projected on a monitor. With the removal of the fiber-optic components, the flexible ureteroscope was transformed, resulting in improvement of image quality and weight. However, the diameters of these digital ureteroscopes have not matched those of their fiber-optic counterparts (Table 40.1).

Digital ureteroscopes were also found to have better illumination and resolution than fiber-optic flexible ureteroscopes, as well as an ability to digitally magnify images up to 1.35 times their original size (Figure 40.2) [11]. With the ability to house the image processing and

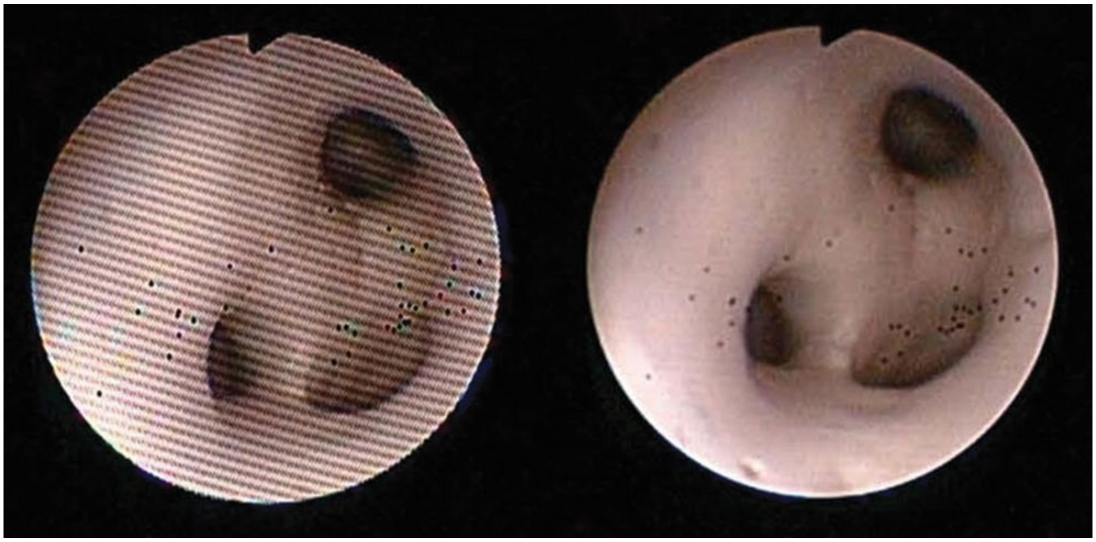

**Figure 40.1** Image through a fiber-optic ureteroscope showing Moiré effect (left) and image after Moiré filtering (right). Note that a number of fibers are broken, leading to dark spots. *Source*: Olympus America Inc. Reproduced with permission of Olympus America Inc.

**Table 40.1** Flexible ureteroscope specifications (as provided by manufacturers).

| Manufacturer | Optics | Model | Working length (cm) | Distal tip (Fr) | Proximal shaft (Fr) | Deflection up | Deflection down | Active 2° | Working channel diameter (Fr) |
|---|---|---|---|---|---|---|---|---|---|
| **Reusable** | | | | | | | | | |
| Gyrus ACMI[a] | Fiber-optic | DUR-8 Elite | 64 | 6.75 | 9.4 | 170 | 180/130 | Y | 3.6 |
| | | DUR-8 Ultra | 67.5 | 8.6 | 9.3 | 270 | 270 | N | 3.6 |
| | Digital | DUR-D® Invisio® | 65 | 8.7 | 9.3 | 250 | 250 | N | 3.6 |
| Olympus[b] | Fiber-optic | URF P5 | 70 | 8.4 | 8.4 | 180 | 275 | N | 3.6 |
| | | URF P6 | 67 | 7.0 | 7.95 | 275 | 275 | N | 3.6 |
| | Digital | URF V1 | 67 | 8.5 | 9.9 | 180 | 270 | N | 3.6 |
| | | URF V2 | 67 | 8.5 | 8.4 | 275 | 275 | N | 3.6 |
| Storz[c] | Fiber-optic | Flex X | 67.5 | 7.5 | 8.4 | 120 | 170 | N | 3.6 |
| | | Flex-X2 | 67.5 | 7.5 | 8.5 | 270 | 270 | N | 3.6 |
| | Digital | Flex-Xc | 70 | 8.4 | 8.4 | 270 | 270 | N | 3.6 |
| Stryker[d] | Fiber-optic | U500 D | 64 | 6.9 | 6.9 | 275 | 275 | N | 3.6 |
| | Digital | URT 7000S/7000Si | 65 | 9.6 | 9.6 | 240 | 190 | N | 3.6 |
| Wolf[e] | Fiber-optic | Viper | 68 | 6.0 | 8.8 | 270 | 270 | N | 3.6 |
| | | Cobra | 68 | 6.0 | 9.9 | 270 | 270 | N | 3.6/2.4 |
| | Digital | Boa | 67 | 8.5 | 9.5 | 270 | 270 | N | 3.6 |
| **Disposable** | | | | | | | | | |
| Boston Scientific[f] | Digital | LithoVue™ | 68 | 7.7 | 9.5 | 270 | 270 | N | 3.6 |
| Lumenis[g] | Digital | PolyScope® | 70 | 9.6 | 8.0 | 270 | | N | 3.6 |
| Maxiflex[h] | Digital | SemiFlex Scope™ | 65 | 8.3 | 8.3 | 270 | 270 | N | 3.4 |

[a] Gyrus ACMI (Gyrus ACMI is now a business division of Olympus).
[b] Olympus Surgical, Orangeburg, NY, USA.
[c] Karl Storz, Tuttlingen, Germany.
[d] Stryker® Endoscopy, San Jose, CA, USA.
[e] Richard Wolf Endoscopy, Vernon Hills, IL, USA.
[f] Boston Scientific, Marlborough, MA, USA.
[g] Lumenis®, Santa Clara, CA, USA.
[h] Maxiflex™ New Orleans, LA, USA.

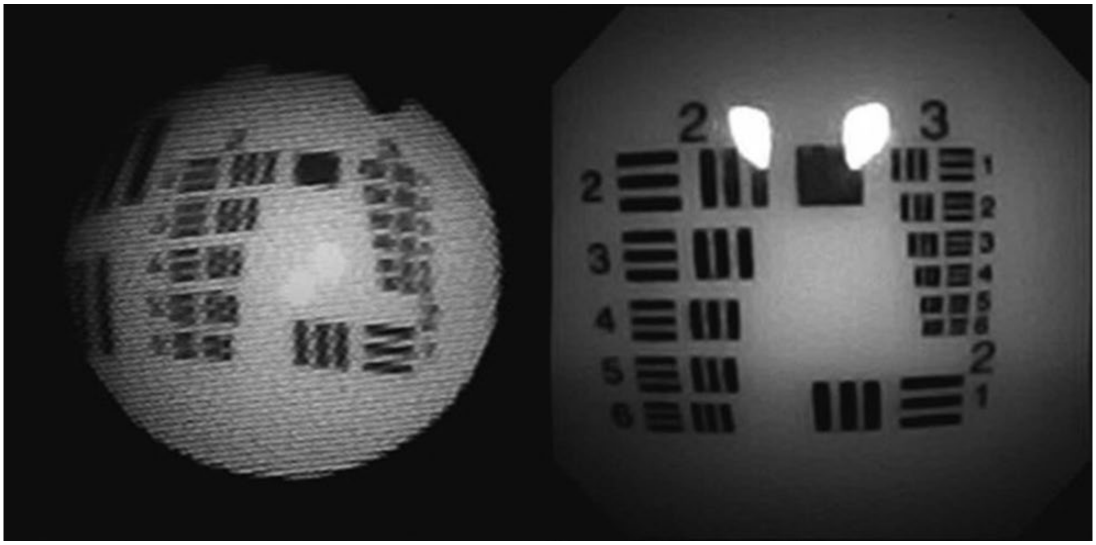

**Figure 40.2** Photographs comparing fiber-optic image of DUR-8 (left) with digital image from DUR-D (right) [11]. *Source*: Andonian S, Okeke Z, and Smith AD. Digital ureteroscopy: the next step. *J Endourol* 2008;22:603–606. Reproduced with permission of Mary Ann Liebert, Inc. publishers.

lighting within one unit, this reduced potential for water leakage into the unit, possible burns from an unattended light source, and number of cables from the unit [11].

## Flexion and deflection

Early flexible ureteroscopes were only capable of passive deflection and were limited in their ability to fully navigate the urinary tract [12]. With improvements, lever/pulley mechanisms were introduced, allowing flexion and deflection of the distal end of the endoscope. The degree of flexion/deflection depends on the configuration and capacity of the optic and illuminating components, as well as the irrigating and working channels within the shaft. This movement is further limited when an instrument such as a laser fiber or basket is introduced into the working channel. In early designs, ureteroscopes relied on both active and passive deflection such that in order to access the lower pole of the kidney, the operator could maximally deflect the tip of the ureteroscope and then, by advancing the ureteroscope further, cause passive secondary deflection by buckling slightly more proximal along the shaft [13]. With constant improvements, the deflection capabilities of ureteroscopes have improved dramatically, reaching as high as 275° for some currently available scopes (see Table 40.1). Deflection is reduced by varying degrees depending on the size and shape of the instruments passed through the working channels, with a resulting variability of impedance upon deflection by a variety of ancillary devices (Figure 40.3), as discussed later in this chapter.

## Irrigation and working channels

The last necessary feature for a flexible ureteroscope is a working and/or irrigation channel. This allows for irrigation of fluid to maintain patency and visualization of the collecting system while passing the ureteroscope through the upper urinary tract [12]. With the development of smaller optics at the distal tip, manufacturers were able

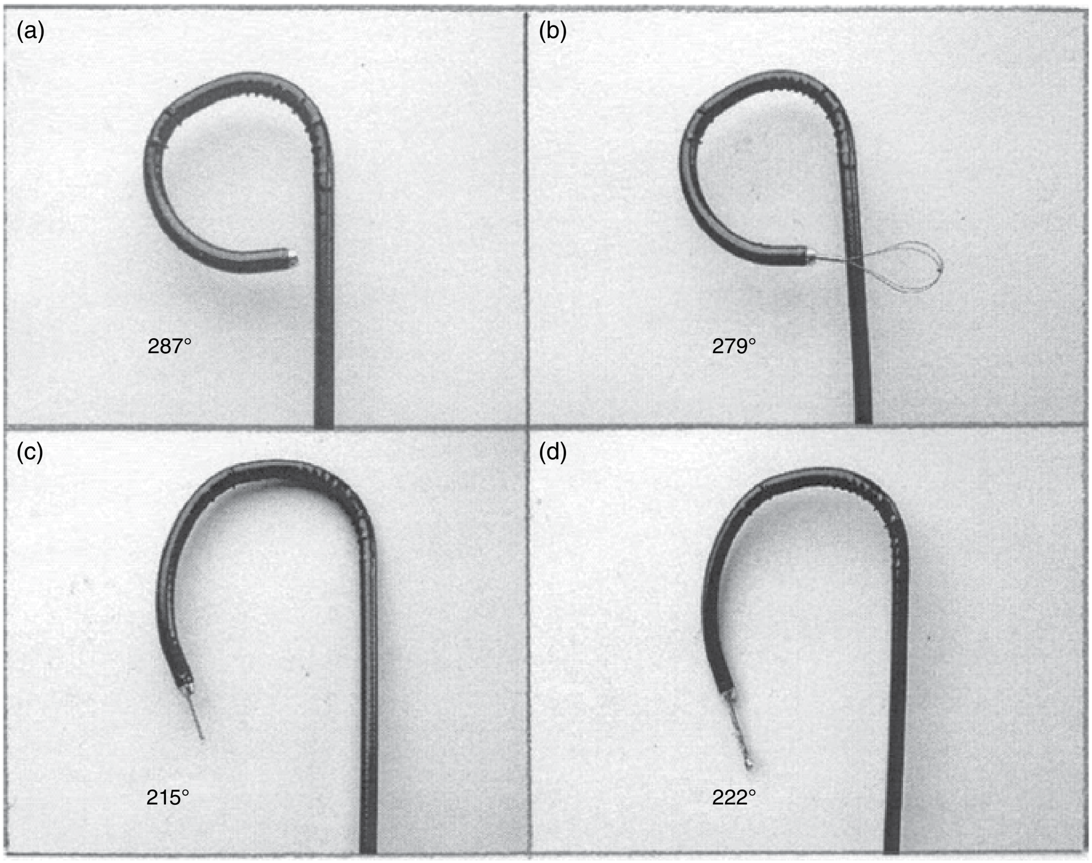

**Figure 40.3** Maximal deflection of distal tip of the DUR-8 Elite flexible ureteroscope with different endoscopic instruments in working channel [14]. (a) Channel empty; (b) 3 Fr nitinol stone basket; (c) 365 μm laser fiber; (d) 3 Fr biopsy forceps. *Source*: Chiu KY, Cai Y, Marcovich R et al. Are new-generation flexible ureteroscopes better than their predecessors? *BJU Int* 2004;93(1):115–119. Reproduced with permission of John Wiley & Sons.

to place the aperture of the working channel in a less eccentrically placed position, ultimately closer to the center, allowing more central protrusion of a passed endoscopic instrument from the working channel.

In 2004, and from this point on, a large number of studies began to evaluate improvements or lack thereof with newer generation flexible ureteroscopes compared to their predecessors [14, 15]. Chiu et al. examined the DUR-8 Elite and the Storz 11278AU, comparing these endoscopes with their older models, DUR-8 and 11274AU, respectively. Their findings showed that the two newer models had considerably better deflection of the distal tip than their respective predecessors. The deflection of all ureteroscopes examined was reduced with insertion of varying endoscopic instruments, with the 3 Fr tipless nitinol stone basket (Cook, Spencer, IN, USA) having the least impact on reduction of deflection, and the 3 Fr biopsy forceps (Richard Wolf, Vernon Hills, IL, USA) having the greatest impact on limiting the degree of deflection (see Figure 40.3). The latest-generation Cobra ureteroscope by Wolf is the first flexible ureteroscope to incorporate two working channels (Figure 40.4) [16]. It contains a 3.6 Fr and 2.4 Fr working channel, allowing unimpeded irrigation when using an endoscopic instrument. The Cobra also comes equipped with a "laser shifter", an apparatus which allows the position of the laser to be locked with minute extension or retraction.

Working channels are subject to considerable wear and tear as they are exposed to the back and forth motion of endoscopic instruments of varying degrees of rigidity and abrasiveness. The working channel is often subjected to laser damage either from misfiring within the channel or collateral damage from the laser firing too close to the aperture at the tip of the scope. Storz has introduced a coating of the distal tip of the working channel with a ceramic compound called Laserite™. This material protects the instrument from thermal damage and reduces the risk of damage and need for repairs [13].

## Current flexible ureteroscopes

There are a number of commercially available digital and fiber-optic flexible ureteroscopes (see Table 40.1). These instruments are similar in construction but have notable differences in parameters such as shaft diameter, working channel diameter, and range of deflection. Although the image and lighting mechanisms of these new generation of flexible ureteroscopes are substantially different, their functional standards with regard to working channels, irrigation, flexibility, and durability remain similar to those of their fiber-optic ancestors. However, their shaft diameters have yet to achieve the smaller sizes seen in fiber-optic flexible ureteroscopes. As the standards continue to improve, competition to make incremental improvements in the core parameters of these endoscopes continues.

### Olympus Gyrus ACMI

The Gyrus ACMI DUR-8 Elite (Gyrus ACMI, now a business division of Olympus Surgical, Orangeburg, NY, USA) ureteroscope was the first ureteroscope to have two points of active deflection. The DUR-8 Elite also offered a Moiré reduction filter which aided in reducing the honeycomb/pixilation pattern secondary to the fiber-optic bundling (Figure 40.1). The DUR-8 Elite was succeeded by the DUR-8 Ultra which offered improvement in distal and proximal shaft size and range of deflection bidirectionally, but removal of the active secondary deflection mechanism. Of significant importance was the development in 2006 of the DUR-D®, the first commercially available digital flexible ureteroscope utilizing the "chip-on-the-tip" mechanism. Its imaging capabilities were superior to those of its fiber-optic counterparts (Figure 40.2), but its deflection was slightly reduced. Nonetheless, this was a milestone achievement for the evolution of flexible ureteroscopes as it set the standard for future digital ureteroscopes.

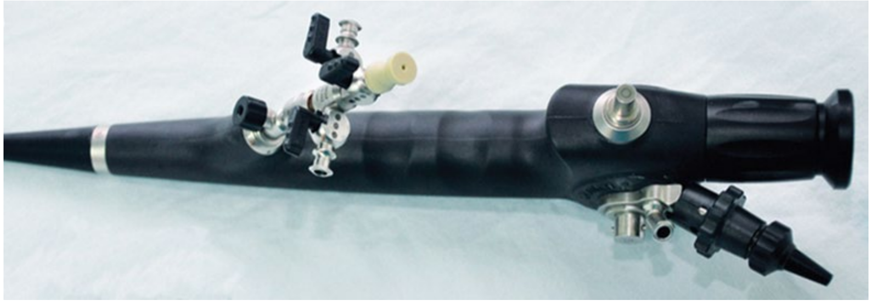

**Figure 40.4** Cobra dual-channel ureteroscope demonstrating two working channels with the laser advancement channel being of longer length and more proximal [16]. In this image, the thumb-operated "laser shifter" is visualized. *Source*: Geavlete P, Multescu R, and Geavlete B. Pushing the boundaries of ureteroscopy: current status and future perspectives. *Nat Rev Urol* 2014;11(7):373–382. Reproduced with permission of Macmillan Publishers Ltd.

In 2011, Gyrus ACMI was acquired by Olympus (Olympus Surgical, Orangeburg, NY, USA), who already had the URF-P5, offering a reduced size in diameter of the distal tip of 8.4 Fr. This was followed by the URF-P6 offering an even smaller diameter distal tip of 7.0 Fr, but also an increased range of flexion of 275° bidirectionally. Olympus has also since produced a new digital ureteroscope, the URF-V, but its specifications show a regression in design optimization with a distal tip diameter measuring 8.5 Fr and upward deflection of 180°. All working channels of the Gyrus ACMI as well as the Olympus ureteroscopes have maintained a dimension of 3.6 Fr.

### Storz

Karl Storz was one of the first manufacturers to bring the distal tip diameter to 7.5 Fr while maintaining a 3.6 Fr working channel (Karl Storz, Tuttlingen, Germany). Storz is also responsible for taking steps to reduce damage and repairs with the integration of Laserite™, giving added protection to the distal tip for thermal damage. The current Flex-X2 also boasts the ability to offer an intuitive or counterintuitive flexion/deflection lever system depending on the operator's preference. The Flex-Xc is the digital flexible ureteroscope offered by Storz. Similar to the digital ureteroscope offered by Olympus, the Flex-Xc distal tip measures 8.5 Fr compared to the 7.5 Fr distal tip offered by its Flex-X2 fiber-optic counterpart.

### Stryker®

Stryker offers the fiber-optic U500 and the digital URT-7000S/7000Si flexible ureteroscopes (Stryker Endoscopy, San Jose, CA, USA). The U-500 or Flexvision™ offers bidirectional flexion of 275° and is equipped with a dual secondary deflection and locking mechanism, allowing the operating hand to relieve strain while fully deflected. The Flexvision optic system is made up of high-density fiber bundles in order to optimize image quality. The URT-7000S/7000SI video ureteroscope utilizes "chip-on-the-tip" digital video technology, is capable of 240° of deflection, and comes equipped with a 3.6 Fr working channel.

### Wolf

The contributions of the Richard Wolf flexible ureteroscopes are of particular interest as the manufacturers have recently introduced the Cobra flexible ureteroscope with a dual working channel system (Figure 40.4). Initially, the channels were fitted to be both 3.3 Fr in diameter, however later models altered the size of these channels to 3.6 Fr and 2.4 Fr. The Cobra is capable of 270° bidirectional deflection like its Viper predecessor. Haberman et al. evaluated the single- and dual-channel Wolf fiber-optic ureteroscopes and found the dual-channel to have superior upward and downward deflection when compared to the single-channel model [17]. Wolf also manufactures a digital flexible ureteroscope, the Boa flexible ureteroscope, equipped with a 3.6 Fr working channel, bidirectional flexion of 270°, and a larger 8.5 Fr distal tip.

### Lumenis®

The standard paradigm of reusable flexible ureteroscopes has come into question, mostly due to their processing, high repair costs, and overall perceived cost effectiveness.

In light of these perceptions, Lumenis (Santa Clara, CA, USA) has manufactured the PolyScope®, a modular flexible ureteroscope. This consists of a single-use flexible multi-lumen catheter and a separate, reusable optical fiber consisting of a 10 000 pixel fiber-optic element. This endoscope is capable of tip deflection of 270° and has a working channel diameter of 3.6 Fr [2]. Yan et al. found that modular flexible ureteroscopy with holmium laser lithotripsy may be considered a feasible method for treatment of calculi with acceptable efficacy, low morbidity, and low maintenance costs [3]. Similar findings were found by Ma et al. and Ding et al. with their use of the PolyScope [4, 18].

### SemiFlex Scope™

Maxiflex™ (New Orleans, LA, USA) manufactures the SemiFlex Scope flexible ureteroscope, a disposable hybrid endoscope with a combination of a rigid proximal shaft and flexible distal shaft and equipped with a reusable eyepiece. This was one of the first ureteroscopes designed with disposability in mind and comes equipped with a 10 000 pixel optical bundle and lighting fiber as well as a 3.4 Fr working channel. It was found to have acceptable active tip deflection, field of view, and flow rate when compared to its reusable competitors [19].

### Boston Scientific

In early 2016, Boston Scientific (Marlborough, MA, USA) launched the first completely disposable digital flexible ureteroscope, the LithoVue™. This ureteroscope exhibits 270° bidirectional flexion, similar to its competitors, along with a 3.6 Fr working channel and 9.5 Fr outer diameter. The impetus for this approach involves the costs accrued due to damage, repairs, and sterilization of reusable flexible ureteroscopes, as well as the associated clinical implications. In a human cadaveric model, the LithoVue was compared with a nondisposable fiber-optic and digital flexible ureteroscope. It was reported that the LithoVue was comparable to this conventional ureteroscopes in terms of visibility and manipulation into the collecting system [1]. A unique feature of an entirely disposable flexible ureteroscope is the elimination of risk of potential transmission of microbial agents to patients via contaminated endoscopes, as has been noted with the use of endoscopes in other subspecialties [20].

## Maintenance, durability, and prevention of damage

Because of their size and components, flexible ureteroscopes are inherently fragile. They are also regularly exposed to repeated stress in the form of twisting and torqueing of the shaft in order to access difficult to reach calyces, repeated passage of laser fibers, baskets and graspers, high-energy explosions at the tip of the ureteroscope, accidental firing within the working channel, laser damage due to laser fiber fracturing, and intense heat and chemical exposure during sterilization. As flexible ureteroscopes have improved, with diminishing shaft diameters, larger and multiple working channels, and increased flexion, their clinical uses and roles have expanded, thus placing even further strain and higher demands on them and resulting in an increasing need for strength and durability.

It has been well documented that the costs involved in maintaining and repairing flexible ureteroscopes are significant and efforts must always be made to minimize instrument breakage [21]. Afane et al. were one of the first groups to evaluate the durability of flexible ureteroscopes, namely those less than 9 Fr in diameter [22]. The authors found that their endoscopes were sent for repair after an average of 6–15 uses, and cited the most common reason for endoscope repair as poor or complete loss of deflection while luminosity and irrigant flow remained relatively unchanged. In 2006, Carey et al. analyzed the frequency of ureteroscope damage at their tertiary care center and noted a number of important findings with regard to maintenance and cost [23]. The authors revealed that after initial damage has occurred, subsequent damage usually occurs more rapidly. They deduced that after a ureteroscope sustained major damage requiring repair, it may be more financially prudent to purchase a new ureteroscope as the cost of maintenance and repair after the initial repair increases significantly per case. They also found it to be more cost-effective for ureteroscopes to be processed and cleaned by dedicated professionals in the endoscopy suite, noting three potentially preventable incidents of damage requiring repair when the ureteroscope was sent for cleaning to a central processing unit. Lasselin et al. also found that significant damage to the fiber-optics occurred during endoscope disinfection [24]. Carey et al. further deduced that flexible ureteroscopes that have undergone comprehensive repair are extremely fragile, a factor which should be considered when purchasing a reusable ureteroscope [25]. Knudsen et al. examined the failure rate of DUR-D® Invisio® digital ureteroscopes over a 12-month period [26]. They found that a total of nine failures requiring endoscope repair occurred, seven of which were not covered under warranty; each repair cost US$6600. They noted that in five of the seven nonwarranty repairs, a damaged distal lens, resulting in flooding of the endoscope, was the main reason for repair.

Knudsen et al. evaluated the durability of four late model flexible fiber-optic ureteroscopes – the Wolf Viper, Olympus URF-P5, Gyrus ACMI DUR-8 Elite, and Stryker Flexvision U-500 – in a randomized prospective multi-institutional clinical trial [27]. They found no significant differences between the four endoscopes in terms of durability. The authors concluded that these newer generation flexible ureteroscopes remained fragile, although it appeared that a comparable degree of durability had been achieved in different scope manufacturers.

Digital flexible ureteroscopes have also been investigated in this regard. In 2009 Al-Qahtani et al. investigated the newer generation Olympus URF-V, used over the course of 60 cases, and noted loss of deflection, while subjective quality of the image remained the same [28]. The digital endoscopes used in this study have significantly different optical systems from those of the fiber-optic scopes in previous studies, and the mechanism for damage may follow a different pattern.

A number of general practices can improve scope durability, including following proposed recommendations for safe use and monitored training of new users [29]. In a recent analysis, Defidio et al. concluded that increased durability can be achieved by adopting a number of strict techniques including minimizing work undertaken with a fully deflected instrument, introduction of instruments through the working channel while maintaining the endoscope in a straight fashion, utilization of a laser catheter sleeve when using the 200 μm fiber, and, critical to their analysis, having a low-risk sterilization method such as Cidex® [30]. The authors duly note that a low-risk sterilization method may not be acceptable universally. In this respect, a study by Johnson et al. examined the effects of repeat sterilization with the Steris System 1® (Steris Corporation, Mentor, OH, USA) and the Sterrad® NX® (Johnson & Johnson, Langhorne, PA, USA) system on the Lumenis Polyscope, common sterilization methods that have been shown to be damaging to the optical properties of flexible ureteroscopes [31, 32]. They found the endoscopes to be durable after 100 cycles of sterilization. Muggeo et al. analyzed the cost of reprocessing flexible ureteroscopes using low-temperature sterilization for heat-sensitive ureteroscopes versus high-level disinfection [33]. They noted that low-temperature sterilization was more cost-effective on a microeconomic scale and also removed any theoretical risk of possible transmission of microorganisms.

As mentioned earlier, various mechanisms have been designed to protect scopes from laser-related thermal damage. One such mechanism is the protective sleeve fitted around laser fibers while in the working channel. Defidio et al. noted that use of the Cook laser catheter sleeve was a contributing factor in maintaining durability of flexible ureteroscopes [30]. Lusch et al. evaluated a similar device, the Scope Guardian Sheath (Mayumana, Netherlands), as well as ScopeSafe™ laser fibers. They found that the ScopeSafe fibers were effective in preventing working channel damage, with limited reduction in deflection and irrigation flow [34]. Chapman et al. showed a significant reduction in repair costs with the use of disposable laser fibers rather than reusable laser fibers, which can sustain microfractures along the fiber, leading to ureteroscope damage [35]. The authors state that although the individual cost of the disposable laser fiber is higher, this is offset by the decrease in damage to the endoscope and fewer repairs needed. Pietrow et al. also noted that their endoscopes averaged 27.5 uses before being sent for repair, suggesting that the advent and use of nitinol devices, ureteral access sheaths, and 200 μm laser fibers helped to lessen the strain placed upon the endoscope and thus minimize damage [36].

Another factor to be considered when trying to prolong the lifespan of flexible ureteroscopes is the utilization of ureteral access sheaths, as was shown by Multescu et al. [37]. It has also been found that performance of a pressure leak test following flexible ureteroscope use helped to identify damage early and avoid further damage, resulting in significant cost savings and reduction in downtime [38].

## Comparison of flexible ureteroscopes

Studies examining the capabilities and functions of flexible ureteroscopes generally focus on the main components discussed earlier: optics, flexion/deflection, and working/irrigation channels. Some further studies are also worthy of note, however. In 2008 Bach et al. evaluated, *in vitro*, five different flexible ureteroscopes and assessed the impact on deflection and irrigation flow with their working channels unloaded and loaded with various instruments [10]. The authors found similar results across all five examined ureteroscopes. They noted that deflection had no impact on irrigation flow when unloaded, and there was no impact seen on the maximum deflection when loaded with a tipless nitinol basket. The authors also noted that laser fibers and biopsy forceps limited maximum deflection, with biopsy forceps interfering with deflection more than laser fibers. Irrigation flow was also interrupted, with flow rates ranging from 62.24% to 99.1% for 1.5 Fr and 3.0 Fr instruments, respectively. Further studies have also investigated the use of smaller instruments in the working channel and their minimal impact on deflection and irrigation [39]. In 2011 Bach et al. examined the effect of instruments within the working channel and their impact on light transmission by measuring the time needed to irrigate clear an inked medium [40]. They noted that the Wolf Cobra, with its dual working channels, had the most rapid restoration of light, and the Olympus URF-P5 had the longest time needed for restoration of light, emphasizing the relationship between visualization and irrigation.

A number of studies have compared fiber-optic and digital ureteroscopes. They reveal that the digital scopes have superior resolution, with better image resolution and quality, and safety with regard to reduction of the fire hazard of xenon lights [11]. Multescu et al. in 2013 examined three different flexible ureteroscopes: the Storz Flex-Xc (digital), Olympus URF-V (digital), and the Wolf Cobra (fiber-optic) [41]. The authors noted a slight advantage with the Flex-Xc with regard to maneuverability, but overall the ureteroscopes performed similarly. The fiber-optic Cobra achieved a lower score for visibility compared to its digital counterparts, but offered adequate irrigation and subsequent visualization independent of the size of the accessory instruments used. This study also demonstrated further the impact of working devices used within the working channels and their effect on the capabilities of the ureteroscope. Lusch et al. compared the fiber-optic Storz Flex-X2 with the digital Flex-Xc, and found the digital Flex-Xc to have superior optics in clear and bloody fields and better illumination than the Flex-X2 [42]. The Flex-Xc also proved to have better overall deflection and better flow with or without accessory instruments in the working channel. A similar study by Zilberman et al. examined the digital Olympus URF-V flexible ureteroscope and compared it with the fiber-optic URF-P3, using an *in vitro* assessment of image resolution, distortion, color representation, grayscale imaging, field of view, and depth of view [43]. The digital ureteroscope was found to have a higher resolution with less distortion, and better color representation. Similar contrast was noted between the endoscopes. The digital ureteroscope produced a 5.3 times larger image and narrower field of view than the fiber-optic endoscope; the depth was not limited by the optics but rather by light for both endoscopes. Another study examining fiber-optic versus digital flexible ureteroscopes done by Somani et al. compared the Olympus

URF-V and the URF-P5 [44]. The authors noted the fiber-optic URF-P5 to have slightly less maneuverability than the digital URF-V, and the URF-V to have a reduced operative time, but overall the two endoscopes had comparable success rates. Shah et al. compared two flexible digital ureteroscopes in 2015, the CCD-based ACMI/Olympus DUR-D and the CMOD-based Olympus URF-V, and found the URF-V to offer better visibility and maneuverability [45]. Both scopes were found to have similar failure rates when compared to previous studies examining fiber-optic ureteroscopes. Improvements in general image quality were well noted with digital flexible ureteroscopes, which is not altogether surprising.

## Future directions and considerations

As flexible ureteroscopes continue to evolve, we see an expanding horizon of increasing technological possibilities both with flexible ureteroscopes as well as their ancillary devices. There is an increasing role developing for disposable flexible ureteroscopes and it is postulated that these disposable scopes may potentially decrease cost by employing them in cases where damage is more likely (i.e. large stone burden, lower pole stones, and complex anatomy) and institutions where repair costs have been found to be relatively high. These endoscopes are only entering the clinical arena, but provisional tests are showing favorable results [1–4, 18, 20]. Robotic platforms for flexible ureteroscopes are also being investigated with a view toward improving instrument stability, ergonomics, and decreased radiation exposure. Desai et al. published their results in 2008 with animal studies and further in 2011, reporting their initial clinical experience using a novel platform with a custom-designed passive ureteroscope, a steerable catheter system, and a remote catheter manipulator [46, 47]. More recently, the Avicenna robotic platform (Elmed, Ankara, Turkey) has been designed with a traditional ureteroscope and a remotely controlled robotic manipulator (Figure 40.5) [48]. This has yielded early clinical results suggesting it to be suitable and safe with significant improvement of ergonomics [7].

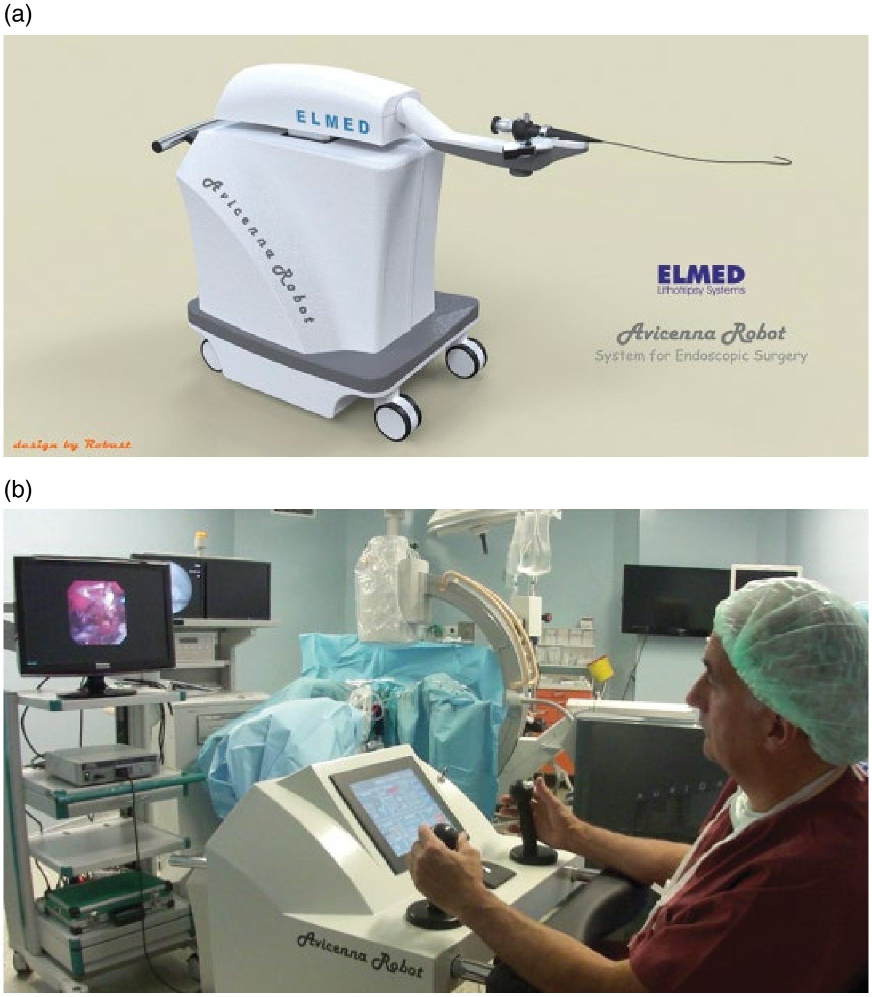

**Figure 40.5** Avicenna robot for flexible ureteroscopy [7]. (a) Manipulator for flexible ureteroscope. (b) Console with joysticks, touch-screen, and armrest. Setup to be used in conjunction with monitor, C-arm, laser, and irrigation. *Source*: Saglam R, Muslumanoglu AY, Tokatli Z, et al. A new robot for flexible ureteroscopy: development and early clinical results (IDEAL stage 1-2b). *Eur Urol* 2014; 66(6):1092–1100. Reproduced with permission of Elsevier.

## Summary

Over the last century, the flexible ureteroscope and its technological evolution has progressed exponentially. Digital ureteroscopy is slowly replacing traditional fiber-optics, and we are already seeing an emerging role for robotics. As these instruments continue to be designed, tested, and redesigned, urologists will be tasked with determining their continued safety, efficacy, and durability.

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# 41

# Rigid Ureteroscope with Flexible Tip and Special Instrumentation

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## Introduction

It is over a century since the first recorded ureteroscopy by Young in 1912. Ureteroscopy has become the preferred surgical treatment modality for managing upper urinary tract stones due to its minimally invasive nature and satisfactory results, particularly for stones <2 cm [1]. Based on endoscope structure, ureteroscopes have developed in two categories. Semirigid or rigid ureteroscopes have a metal shaft and a synchronous tip response. These scopes have the advantages of ease of manipulation and the short learning curve that is required to use them. However, semirigid/rigid ureteroscopes still have several limitations. Semirigid scopes have a rigid and straight shaft that is capable of treating ureteral stones with satisfactory results [2]. However, the stone-free rate is relatively low for treating proximal ureteral stones due to the potential risk of retropulsion [3]. In this condition, ureteral occlusion devices are effective in reducing proximal ureteral stone migration; however, there are additional side effects [4]. Flexible ureteroscope replacement is an another solution to settle the problem of stone migration. Nevertheless, endoscope replacement during the procedure is not convenient and is likely to cause contamination as well as prolonged operation time.

Flexible ureteroscopes have a fully deflectable shaft and actively flexible tip and are thus capable of treating renal stones. However, since the flexible shaft leads to difficult manipulation, flexible ureteroscopes are not suitable for treating distal ureteral stones. Furthermore, poor maneuverability, extra costs for the ureteral access shealth, and high device vulnerability preclude flexible ureteroscopes from wider distribution [5].

To overcome the deficiencies of traditional rigid and flexible ureteroscopes, Yinghao Sun has designed and developed a hybrid ureteroscope integrating rigid and flexible features. The greatest innovation of this novel ureteroscope, is that within the body of a rigid ureteroscope is the distal flexible tip capable of active deflection, functioning with the unique capacity of both rigid and flexible ureteroscopes. Since it debuted 15 years ago, the second generation of this novel ureteroscope has come into production. After 3 years, Sun's tip-flexible semirigid ureteroscope has spread across China and is being used in more than 80 domestic urological centers, and the the number is growing. Moreover, Sun's ureteroscope has been introduced in speeches at 2014, 2015, and 2016 World Congress of Endourology annual meetings and is highly valued by international counterparts. For now, it is an alternative to a rigid or flexible ureteroscope for endoscopic lithotripsy.

## Endoscope development

In 2003, with technical help from the Olympus Corporation, Yinghao Sun and his colleague developed the first generation of the tip-flexible ureterorenoscope. This novel endoscope intergrated the flexible tip of the Olympus URF-P3 flexible ureteroscope with a rigid shaft tip. The caliber of the endoscope is 8.5 Fr at the deflectable tip and 10 Fr at the proximal end of the tapered shaft. The flexible tip is maintained in a straight axis when an accessory rigid probe is inserted in the working channel, thus making it feasible for ureteroscopic access. When the probe is withdrawn, the flexible tip can be controlled for active deflection to explore the renal collecting system. The flexible part on the tip is 60 mm in length, which allows active dual deflection up to a maximum of 180°. When a 200 mm laser fiber is inserted, the maximal deflection angle decreases to 110°. This active deflection performance is almost the same as the Olympus URF-P3 flexible ureteroscope. In addition, the active deflection manipulation was parallel to that of the URF-P3. The operator is able to deflect the flexible tip upwards

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

and downwards by activating the deflection lever on the handpiece. In order to fit the flexible part, the working channel of the composite ureteroscope is 3.5 Fr in diameter. Although it is rather smaller than some rigid/semirigid ureteroscopes, the caliber is sufficient for most ancillary instruments [6].

In the subsequent clinical application reported in 2010, a total of 175 patients with renal calyceal calculi who underwent ureteroscopic lithotripsy using this first-generation tip-deflectable ureteroscope with a holmium laser were retrospectively reviewed. Some 87.5% of the patients were treated successfully using the ureteroscopic approach. Failures included 4.6% of the patient who had severe torsion of the ureter, and in another 7.4% patients the procedure failed to find a lower pole calyceal calculus. The success rate of stone clearance (defined as any single residual fragment less than 2 mm) after 1 month was 83%. Based on the initial study result, this new ureteroscopic technique was seen to have some definite advantages when compared with other types of traditional stone treatment. First, patients requiring a ureteroscopic approach with multiple stones in the renal calyces and the proximal ureter can have them removed within a single procedure using the novel ureteroscope. This avoids the necessity for secondary procedures or a change to flexible ureteroscopy modalities. Second, the composite ureteroscope is manipulated in the same way as the traditional semirigid ureteroscope, only with an added lever for deflection control. This is considered to make the endoscopic procedure easier. Third, this hybrid ureteroscope might have a longer life expectancy than a traditional flexible ureteroscope, which will have economic benefits in lower-income countries in particular.

Some limitations were found that require improvement. For example, only if the rigid accessory probe was inserted could the flexible tip be maintained in a straight axis, allowing easier passage through the intramural ureter and then anteriorly over the iliac vessels with enough maneuverability to negotiate narrow ureters. As the hybid ureteroscope had only one working channel, there was a lack of space for working instruments in the working channel for lithotripsy when the probe was inside. Additionally, the 180° dual deflection did not allow a full exploration of the collecting system in some cases. Moreover, the flexible part of the endoscope was found to be not long enough to fully inspect the renal calyces since it was only 60 mm in length.

## Current Sun's scopes

In 2012, Yinghao Sun, cooperating with the Hawk Endoscopes Corporation (Hangzhou, China), developed and produced a new version of the tip-flexible semirigid ureterorenoscope, which became known as Sun's ureterorenoscope. This endoscope on improved some of the deficiencies of the previous version and demonstrated strong practicality and universality. In the 4 years after that, Sun's ureterorenoscope spread rapidly across China and it is now gaining momentum not only in China but also in the wider Asian commercial endoscope market.

### General properties

Sun's ureterorenoscope involves similar basic components as a common semirigid ureteroscope, including an optical channel for image provision, fiber-optic bundles for light transmittal, and a working/irrigation channel. Sun's ureterorenoscope has an additional deflection mechanism for active flexible tip movement. To achieve the intergrated functions of both traditional rigid and flexible ureteroscopes, Sun's ureterorenoscope has a unique combination structure that consists of a semirigid ureteroscope with a deflectable part on the tip of the shaft and a rigid metal sheath. These two parts are disassembled during sterilization and reassembled for use. The semirigid and flexible working modes can be switched between by setting the sheath in a retracted or nonretracted position. With development in fiber-optic systems and use of materials, Sun's ureterorenoscope provides better imaging quality, increased active deflection, and larger working channel within an even smaller shaft compared with the previous version. Details of some main properties are discussed in the following sections. See Figure 41.1.

### Optics, angle, field of view, and eyepiece

Similar to the most current semirigid and flexible ureterorenoscopes, Sun's ureterorenoscope has a fiber-optic system that includes two light bundles and one optical bundle to provide light and image transmission. This maintains full visualization during scope passage through the tortuous ureter without leading to crescent-shaped defects on the scope eyepiece if using the traditional rod-lens system, and even allows navigation with a large range of active deflection in the renal collecting system. The two sets of light bundles are helpful to eliminate shadows when any working instrument is inserted. The fiber-optic bundles' pixel count is 10 000, which is much more than that of most current fiber flexible ureteroscopes (6000 for Olympus URF-P5 and 6000 for Karl Storz Flex-X2) [7]. Thus it provides better image quality than most fiber flexible ureteroscopes (see Video 41.1).

The angle of view of Sun's ureterorenoscope is 10°. This facilitates passage of the scope when encountering a tortuous ureter and allows immediate visualization when a working instrument emerges from the tip. Sun's ureterorenoscope has a field of view of 90°, comparable with the current flexible ureteroscopes on the market.

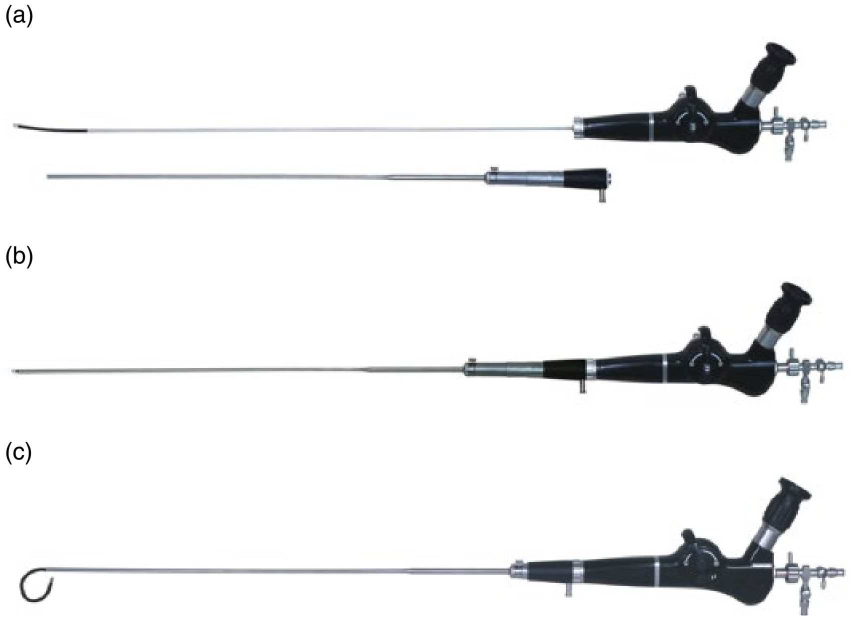

**Figure 41.1** Components of Sun's semirigid ureterenoscope. (a) Dissembled components of the ureterenoscope including a semirigid ureteroscope and a rigid sheath; (b) ureterenoscope in rigid endoscope mode; (c) ureterenoscope in flexible endoscope mode.

To permit introducing a straight working instrument, an offset ocular eyepiece design was included. This eyepiece is fixed on the handpiece and can be connected to the camera.

## Dimensions and the scope tip

Similar to most current semirigid ureteroscopes, Sun's ureterorenoscope is designed with a graduated stepless tapered design, so the shaft is small in diameter at the distal tip and the caliber enlarges gradually towards the proximal end. As the outer rigid sheath and the inner tip-flexible ureteroscope have to be assembled together when the endoscope is in use, it is the caliber of the sheath that affects the ureteroscope's advancement. The diameter of the ureterorenoscope, which is 8.4 Fr at the distal tip and 9.8 Fr at the proximal end, is bigger than that of some flexible ureteroscopes and it might be thought that it would require ureteric orifice dilatation more frequently. In clinical application, Sun's ureterorenoscope still proved to have a 91.9% success rate for endoscope advancement without dilation [8]. This result is even better than that of the 8/9.5 Fr semirigid ureteroscope, as reported in [9]. Despite the current available flexible ureteroscopes having an even smaller shaft [10], it should be noted that the ureteral access sheath (UAS) is recommended in flexible ureteroscopy [11]. When compared with the most commonly used UAS (12/14 Fr), the caliber of Sun' ureterorenoscope is smaller, showing no disadvantage in endoscope dimension for advancement.

The length of Sun's ureterorenoscope shaft is 425 mm, allowing full access to the renal calyces in most patients. Also, it is worth mentioning that the rigid sheath of Sun's ureterorenoscope has a three-stage retractable structure in the proximal part of the shaft. This allows the sheath be locked at three different lengths, allowing variable extension of the deflectable tip to accommodate different requirements. As the retractable sheath can be fixed to the inner scope but with separate full 360° rotation, the sheath bears most of the torque resistance, allowing the inner shaft to rotate freely. All the rotation manipulation movements transfer directly to the tip of the endoscope, greatly improving the torque stability.

When the rigid sheath and the inner endoscope are assembled, the inner flexible tip is 3 mm beyond the distal end of the rigid sheath. Like with current semirigid ureteroscopes, Sun's ureterorenoscope has a beveled tip design which is only 8.2 Fr in diameter. This facilitates entrance into the ureteric orifice and minimizes iatrogenic damage.

## Working channel and irrigation

Sun's ureterorenoscope incorporates a single working channel. This 3.6 Fr working channel passes through from the lower part of the handle to the tip of the endoscope. This size is the same as that of the majority of flexible ureteroscopes, and is capable of introducing most accessory instruments including the guidewires, laser fibers, stone baskets, and biopsy forceps often involved in ureteroscopic surgery. This working channel is eccentrically located in the shaft and thus has less impact on deflection when working instruments are inserted and reduces distortion of the deflectable tip.

When a working instrument is being used, the larger the endoscopic working channel is, the more space is left in the lumen. This suggests that ureteroscopes with larger working channels provide more irrigation flow than those with small channels [12]. Comparisons of Sun's ureterorenoscope (working channel 3.6 Fr), a semirigid ureteroscope (OES Pro, Olympus, Japan; working channel 4.2 Fr), and a flexible ureteroscope (URF-P5, Olympus; working channel 3.6 Fr) showed that, due to the smaller working channel, Sun's ureterorenoscope had a lower irrigation flow rate than the semirigid ureteroscope. Nevertheless, Sun's ureterorenoscope provided more irrigation flow than the most common fiber-optic flexible ureteroscope which had the same working channel in size. This might be attributable to the total flexible lumen generating more resistance than a straight tract [13].

Despite there being only one working channel in the shaft, Sun's ureterorenoscope has a unique method for outflow not seen in other ureteroscopes. The little space between the inner scope and the rigid sheath has been taken full advantage of as a separate "outflow channel," which passes along the sheath from the holes around the distal end to the outlet at the proximal end. This novel design is considered to be helpful in providing continuous irrigation flow for a clear view.

## Deflection mechanism

As it was designed to be capable of inspecting the collecting system and treating renal stones, Sun's ureterorenoscope has an actively deflecting tip at the distal end of rigid shaft. When the outer sheath and the inner endoscope are assembled together and the sheath is fully retracted, the 90 mm deflectable tip can be used for retrograde intrarenal surgery. Similar to a flexible ureteroscope, the flexible tip of Sun's ureterorenoscope is controlled by moving the lever on the handpiece (upward deflection on the lever causes the scope tip to move downward, and vice versa). The ureterorenoscope has a dual deflection of 250° upward and 270° downward to secure full access to all calyces (see Figure 41.2). According to a previous test reported by Sun et al. [6], a decrease in deflection with various working instruments was observed in both Sun's ureterorenoscope and a flexible ureteroscope (URF-P5). However, Sun's ureterorenoscope showed less deterioration in deflection than the flexible ureteroscope with the same working instrument. The maximum downward deflection with a 200 μm laser fiber was 249° for Sun's ureterorenoscope and 226° for the flexible ureteroscope. Similar results were also found when a 1.7 Fr stone basket was used with the two endoscopes (see Figure 41.3). This demonstrated that Sun's ureterorenoscope has identical active deflection to a conventional fiberoptic ureteroscope, and that relatively high deflection is still retained when certain working instruments are inserted.

## Column strength

It has already been demonstrated that the more rigid the shaft is, the more column strength the endoscope should have. Due to their totally flexible structure, flexible

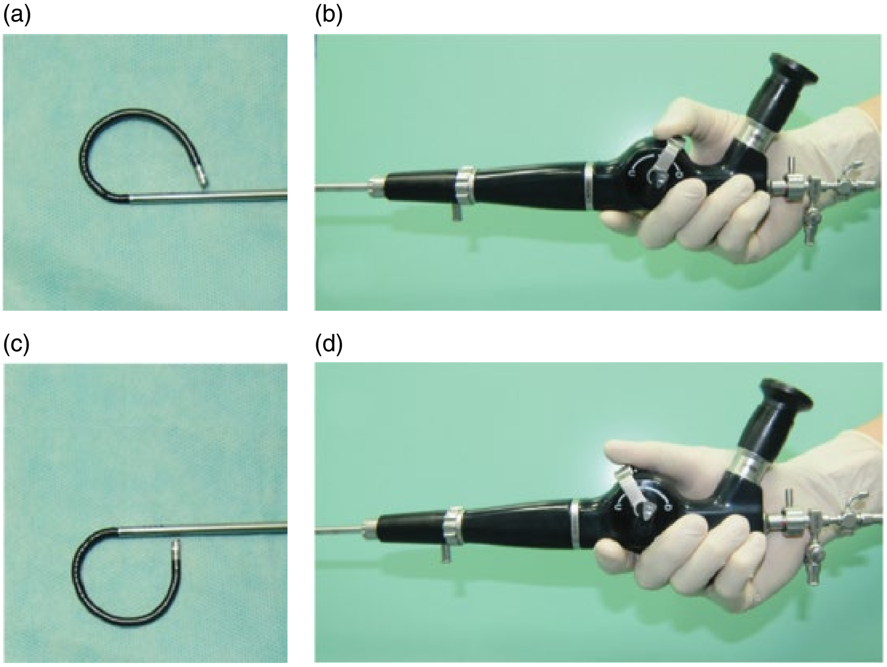

**Figure 41.2** Tip manipulation of the Sun's tip-flexible ureterorenoscope. (a, b) Lever moves downwards to control the upward deflection on the flexible tip; (c, d) lever moves upwards to control the downward deflection.

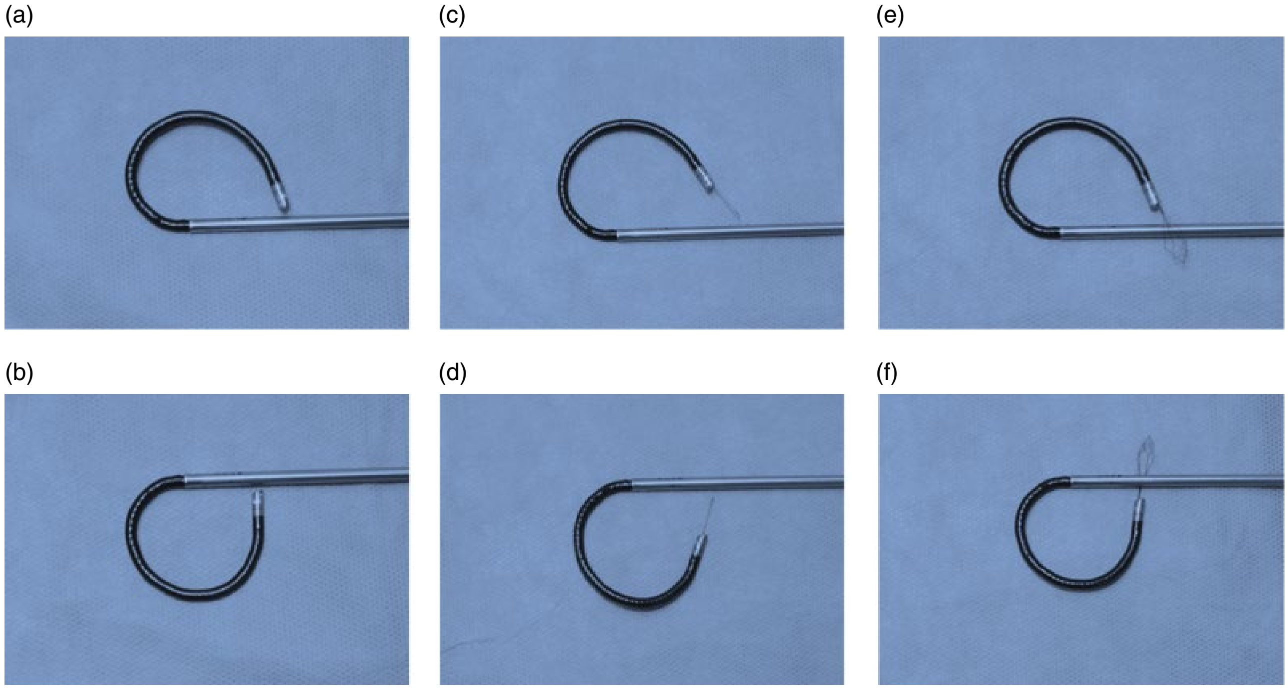

**Figure 41.3** Dual deflection of Sun's ureterorenoscope with different auxiliary instruments. (a, b) With empty working channel; (c, d) with 200 μm laser fiber; (e, f) with 1.7 Fr basket.

ureterorenoscopes are more fragile than semirigid ureteroscopes. Despite the shaft strength of the latest flexible ureteroscopes having been greatly improved through technical developments, they are still more likely to buckle [14]. As a novel composite ureteroscope, the majority of Sun's ureterorenoscope shaft is made of rigid materials, which contributes to a crush resistance that is approximately comparable to a common semirigid ureteroscope. In a study by Yinghao Sun [13], endoscope stability was assessed and compared between Sun's ureterorenoscope and a semirigid ureteroscope (OES Pro), which has the shaft caliber. Several bending forces up to 1.5 kg were applied at the proximal third of the shaft of both scopes. The subsequent deviation, defined as the angle of the endoscope tip from the baseline horizontal position, was tested as a measure of the column's strength. Both the Sun scope and semirigid ureteroscope presented a force-dependent increase in deviation angle. Although Sun's ureterorenoscope showed relatively higher deviation, the difference between the two ureteroscopes was only less than 1°. Plus, as the maximum deflection caused by the bending forces was no more than 50 mm and would not lead to scope failure, Sun's ureterorenoscope was proved to be sturdy enough for retrograde ureteroscopy.

## Light source

Traveling through the fiber bundles, the light is transmitted to the tip of the endoscope from the source lamp. Sun's ureterorenoscope incorporates two fiber light bundles on the left and the right side of the optic-transmitting bundle, eliminating any shadows cast by working instruments. Sun's ureterorenoscope has a universal light port that can use most current light sources including halogen (150 W) and xenon (300 W). With automatic light-sensing functions, these light sources can adjust the brightness to current requirements during ureteroscopic procedures.

## Passive deflection

In 2015, the latest version of Sun's ureterorenoscope released onto the market. In addition to the common features and structure of the previous version, this third-generation hybrid ureteroscope incorporated a secondary passive deflection structure (see Figure 41.4). This mechanism was achieved by adding a deflectable shaft of 40 mm in length proximal to the point of the actively deflectable tip. This segment cannot be controlled for dual deflection but is passively deflected on contact with renal tissue. This structure has the same function its the counterpart in flexible ureteroscopes, permitting an even larger range of deflection for access to lower pole calyces [15]. Additionally, the passive deflection part effectively lengthens the flexible shaft, allowing better inspection in cases with moderate hydronephrosis or with a long lower infundibulum.

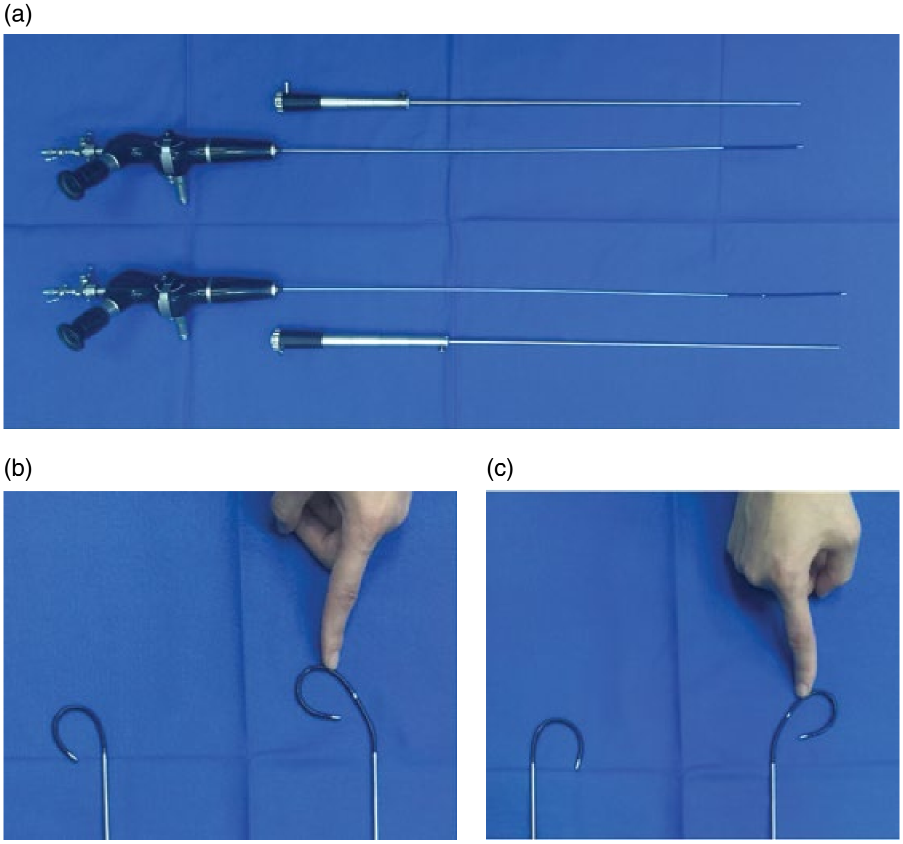

**Figure 41.4** Comparisons between the second and third versions of Sun's ureterorenoscope. (a) Overall appearance of the two endoscopes (the second-generation scope is shown at the top); (b, c) dual passive deflection of the latest version of the endoscope.

## Ureteroscopic surgery with a flexible-tipped ureterorenoscope

In the past two decades, technical improvements, such as endoscope miniaturization and imaging quality enhancement, as well as a wider variety of accessory tools, have led to a rapid gain in the popularity of ureteroscopy. These revolutionary advances have widely increased the indications for ureteroscopy, and made it possible to manage all ureteral and renal stones.

As the stone-free rate (SFR) of endoscopic surgery is considered superior to that of extracorporeal shock-wave lithotripsy and comparable to that of percutaneous nephrolithotomy for the management of either ureteral or renal stones of less than 20 mm, the European Association of Urology and American Urological Association guidelines [11] have suggested that ureteroscopy may be considered as a first-line treatment modality for upper urinary tract stones. Although the SFR for upper urinary tract stones is satisfactory, some limitations still remain. Semirigid ureteroscopy for distal or mid-ureteral stones achieves good stone clearance; however, when stones are located in the proximal ureter, stone fragments may easily migrate into the kidney during lithotripsy. Although flexible ureteroscopy has demonstrated high levels of renal stone clearance, it remains a less durable modality due to the totally flexible shaft.

In order to overcome the limitations associated with conventional ureteroscopy, Sun's ureterorenoscope was developed to be used in the treatment of ureteral and renal stones with no requirement for endoscopic alternation. In this section, details of the ureteroscopic surgery using Sun's ureterorenoscope are discussed.

### Indications

As the SFRs from distal and mid-ureteroscopic lithotripsy are claimed to be superior to that from shock-wave lithotripsy, ureteroscopy has become the first choice for treatment of stones [16]. In ureteroscopic surgery using Sun's ureterorenoscope, the inner endoscope and the outer sheath are assembled together. When the outer sheath is not retracted and the inner deflectable tip is fully inside, the endoscope has a fully rigid shaft, and can be used as a common semirigid ureteroscope. Stones located in the distal or mid ureter can be disintegrated by laser lithotripsy and extracted using a stone basket with ease during ureteroscopy.

Although SFRs of approximately 81–94% can be achieved by semirigid ureteroscopy for distal and middle ureteral stones, this decreases to 77% for proximal ureteral stones due to the potential for retropulsion [17]. Since semirigid ureteroscopes are not capable of active deflection and so cannot give access to the renal calyx, ureteral occlusion devices are always required to reduce proximal stone migration [2]. With Sun's ureterorenoscope the problem of stone migration is easily solved. Once stone retropulsion occurs, the surgeon can advance Sun's endoscope to the pelvic brim and retract the sheath, using the deflectable tip to allow access to the renal calyx to continue stone fragmentation. This advancement greatly improves the SFR for proximal ureteral stones by ureteroscopy, and thus allows Sun's ureterorenoscope to cover all parts of treating ureteral stones.

Being 90 mm in length, with a 250°/270° dual deflection tip, Sun's ureterorenoscope can allow access to almost any part of the renal collecting system. This makes it possible to treat renal stones as if using a flexible ureterosocope. Nevertheless, it should be noted that patients with hydronephrosis of >30 mm in diameter on ultrasonography are usually excluded because of the increased difficulty in inspecting the collecting system and in accessing some lower pole calyces [11].

## Equipment

Like all endourologic surgery, a procedure involving Sun's ureteroscope should always take place in a lead-shielded operating room, as retrograde pyelography and X-ray examination are routinely required. Other basic equipment is essential, including guidewires, contrast medium, laser lithotripsy, stone retrieval devices, irrigation system, as well as biopsy forceps (if needed).

Although an open-end ureteral catheter is not required as retrograde pyelography can be directly performed with the ureterorenoscope, guidewires are still necessary as they enable the ureteroscope or the ureteral dilator to advance through the ureter. Super-stiff wires are more likely to be used when a tortuous ureter needs to be straightened. A 0.035 inch angled-tip hybrid hydrophilic guidewire is always recommended as they can become be very slippery and atraumatic when absorbing water. Besides, this type of guidewire has sufficient rigidity for endoscope advancement and easy passing of impacted stones in the ureter.

Many lithotripsy devices have had technical developments, and proved to be safe and effective for ureteroscopy. As for Sun's ureterorenoscope, holmium:YAG laser is the preferred device. The laser fiber has smaller size than other lithotripsy devices such as in pneumatic and ultrasonic lithotripsy, which is suited to the 3.6 Fr working channel of the Sun's endoscope. In addition, the 200 μm laser fiber is very flexible and does not hinder the active deflection of the flexible tip. With these features, a holmium:YAG laser allows renal stone fragmentation through Sun's ureterorenoscope even if the stone is located in the lower renal calyx.

According to a matched-pair study, a semirigid ureteroscope that was almost the same size as Sun's ureterorenoscope required a ureteral dilation rate of 15% [18]. This result might suggest that the potential dilation requirement for tip-flexible ureteroscopy is likely to be over 10%. By now, it is widely accepted that ureteral balloon dilators are much safer for accessing anatomically tight or strictured segments of ureter than traditional ureteral dilators. Generally, a 40 mm dilator with 12 Fr balloon is sufficient for application of Sun's ureterorenoscope.

It remains controversial whether or not fragment extraction should be performed during endoscopic surgery. Despite the fact that most stone retrieval devices could be inserted into Sun's ureterorenoscope, stone fragment retrieval is not recommended as a routine procedure during tip-flexible ureteroscopy. As the inner diameter of the rigid sheath of Sun's endoscope is only 8.2 Fr, which is not large enough for stone extraction, like the UAS used in flexible ureteroscopy, it is required that Sun's ureterorenoscope is totally withdrawn and readvanced when retrieving stone fragments. This may significantly increase the operation time, and may also be associated with increased potential for damage. Thus, nitinol tip-less baskets and graspers are only used for stone relocation when treating difficult lower pole stones or whenever stone component analysis is required.

Irrigation devices are used to actively create a space either in the renal collecting system or in the ureter, to work in and to provide clear visualization. Several varieties of irrigation device can be selected for tip-flexible ureteroscopy. Some sorts of irrigation pump are capable of providing continuous-pressure controlled flow, warmed to body temperature. These devices are easy and convenient in use, but they do have a potential risk of over-infusion that might cause pyelolymphatic or pyelovenous backflow, which is associated with subcapsular effusion or subcapsular hematoma [19]. Besides, pump irrigation is more likely to cause stone retropulsion in the treatment of proximal ureteral stones [20].

An irrigation hanging bag is another simple irrigation device and provides flow with stable pressure. It has the obvious advantage of safety whereby the irrigation flow will stop by itself if the intrarenal pressure exceeds the pressure associated with the bag height, helping to prevent over-infusion. However, it also has the vital disadvantage that irrigation is not flexible and constant visualization of the pressure might not be maintained in complicated situations. During tip-flexible ureteroscopy, irrigation by an assistant using a hand-held syringe is preferred, as it allows safe and flexible control of the force with which the irrigation flow is delivered. Nevertheless, this irrigation modality requires the assistant to be experienced and judicious. Normally, saline is the best choice.

### Step-by-step ureteroscopic access

Before use, Sun's ureterorenoscope should be carefully examined to ensure its encapsulation, deflection, retractable configuration, and image clarity are in order. The endoscope should be sent for repair if major damage is found. The surgeon should hold the endoureterorenoscope handpiece with the dominant hand, keeping the thumb on the deflection lever. The other hand should be used to hold the penis while advancing the endoscope and rest in a comfortable position during inspection and lithotripsy. The surgeon should be seated during tip-flexible ureteroscopy rather than standing, as for flexible ureteroscopy [21].

Usually, the ureteroscopy begins with a cystoscopy. As Sun's ureterorenoscope offers satisfactory image quality, it could be used for full assessment of the bladder instead of using a rigid cystoscope. After the relevant ureteral orifice is located, a 0.035 inch hybrid guidewire is advanced through the ureteroscope to access the ureter. If a small orifice is encountered, the endoscope could be rotated 180° to lift the ureteral orifice, enlarging the space into which the ureteroscope advances. In addition, balloon dilators can also be used, allowing the scope to access across the small orifice with ease. In most causes, there is no need to worry about ureteral injuries, as a recent study suggested that balloon dilatation is not a risk factor for ureteral wall injury during ureteroscopy [22]. A second ureteroscopy after 1–2 weeks of double-J stenting should also be considered if the ureter is so small that any ureteroscope access attempt would cause severe ureteric injury.

Generally, scope access to the orifice is followed by a retrograde pyelogram procedure [23]. However, if ureteroscopy is being performed for treating mid or distal ureteral stones, a pyelogram might be skipped as there is no need to determine the layout of the collecting system and it has a potential risk of stone retropulsion as well as unnecessary increased radiation exposure. For safety, the guidewire is advanced gently under X-ray guidance and endoscopic vision. After the guidewire is properly placed, Sun's ureterorenoscope is then advanced alongside the wire with great caution. If there is any resistance, the temptation to push the ureteroscope should be avoided without identifying the caliber of the ureter.

Occasionally, due to severe tortuous ureteral conditions caused by stone obstruction or anatomical features, advancement of the ureteroscope might be particularly challenging. Under such circumstances, the Trendelenburg position is useful as it moves the kidney to the head side which will decrease ureter tortuosity. Other tips such as pressure on the abdomen could also be helpful for straightening the ureter.

During conventional semirigid ureteroscopy, once the ureteral stone is visualized the guidewire is widely recommended to pass across the stone obstruction and coil in the renal collecting system as a safety wire. This will not only maintain access to the upper urinary tract but also straighten the tortuous ureter. As for Sun's ureterorenoscope, if there is no potential risk of iatrogenic injury, the safety guidewire can be omitted. Benefiting from the three-stage retractable configuration of the outer sheath, the deflectable tip of the Sun's endoscope can be extended out in three different lengths in order to accommodate different requirements (see Figure 41.5). This unique design allows the flexible tip to deflect in a rather small range without losing rigidity, and is useful when treating difficult ureteral stones in particular. With this slight deflection, a better line of sight is likely to be obtained and the laser fiber can be placed onto the stone's surface instead of the ureteral mucosa, even when there is no safety guidewire left in place.

When the tip-flexible ureteroscopy is performed for intrarenal endoscopic surgery, the retrograde pyelogram should be performed to delineate the collecting system map. After Sun's endoscope is advanced and has reached the ureteropelvic junction, the assistant helps to inject

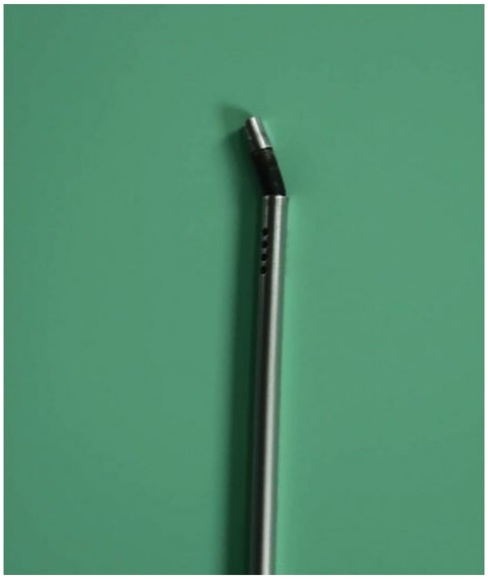

**Figure 41.5** The deflectable tip of Sun's ureterorenoscope can be extended to a variety of lengths.

the diluted contrast medium through the working channel. A retrograde pyelogram should be visualized dynamically to control a proper contrast dose, whereby a clearly visible collecting system anatomy and renal stones are identified without causing contrast extravasation.

Before using the deflectable tip of Sun's ureterorenoscope to inspect the kidney, the outer rigid sheath should be fully retracted to extend the entire 90 mm inner deflectable tip. Movement of the deflectable shaft is carried out using two synchronized methods. Active deflection (up and down) is manipulated by the lever on the handpiece, and horizontal steering is controlled by axis rotation of the endoscope. Under the guidance of the retrograde pyelogram, inspection of the collecting system progresses from the renal pelvis to the upper, middle, and lower renal calyces.

During the procedure, the assistant should maintain proper saline irrigation using a syringe to provide optimal visualization. Over-pressurizing should be avoided as it might cause pyelovenous backflow and secondary infection. Care should be taken to ensure continuous outflow at the outlet port. If outflow stops then it suggests that the edge of the rigid sheath has not passed across the level of ureteropelvic junction and that the position needs to be adjusted.

## Lithotripsy

After the ureteral or the renal stones have been located, lithotripsy should be performed. Since Sun's ureterorenoscope has an active deflectable tip that can be used for treating calyceal stones, holmium:YAG laser is the best lithotripsy equipment in tip-flexible ureteroscopy. Among the available varieties of laser fibers, 200 μm laser fiber is mostly recommended, as its small diameter has very limited impact on endoscope deflection as well as on adequate irrigation. Additionally, 200 μm laser fiber carries up to 45 W power, which is capable of disintegrating or ablating all stones irrespective of composition. By now, most urologists have accepted the standard of "stone free," defined as residual fragments not exceeding 4 mm by X-ray. Since fragment retrieval does not suit tip-flexible ureteroscopy, stone particles must be small enough to ensure complete postoperative expulsion. Therefore, "stone dusting" is preferred as the ideal lithotripsy modality for fragmentation in tip-flexible ureteroscopy, Generally, laser power should be initially set to a "low energy/high frequency" mode of 0.5–1.0 J/20–30Hz, which will suit stone dusting and vaporization. If the stone is hard, the power is increased to 1.0 J at 10 Hz. One thing to always be aware of is that the laser fiber should be advanced when the deflectable tip is in a straight position instead of being deflected, so as to avoid scope or working channel perforation of the surrounding tissue. Laser lithotripsy should be synchronized to respiratory movements, thus avoiding injury to the mucosa. In patients with significant respiratory movements, temporary breath holding with assistance from the anesthetist might facilitate accurate stone fragmentation.

Sung et al. reported that lower calyceal stones contributed to approximately 49% of total renal stone cases and had a worse SFR than upper and mid calyceal stones [24]. This result suggested that lower pole stones are not only the most commonly encountered cases, but also are the most difficult scenarios for ureteroscopy. Despite certain tests demonstrating that Sun's ureterorenoscope has satisfactory deflection, it is recommended to perform stone relocation before fragmentation, as it reduces the duration of the endoscope working in maximum deflection. Working instruments such as baskets and graspers should be used to move the lower calyceal stones to a more favorable position such as the mid or upper calyx.

After complete lithotripsy, a final retrograde pyelogram should be performed to determine whether any calyx is missed on entry. Sun's ureterorenoscope should be withdrawn, with its deflectable tip kept in the neutral position. The rigid sheath of the scope should be retracted during this procedure, and should not be extended until the endoscope has been withdrawn completely.

A double-J stent placement is recommended in some complicated situations, including large stone burden, a tight ureter, evidence of extravasation, and solitary kidneys.

## Technical failure

Since the majority of the ureterorenoscope shaft is covered by metal, it has a low risk of shaft damage in comparison with its flexible counterparts. Based on the results from a multicenter study by Yinghao Sun [8], and our experiences, the average usage for Sun's endoscope before major repair is over 60 procedures. A broken shaft at the rigid/deflectable junction contributes to the majority of endoscopic failures. There are several principles that are helpful in maximizing the ureterorenoscope's life span. Firstly, the endoscope should not be advanced through the ureter with the outer sheath fully retracted. The view from the endoscope indicates only whether there is any obstruction directly beyond the tip; if the sheath is retracted operators will not be aware if a junction site has already buckled the tip, or to what angle. This is the most common failure for surgeons who are not familiar with the endoscope's features in particular. Secondly, the outer sheath should never be extended *in vivo* once it has been retracted in the procedure. Sheath extension must be performed with the deflectable tip in the straight position, under direct vision when it is fully withdrawn outside the body. Thirdly, overdeflection and prolonged duration in lower pole calyces should be avoided when accessing the lower pole calyces, especially with a working instrument inside. This might lead to the active deflection unit being broken.

### Care, maintenance, and sterilization

After utilization, the outer sheath and the inner shaft of Sun's ureterorenoscope should be dissembled and carefully cleaned. The deflectable tip should be maintained in the straight position to avoid damage and degradation of its deflection angle. A leak test should always be performed before and after every utilization, ensuring that minor damage to the shaft or the working channel is not neglected. During gas sterilization, the venting system, mostly via a valve, should be equipped to equalize pressures and prevent damage to the scope.

## Future trends

Similar to semirigid and flexible ureteroscopes, Sun's ureterorenoscope is under constant development towards smaller caliber, better image quality, and better deflection. To improve deflection for access to lower pole calyces with a very difficult ureteroinfundibular angle or great infundibular length, the latest version has been developed with an additional passive flexible part. It is undergoing perspective study. Future improvements, including the use of digital video technology, are under consideration.

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# 42

# Digital Ureteroscopes

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## Introduction

Flexible ureteroscopes are widely used in daily practice by urologists for treatment of calculi and for diagnosis and treatment of ureteral and upper urinary system disorders. The less invasive nature of the procedure makes it a favorable choice for surgeons compared with more invasive alternatives such as percutaneous nephrolithotomy or even other minimally invasive techniques. Since its introduction, many technological advancements have been made. Better imaging quality and deflection angles, more functional working channels, and more durable instruments have been introduced. Currently, flexible fiber-optic ureteroscopes, flexible digital ureteroscopes, and the recently introduced disposable digital flexible ureteroscopes are all being used in daily practice. In this chapter we review the details of digital ureteroscopes, which have a characteristic advantage of superior imaging thanks to their "chip on the tip" technology.

## Reusable digital flexible ureteroscopes

Digital flexible ureteroscopes are widely used in clinical practice and stand out because of their enhanced high-quality images. Previous ureteroscopes transmitted images via fiber-optic cables, with an external light source and an attached camera. Today's digital ureteroscopes do not necessitate such bulky devices; instead, digital images are transferred to a screen via a single cable (Figure 42.1). This feature reduces the effort required by the surgeon, and better quality images make the operation easier to perform. Pixel resolution of digital ureteroscopes is nearly ten times better than that of fiber-optic ureteroscopes and the images can be magnified digitally and viewed during the operation (Figure 42.2). ACMI DUR-D Invisio was the first digital flexible ureteroscope introduced for urologic practice. It contained a complementary metal oxide semiconductor (CMOS)-based chip at its distal end. Even though ACMI DUR-D had better image resolution than previous ureteroscopes, there were some disadvantages, such as increased instrument diameter. This sometimes prevented the surgeon from reaching the desired lower calyx and produced a deteriorated image when the red laser beam was activated. Technological advancements have led to the production of newer and better quality digital ureteroscopes. The Olympus URF-V, which contains a charge-coupled device (CCD)-based chip, and the Karl Storz Flex-Xc, which contains a CMOS-based chip, were introduced in the following years.

Better contrast discrimination, color differentiation, and higher-resolution images obtained by digital ureteroscopes lead to better diagnosis of millimetric lesions and increased comfort for the surgeon during renal stone fragmentation. Focusing on the stone and identifying the calyceal anatomy is much easier with these ureteroscopes, which leads to decreased risk of mucosal injury and bleeding during stone fragmentation with a holmium laser (Figure 42.3). Enhanced imaging achieved by digital ureteroscopes also decreases the operation time when compared with fiber-optic ureteroscopes [1].

Although technological advancements have led to better quality images and more durable ureteroscopes, there are still certain problems owing to the fragile nature of these instruments. Many studies have compared the durability of digital ureteroscopes with fiber-optic ureteroscopes and have proven that digital ureteroscopes are more durable. However, flexible ureteroscopes are all fragile instruments. Repetitive use of these instruments

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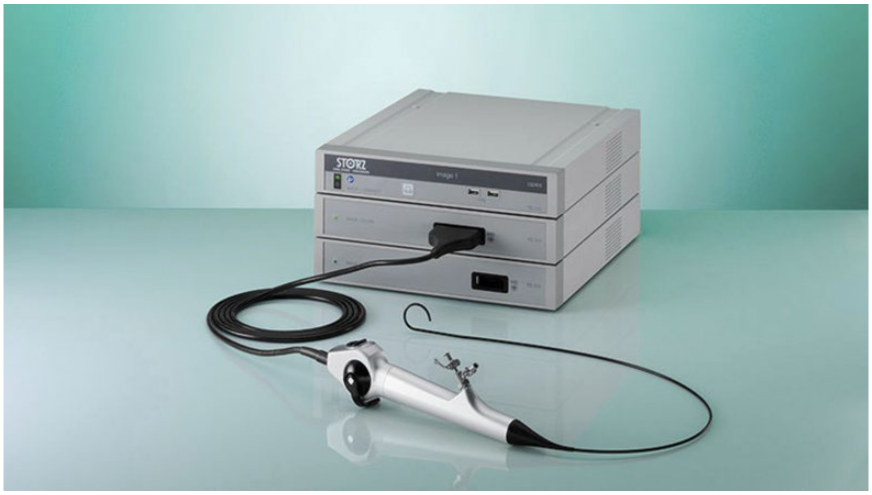

**Figure 42.1** Karl Storz Flex-Xc single connection cable.

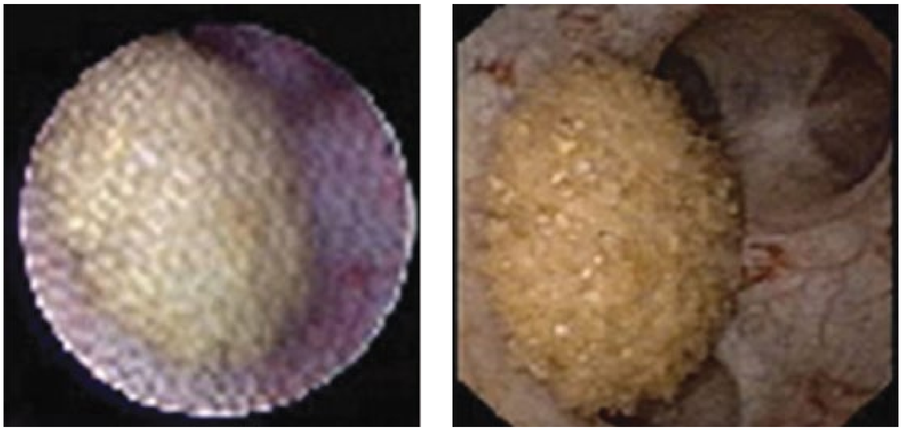

**Figure 42.2** Fiber-optic ureteroscope image (left) versus a digital ureteroscope image (right).

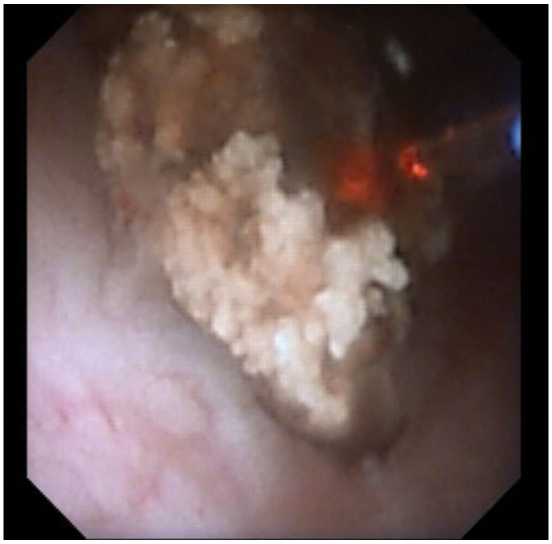

**Figure 42.3** Flex-Xc ureteroscope; digital image of a stone and laser fiber.

eventually decreases the angle of maximal deflection. Proper handling of the instruments by experienced surgeons significantly increases their durability. Use of an access sheath during the introduction of the instrument into the upper urinary tract also increases its life span. Avoidance of maximal deflection and relocating stones before fragmentation are also beneficial precautions. Another problem with these instruments is possible damage to the digital chip and ureteroscope by the holmium laser if unintentionally retracted into the instrument during stone fragmentation. Turning the laser off while retracting it into the ureteroscope or fixing the laser after appropriate placement are possible precautions, but they are not guaranteed. Use of an "endoscope protection system" (EPS) is a better option. When the laser is retracted into the instrument, and therefore disappears from sight of the CMOS-based chip, the EPS recognizes the absence of the blue cladding of the active laser fiber and automatically switches it off. All of these precautions lead to increased life span of these expensive instruments and reduce repair costs.

Digital ureteroscopes have become the subject of many studies. Newly introduced "chip on the tip" technology, superior imaging quality, newly introduced working channels, and maneuverability abilities are the main features that have been evaluated. Binbay et al. and Somani et al. made a comparison between digital and conventional ureteroscopes, discussing the slightly limited maneuverability and shorter operation times of digital scopes [1, 2]. Shah et al. compared the ACMI DUR-D with the Olympus URF-V and found better visibility and maneuverability of the CCD-based Olympus URF-V [3]. Lusch et al. compared the performance and characteristics of the dual-channel Wolf Cobra fiber-optic ureteroscope with two single-channel fiber-optic ureteroscopes and a single-channel URF-V digital ureteroscope. They found better image resolution with the URF-V owing to its digital sensor chip and increased irrigation flow of the Wolf Cobra as a result of its separate working channel. They also noted the increased thickness of the Wolf Cobra when compared with other ureteroscopes [4]. Richard Wolf has since introduced a digital version of this unique instrument called Cobra Vision. Technical details of available digital ureteroscopes are listed in Table 42.1.

Humphreys et al. [5] published a unique article about the use of these novel digital ureteroscopes. They conducted this study using the ACMI DUR-D digital ureteroscope and mentioned the possible use of these instruments, which produce high-quality images, in detecting the early stages of calcium oxalate stone formation and possibly understanding the mechanism of stone formation [5]. Multescu et al. compared the Flex-Xc, URF-Vo, and Wolf Cobra in terms of maneuverability, imaging, and deflection mechanisms. They stated that the most important difference was image quality, but another important difference was the more effective irrigation flow of the Wolf Cobra [6]. Bach et al. compared the need for an access sheath in two different ureteroscopes, the ACMI DUR-D digital flexible ureteroscope and the DUR-8 fiber-optic flexible ureteroscope. They noted an increased need for ureteric access sheath use with digital ureteroscopes due to their increased tip diameter, which may increase morbidity and cost of the operations [7].

## Disposable digital flexible ureteroscopes

The high price and repair costs of flexible ureteroscopes led to the creation of disposable, single-use versions. Bagley first introduced the flexible disposable modular ureteropyeloscope in 1987 [8]. This ureteroscope contained a replaceable flexible tip, available in 6.0, 8.5, and 11.0 Fr diameters. He cited his indications for the use of this disposable instrument as surveillance for fragments after lithotripsy and for diagnosis of radiographic abnormalities in the upper tract. He introduced the instrument into the ureter successfully in 37 out of 38 patients, a promising success rate. In 2009, Boylu et al. compared the efficacy and quality of the disposable flexible SemiFlex Scope, which contains a reusable eyepiece and a semiflexible shaft with a 3.3 Fr working channel, with currently used fiber-optic ureteroscopes [9]. They noted that the SemiFlex Scope had acceptable features and showed promising results. A year later, the PolyScope, a semidisposable flexible ureteroscope, was evaluated by Bader et al. [10]. They mentioned the lower costs of this instrument compared with the high repair costs of other reusable flexible ureteroscopes. The more recently introduced Boston Scientific LithoVue single-use digital flexible ureteroscope is a newer disposable ureteroscope and stands out because of its high resolution images provided by the digital CMOS-based chip at its distal end (Figure 42.4). The tip diameter of the scope is 7.7 Fr and the outer diameter is 9.5 Fr. It offers 270° deflection in both directions and similar image quality to other reusable scopes. It contains a built-in light source and is connected to a rolling mobile workstation with a single cable. The workstation contains integrated image-transferring software and provides high-definition images. Life span of these instruments are restricted with 4 hours of usage by the producer. Proietti et al. compared the efficacy of the newly introduced LithoVue disposable digital ureteroscope with the reusable URF-V digital ureteroscope and the URF-P5 fiber-optic ureteroscope, and stated that the LithoVue is comparable with other conventional ureteroscopes in terms of visibility and manipulation [11] (Figures 42.5 and 42.6). Because this technological device was recently introduced, their cost-effectiveness and usefulness remains to be analyzed with further clinical trials.

## Technical features of digital ureteroscopes

### Setup

Digital ureteroscopes differ from standard flexible fiber-optic ureteroscopes, especially in image-transfer technologies. A digital ureteroscope is composed of a proximal handle and an articulation lever at its proximal end, similar to standard flexible ureteroscopes. Digital ureteroscopes are connected to a digital high-quality screen and light source without the need for an additional optical eyepiece or a camera head. The distal end of the cable attaches both to the light source and to the video monitoring system and

Table 42.1 Technical details of available digital ureteroscopes.

| | Length (mm) | Shaft diameter (Fr) | Tip diameter (Fr) | Channel size (Fr) | Active deflection (up) | Active deflection (down) | Chip technology | Number of working channels |
|---|---|---|---|---|---|---|---|---|
| **Reusable digital flexible ureteroscopes** | | | | | | | | |
| Olympus URF-V | 980 | 9.9 | 8.5 | 3.6 | 180 | 275 | CCD | 1 |
| Olympus URF-V2 | 980 | 8.4 | 8.5 | 3.6 | 275 | 275 | CCD | 1 |
| Stryker Flexible Vision | NA | NA | 9.6 | 3.6 | 240 | 240 | NA | 1 |
| Karl-Storz Flex-Xc | NA | NA | 8.5 | 3.6 | 275 | 275 | CMOS | 1 |
| Richard Wolf BOA Vision | 680[a] | 8.7 | 6.6 | 3.6 | 270 | 270 | NA | 1 |
| Richard Wolf Cobra Vision | 680[a] | 9.9 | 5.2 | 3.6 | 270 | 270 | NA | 2 |
| **Disposable digital flexible ureteroscopes** | | | | | | | | |
| SemiFlex Scope | 650 | 6 | NA | 3.3 | 180 | 180 | NA | 1 |
| The PolyScope | 850 | 8 | NA | 3.5 | 180 | 180 | NA | 1 |
| Boston Scientific LithoVue | NA | 9.5 | 7.7 | 3.6 | 270 | 270 | CMOS | 1 |
| Cook Medical The Flexor Vue | NA | NA | NA | NA | NA | NA | NA | NA |

NA, not applicable.

[a] Working length.

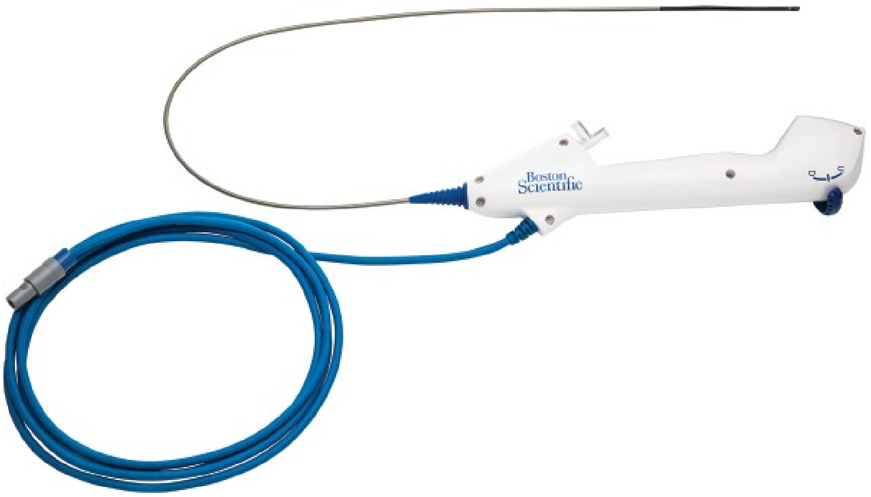

**Figure 42.4** LithoVue disposable flexible ureteroscope.

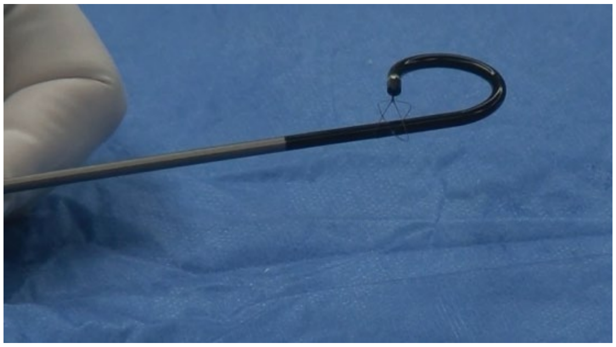

**Figure 42.5** The 270° of deflection of a disposable ureteroscope during nitinol basket use.

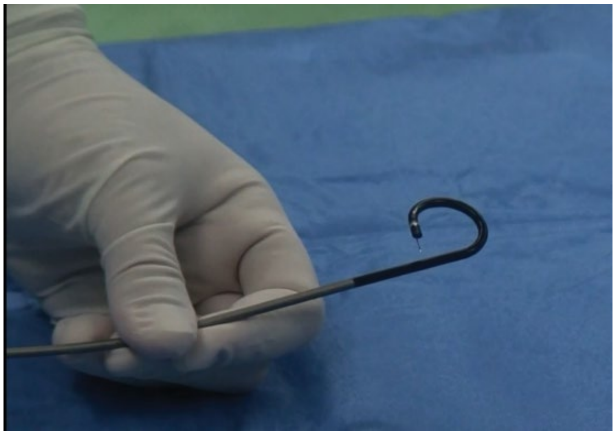

**Figure 42.6** The 270° of deflection of a disposable flexible ureteroscope during laser fiber use.

data are transferred to the monitor. The Olympus URF-V and URF-V2 have an additional illumination cable attachment using a newer technology, which is discussed under Illumination, below. Two working channels are available on these ureteroscopes; one is used for irrigation and the other for instrumentation. Access sheaths are placed into the desired ureter via guidewire placement and the rest of the procedure is similar to standard flexible ureteroscopy. Disposable digital ureteroscopes also have similar properties but have a single attachment cable to their unique monitoring system, which includes the illumination device.

## Imaging

A unique feature of digital ureteroscopes is their enhanced imaging ability. They achieve this better imaging with a chip at their distal end, and thereby this feature is called “chip on the tip” technology. The first flexible ureteroscopes were introduced in the early 1960s and delivered the image to a screen via fiber-optic cables. Each fiber-optic cable delivered a certain part of the entire frame, giving the final image a “honeycomb” or “chicken wire” appearance. These fiber-optic flexible ureteroscopes are still used widely. In 1969 at AT&T Bell Labs, Boyle and Smith invented a microchip that transfers information by storing an electrical charge in itself, allowing the data to be retrieved when desired, and thus creating digital imaging and image-transferring technologies [12]. These microchips are called CCDs and won Boyle and Smith the Nobel Prize for Physics in 2009. These devices convert incoming photons by p-doped metal oxide semiconductor (MOS) capacitors into an electrical charge, and then convert this information into a digital format. Another similar technology called CMOS was patented by Frank Wanlass in 1963 and also used for digital image transferring purposes [13]. CMOS chips are semiconductor battery-powered chips which store information and are used in computers as microprocessors, data converters, and image sensors. Both of these technologies are being used in many different fields, but they were first used for medical purposes in

2005 for the ACMI DCN-2010 digital flexible cystoscope. This device allowed better visualization and provided better images of the urethra and bladder. A year later, in 2006, the ACMI DUR-D digital ureteroscope was introduced, which carried a CMOS chip at its distal end (chip on the tip technology). Different digital flexible ureteroscopes carrying CCD or CMOS chips have since been introduced.

### Illumination

Illumination is mandatory for flexible ureteroscopy, as it is in all endoscopic procedures. Illumination is achieved through a light source connected to the flexible ureteroscope. In fiber-optic scopes, this connection was achieved by plugging in one end of the light cable to the illumination unit and the other end to the instrument. In digital scopes, there is no additional plug-in unit on the instrument. The distal ends of digital ureteroscopes have a socket that is plugged into the control unit, which is responsible for both image transferring and illumination. However, the Olympus URF-V and URF-V2 have an additional extension of this single cable that is separately plugged into the illumination unit and uses different illumination technology than the others (Figure 42.7). Most digital ureteroscopes use light-emitting diode (LED) technology, whereas the Olympus digital ureteroscopes use xenon technology for illumination. The additional cable extension is connected to a xenon light source. Prospective trials are needed to evaluate any functional differences between LED and xenon illumination.

### Deflection mechanism

Another unique feature of flexible ureteroscopes is their deflection ability. The distal end of flexible ureteroscopes can deflect up to 275° and this deflection is controlled by a lever located at the proximal part of the instrument. This type of deflection is called "active deflection." Small wires are present between the distal part and the lever, and movement of these wires creates up and down deflection of the distal scope. The first flexible ureteroscopes only had the ability to deflect 170°.

Another type of deflection is called "passive deflection," achieved by the contact of the intrarenal collecting system with a softer segment of the instrument located proximal to the deflecting region. This softer segment allows additional deflection and facilitates reach of the entire collecting system.

Rotation of the instrument during the operation allows the surgeon to relocate it by changing the shaft's angle and increase the maneuverability. This maneuver is achieved by inward or outward rotation of the surgeon's hand. As an example, while fragmenting a large stone, rotating the instrument will change the position of the laser fiber and thereby facilitate effective stone fragmentation. This manual hand maneuver can be challenging for surgeons after longer operation times. The Olympus URF-V2 digital flexible ureteroscope overcame this problem by adding a special rotation control ring to the distal part of the handle. This ring achieves 120° of rotation to the left and right, and aims to reduce the effort required by the surgeon.

## Care, maintenance, and sterilization

Flexible ureteroscopes are delicate and expensive instruments and are more fragile than semirigid and rigid ureteroscopes. Proper handling and careful sterilization are very important for extending the life span of these instruments. Fiber-optic flexible ureteroscopes had the

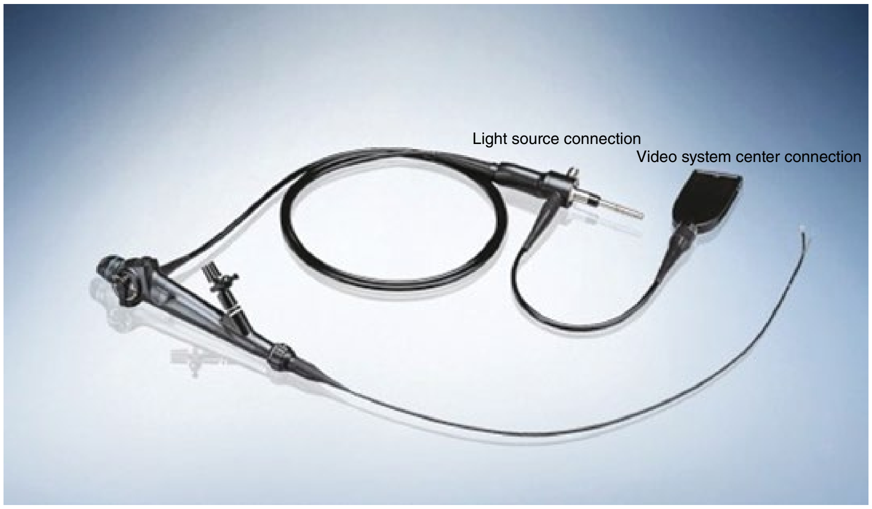

**Figure 42.7** Olympus URF-V connection cables.

disadvantage of easily damageable optic fibers, but the CDC and CMOS technology and lack of optic fibers avoids this flaw in digital ureteroscopes. When even a single fiber of a flexible fiber-optic ureteroscope becomes damaged, the part of the image frame it covers does not appear on the screen, resulting in an incomplete image. Even though this optical fiber problem is solved in the newer technology, there are many other ways these instruments can be damaged. Over-deflection of the instrument, especially during the struggle to reach the lower calyceal system with a narrow infundibulopelvic angle, loose handling, retracting the active laser fiber into the instrument, and inappropriate cleaning sterilization and storage methods are all typical ways in which these instruments can be damaged. Well-trained operating room staff, residents, and specialists are crucial for increasing the life span and durability of flexible digital ureteroscopes.

The experience of the surgeon is a very important factor in the durability of these instruments. A study published by Binbay et al. compared the durability of the Karl-Storz Flex X2 with the ACMI DUR-D, and found equal need for repairs when operations were performed by equally experienced surgeons [1].

Another potential cause of damage is introduction of the laser fiber into the instrument. The laser fiber should be introduced into the instrument only if the instrument is in a fully straight position, which can be confirmed by fluoroscopy. If the laser fiber is introduced when the instrument is deflected, the tip of the laser fiber can cause serious damage to the working channel and to the shaft of the instrument. Another way to improve the durability of both the instrument and the laser fiber is to use high-frequency, low-energy settings during laser fragmentation. This energy setting prevents breakage of laser fiber inside the instrument. Using a safe seal port is also beneficial. Fixing the laser fiber gently by this safe seal port prevents the laser fiber from retracting into the instrument and causing further damage. Before starting laser fragmentation, the focus point of the laser fiber on the stone should be confirmed to avoid damage to the distal end of the instrument and to the epithelium of the renal collecting system. Some areas of the collecting system can be very hard to reach with flexible ureteroscopes and surgeons should keep in mind that there are alternative methods like shock-wave lithotripsy or percutaneous nephrolithotomy to clear these stones. Applying too much pressure and torque on the instrument to reach the calyx will decrease its life span. Offering other treatment modalities to patients is another way to increase the instrument's life span. Placing an access sheath in the ureter before introducing the instrument will also help avoid damage and is highly recommended. After the introduction of the instrument through the access sheath, the outer portion of the instrument should be kept as straight as possible and extreme bending of that portion should be avoided to avoid unintentional laser fiber injuries and to increase the durability of the instrument. Flexible ureteroscopes should be used for appropriate cases and their advantages, disadvantages, and cost-effectiveness should be evaluated on a case-to-case basis.

Proper maintenance and sterilization of these instruments are as important as their surgical handling. A dedicated and experienced sterilization staff is mandatory. Unnecessary bending and deflection of the instrument should be avoided during sterilization. Instruments should be stored in their special cases. Use of formaldehyde should be avoided, as it may cause damage.

Flexible ureteroscopes have the advantage of having a deflection mechanism at their tip. This enables the surgeon to reach the desired calyx and make appropriate movements during surgery. However, this advantage can turn into a disadvantage if over-deflection occurs. This situation typically occurs during maneuvers to reach the lower calyceal system. Karaolides et al. mentioned this problem [14]. Most of the instrument injuries and repair needs occurred after over-deflection. They also mentioned that these instruments needed repair after an average of 18 uses and that appropriate handling and monitored training of new users can decrease the chance of damage and increase the life span of the instruments. As a result, Karaolides et al. concluded that overall longevity depends on correct handling and appropriate training of surgeons. Multescu et al. also noted this [15]. They evaluated patients who underwent flexible ureteroscopy with a Storz Flex-Xc flexible ureteroscope and advised the importance of using a ureteral access sheath, avoiding over-deflection, and relocating lower pole stones when possible. They concluded that these preventions prolonged the life span of the instruments. They also cited the importance of removing the flexible ureteroscope en bloc with the access sheath, to avoid damage to the tip of the instrument if it is deflected and comes in contact with the distal end of the access sheath.

When the ACMI DUR-D was introduced, it had a certain disadvantage during laser fragmentation referred to as the "sunset effect" (Figure 42.8). The tip of the laser fiber appeared as a red light, which indicated the active state of the laser fiber. This red light caused a prominent glare and visual artifact not seen with other flexible ureteroscopes. This sunset effect made it more difficult to focus on the stone and caused trouble for surgeons during stone fragmentation. Surgeons generally overcame this problem by deactivating the red light of the laser fiber, which posed possible damage risk to the instrument if the laser fiber was broken. The surgeon would not be aware of laser malfunction because of the always-inactive

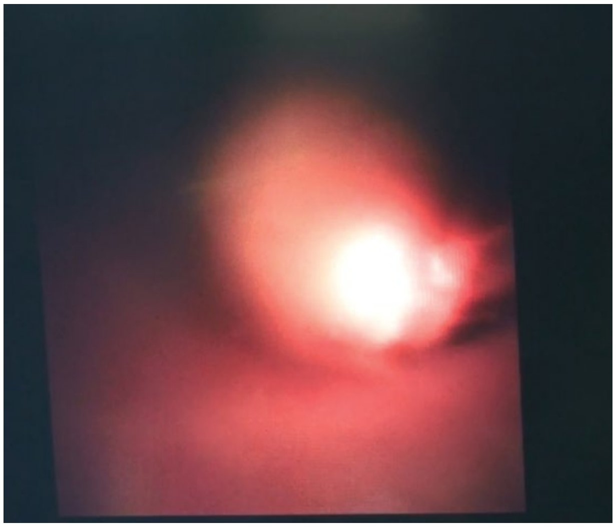

Figure 42.8 Sunset effect during ureteroscopy.

red light. The ACMI DUR-D flexible ureteroscope also caused artefactual images during fluoroscopy screening, but both these unwanted images and the previously mentioned sunset effect have been overcome in newer digital ureteroscopes.

There are other avenues for possible instrument damage during use. Retracting the laser fiber into the instrument during stone fragmentation may cause serious damage to the working channel and inevitably require repair. The traditional way to overcome this problem is referred to as the "safe laser technique" and is achieved by fixing the proximal end of the laser fiber to the entrance part of the working channel by screwing it to the distal part of an adjustable Tuohy-Borst adapter. EPS can also be used to prevent this situation, terminating the laser energy when the laser fiber is retracted into the ureteroscope. Sung et al. evaluated the efficacy of this system in an *in vitro* study and found it highly effective, except in situations of high-density blood concentration [16]. Xavier et al. also evaluated the efficacy of this system in an *in vivo* study and concluded it to be highly effective and able to replace the standard safe laser technique [17].

## Conclusion

Digital technology is widely used in medical and nonmedical fields and it keeps developing day by day. Digital ureteroscopes are being used by urologists with high success and low complication rates. Better imaging quality can reduce operation times. Overcoming the issues about high repair costs of these instruments, developing more effective stone fragmentation methods to treat bigger stones, and creating thinner instruments will replace fiberoptic ureteroscopes with digital ureteroscopes completely.

See accompanying Video 42.1.

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# 43

# Ureteroscopy Working Instruments

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## Introduction

Before the collaborative efforts between engineers and urologists spurred by the birth of endourology in the early 1980s, upper urinary tract diseases were managed through large open incisions and were associated with significant associated patient morbidity [1]. The advent of flexible and semirigid ureteropyeloscopy has lead to less invasive treatment options for the upper collecting system. Over the course of time, lead by the interaction between engineering and medicine, the instrumentation and technique of endourology has continued to be refined and improved.

## Patient preparation

After induction of anesthetic, the patient is placed in a lithotomy position with the ipsilateral leg slightly extended [2]. Although recommended primarily for patients with a moderate risk of thromboembolism [3], we routinely utilize pneumatic compression boots in all patients in the lithotomy position to decrease the risk of deep venous thrombosis and decrease the risk of intra-compartment pressure [4].

The C-arm monitor, video monitor, and holmium laser machine are positioned on one side of the patient such that the surgeon's attention to the C-arm image, endoscopic image, and laser foot pedal are all "in line," requiring little movement of the head but rather subtle movement of the eyes. It is helpful to utilize software that draws the fluoroscopic image into a "picture-in-picture" format on the endoscopic image. Typically a flat-screen monitor mounted on a swivel arm is utilized. The C-arm device is positioned on the other side of the patient to allow for free movement of the image intensifier from the kidney to the pelvis.

On occasion, if there is uncertainty as to whether the pathology may require a percutaneous approach, the patient may be positioned in a prone-split leg position, so that it is easy to proceed with posterior percutaneous renal access if needed [5].

## Ureteral access

The use of a safety wire is encouraged for all urological endoscopic procedures, although some authors suggest it is not needed if active stone basketing is not planned as part of the procedure [6]. Guidewires facilitate and maintain access to the upper urinary tract and may straighten an otherwise tortuous path. The ideal guidewire would require little force to bend in response to obstruction, and a large force to perforate through tissue. These properties were examined in an *in vitro* study with nine commercially available guidewires and the lubricous, soft-tip nitinol Glidewire (Boston Scientific, Natick, MA, USA) was the safest wire for initial access to the ureter, as it is less likely to perforate and more likely to bend before a point of obstruction [7]. Another study has evaluated a new set of straight-tip hydrophilic guidewires that has been recently launched in the market based on the same properties as described later and in comparison to Glidewire (Boston Scientific). The Glidewire and the EZ Glider (Olympus) required the most force to perforate the *in vitro* model and presented the lowest tip bending forces. Moreover, in the same study five stiff wires were also tested and the GlidewireS (Boston Scientific) required the greatest force in the perforation test and the lowest tip bending force, as did the EZ GliderS (Olympus) [8].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

A standard guidewire would also have a fairly stiff midshaft to straighten the ureter and facilitate coaxial passage of other devices (e.g. sheaths, stents). It would have a floppy tip on the external end to facilitate atraumatic back-loading of the flexible ureteroscope if needed. The Bard Sensor guidewire (Boston Scientific) is a hybrid wire that combines these components; a hydrophilic distal tip, shift shaft (nitinol core with polytetrafluoroethylene coating), and floppy proximal tip [9]. We typically utilize a 0.035 inch Olympus UltraTrack guidewire as our initial guidewire to cannulate the ureteral orifice and advance up to the level of the renal pelvis. If resistance is encountered, a 5 Fr open-ended catheter is advanced to the level of resistance under fluoroscopic guidance and retrograde pyelography is performed to delineate the ureteral anatomy. A 0.035 inch straight-angle hydrophilic Terumo Glidewire (Terumo Interventional Systems, Somerset, NJ, USA) is then placed through the open-ended catheter and advanced beyond the site of obstruction. For coaxial passage of ureteral access sheaths and large caliber stents and catheters an Amplatz Superstiff in utilized to minimize the risk of wire buckling or kinking (Boston Scientific).

The Orchestra (Coloplast, Humlebaek, Denmark) is a new hydrophilic guidewire that has demonstrated, in an *in vitro* analysis, similar safety performance while providing a stiff shaft and more lubricous coating when compared to Glidewire [10].

In conclusion, each hydrophilic guidewire has particular properties that can be translated into advantages for a specific case; therefore it is important for the endourologist to be attentive to technological advancements and performance reports.

### Torqueable catheters

At times the ability to guide a wire past a point of particular tortuosity may prove beneficial to establish secure guidewire access. One alternative would be to utilize an angled-tip guidewire and a torque device which attaches to the external end of the wire. Rotating the torque device reorients the tip of the wire to direct it towards the anticipated path of the lumen as outlined on retrograde pyelography. Alternative, a variety of torqueable angled catheters (Kumpe catheter, JB-1 catheter, Cobra catheter) can be utilized to help guide the wire in the correct direction.

## Ureteral access sheaths

Ureteral access sheaths (UAS) facilitate expeditious and atraumatic entry and re-entry to the upper collecting system with the flexible ureteroscope, while eliminating the risk of buckling of the endoscope in the bladder. The use of a UAS has been demonstrated to decrease operative time and cost, minimize patient morbidity, and optimize overall success of flexible ureteroscopy [11]. Specifically, a retrospective case series has demonstrated superior stone-free rates in a contemporary series of patients undergoing ureteroscopy with the use of an access sheath compared to no access sheath [12].

The access sheath also protects the upper urinary tract from increased peak intrarenal pressure even with irrigant fluid pressurized to 200 cm$H_2O$, as it allows efflux of irrigant fluid through the sheath and around the ureteroscope, maintaining intrapelvic pressures below 20 cm$H_2O$ [13]. Finally, some authors have suggested that the use of a UAS decreases the risk of endoscope damage [14]. Conversely, UAS insertion has recently been associated with ureteral injuries of various magnitudes [15], endorsing the importance of knowing the characteristics of each UAS available in the market so as to choose the most appropriate one for a particular case.

*In vitro* and randomized clinical studies have demonstrated that the Cook Flexor® sheath (Cook Urological, Bloomington, IN, USA) is superior with regards to ease of placement, instrument passage, and stone extraction [16], is more resistant to both buckling at the ureteral orifice and kinking after removal of the inner dilator [17], and has one of the largest inner diameters in the most common bending positions of straight and 30° bends, which further facilitates stone extraction [18]. Nevertheless, in a recent *in vitro* study, the Navigator HD (Boston Scientific) was found to be the most resistant to buckling and have the most slippery sheath when compared to other new-generation UAS, whereas Cook Flexor sheaths were the least traumatic [19].

New UAS models have been designed, such as Re-Trace® (Coloplast) and Cook Flexor Parallel® (Cook Urological); both can slide over a stiff guidewire placed only at the tip of the inner sheath (outside the sheath shaft). This new design allows for an easy extraction of the inner sheath without taking out the working wire, which, in turn, becomes the safety wire. Additionally, the Cook Flexor®DL (Cook Urological) UAS offers an additional 3 Fr working channel. The extra working channel can be used for irrigation, to deliver contrast, and for introduction of wires and baskets in parallel to the sheath itself.

A 12/14 Fr UAS is the standard size utilized for adults, as studies have demonstrated that this internal diameter optimizes irrigant flow and intrapelvic pressures [20]. Typically a 35 cm long sheath is utilized for women and 45 cm is utilized in men if the goal is to reach the ureteropelvic junction. If the sheath does not go up the ureter, the inner dilator can be used without the outer sheath to dilate the ureter over a superstiff guidewire. If unsuccessful one might utilize a ureteral balloon (see below) through the sheath or place a ureteral stent to passively dilate the ureter.

## Intracorporeal lithotrite

While a number of different endoscopic lithotrites, such as ultrasonic, electrohydraulic, pneumatic, and laser, have been utilized for ureteroscopic lithotripsy, the holmium laser has become established as the standard of care, due to its efficiency, versatility, and safety. *In vitro* analyses have demonstrated that the holmium laser fragments all stone compositions and produces smaller stone fragments than pneumatic, electrohydraulic, and pulsed-dye (Candela) lithotripsy [21]. While electrohydraulic can cause damage even if fired from several millimeters away, holmium laser can be safely activated at a distance of 0.5–1 mm from the ureteral wall without risk of perforation as the energy is effectively absorbed in the fluid medium [22].

Holmium:YAG laser lithotripsy generates a photothermal process that leads to direct absorption of the laser energy by the stone and thermal combustion. It also creates a vaporization bubble that subsequently destabilizes and decomposes the stone [23]. It has been published in clinical trials that the stone-free rates both at the end of the ureteroscopy and 3 months postprocedure were significantly higher for holmium than either electrohydraulic [24] or pneumatic [25] lithotripsy. Currently, dual-pulse-width laser lithotripsy has shown in *in vitro* studies to cause less stone retropulsion with the same stone fragmentation rates [26].

Laser energy is brought to the target (stones) with the aid of laser fibers, which are thin and flexible, the optimal characteristics for passing through the working channel of a flexible ureteroscope. Studies on performance and safety of commercially available holmium laser fibers demonstrated that the Dornier Lightguide 200 was the most likely of small fibers (200–273 mm) to fracture and damage a flexible ureteroscope, while the Lumenis 272 (Coherent) and the Innova Quartz 400 (Gyrus-ACMI) were the most durable in their size class [27].

The 365 μm laser fiber is more durable and results in the best stone fragmentation efficiency [28, 29]. However, the increase in size leads to a decrease in active deflection of the flexible ureteroscope; only 7–16% of maximum deflection (−9 to −19°) is lost with the 200 μm fiber compared to 18–37% (−24 to −45°) of maximum deflection with the 365 μm fiber [30, 31].

Flexxiva® (Boston Scientific) is a newly designed ball-tip laser fiber. Its atraumatic tip is protective of the working channel and has shown reduced insertion forces when compared to standard, flat-tip fibers [32]. Flexxiva passes through a deflected scope without puncturing or tearing the scope coating [32].

Pneumatic lithotripsy has the advantage, especially in areas where resources are limited, of low maintenance and disposable costs. The disadvantages of pneumatic lithotripsy are the increased risk of stone migration and the inability to apply this modality through a flexible ureteroscope.

Electrohydraulic lithotripsy generates a spark which results in plasma expansion at supersonic speed, propagating a hydraulic shock-wave and cavitation bubble. Collapse of the cavitation bubble leads to a second shock-wave, which if asymmetric leads to formation of a liquid jet. Each of these mechanisms results in stone fragmentation [33, 34]. However, the safety of the device is the primary concern, with one series reporting a 3% conversion rate to open surgery due to ureteral perforation in conjunction with a stone-free rate of only 58% at 3 months [35].

## Ureter-occluding devices

A variety of devices have been developed to prevent stone migration during intracorporeal lithotripsy. The Stone Cone (Boston Scientific) consists of concentric coils which act to prevent proximal retropulsion of stone fragments, and it has proved to reduce the incidence of residual stone fragments >3 mm in size [36]. The 2.8 Fr Cook N-Trap is composed of 24 interwoven nitinol wires that has been shown in *ex vivo* pig ureters to prevent the migration of small plastic beads as small as 1.5 mm [37]. Each device is designed to release any larger fragments as the device is withdrawn. It has been demonstrated that the Stone Cone releases the stone with a mean of 0.19 lb of force while the N-Trap releases the stone with a mean of 0.86 lb of force, suggesting a potential safety advantage with the Stone Cone [38]. More recently, the Percsys Accordion has been launched and was proved in an *in vitro* comparative study to be as safe and efficient as the Cook and Boston Scientific counterparts [39].

*In vitro* studies have evaluated a biogel polymer that is delivered using a 3 Fr ureteral catheter above the stone to occlude the more proximal ureter. The triblock polymer of polyethylene oxide is a liquid at low temperatures and turns into a gel at body temperature.[40] Warm irrigation must be utilized during the procedure, then cold saline is instilled to liquefy the polymer at the completion of lithotripsy. Residual polymer dissolves in urine after 2 hours and is expelled [34]. In a recent randomized clinical trial, Rane et al. reported the successful use of a water-soluble polymer (BackStop) to prevent stone migration during semirigid ureteroscopy. The study showed that this polymer was efficient in stabilizing the stone during laser or pneumatic lithotripsy; moreover, no adverse events were associated with its use compared to conventional ureterolithotripsy [41].

Each of these devices and techniques require additional manipulation prior to ureteral lithotripsy, so the benefit of their use should be weighed against the additional risks of perforation in the face of a large ureteral stone. Specifically, their use may be most warranted in situations where pneumatic lithotripsy is planned and the risk of migration is higher, or if there is significant hydroureteronephrosis above the stone, or if there is limited availability of flexible ureteroscopy to retrieve stones that migrate.

## Stone retrieval devices

A stone retrieval device is essential in ureteroscopy. Each device can be evaluated and distinguished by its ability to be visualized during stone manipulation, to provide radial force to open in the ureter, and to capture, retain, or, if necessary, disengage a stone. Alligator or rat-tooth forceps are preferred by some due to their reversible grasp and reusability; however, the large size and weak grasp impact their effectiveness [41].

Nitinol-based baskets are more versatile due to the unique pliability of the wires and to the flexibility that allows full lower pole deflection of a flexible ureteroscope in the majority of cases [42, 43]. *In vitro* studies have shown that the Cook N-Circle 2.2 Fr (Cook Urological) was the most efficient in stone capturing in a ureteral model while the Sacred Heart Halo 1.5 Fr (Sacred Heart Medical, Minneapolis, MN, USA) was most efficient in a calyceal model compared to 12 other baskets [44–46]. If there are stone fragments adherent to the renal papilla, the Cook N-Circle 2.2 Fr basket wires are more pliable and can be distorted with gentle pressure until they embrace and grab the adherent stone.

The Cook N-Compass (Cook Urological), with its webbed configuration, is designed to optimize the retrieval of multiple small (1 mm or less) stone fragments that may result from lithotripsy of a large burden intrarenal stone.

The Bard Dimension basket has a unique lever that extends two wires to "deflect" the cage of the basket. It has been proposed that this facilitates retrieval from stones in hard-to-reach calyces and facilitate stone release if needed [47]. However, other investigators have reported that this affords no advantage for either stone capture or stone release [48]. The Boston Scientific Graspit and Cook NGage are two devices that have coupled the properties of a three-prong grasper with the entrapment capability of a regular tipless nitinol basket. It has been proposed that they provide a better ability to grasp and release the stone [49].

The 1.5 Fr Sacred Heart Halo has been demonstrated to be the most efficient at stone retrieval of smaller fragments and provides superior irrigation compared to the Microvasive Zerotip 1.9 Fr [50]. In addition, it allows rotation of an engaged stone via a rotary wheel on the basket handle, and simultaneous laser lithotripsy, as a 200 μm laser fiber can be passed alongside the Halo basket, a technique that is utilized if a stone is too large for removal down the ureter. The 1.9 Fr Escape nitinol stone retrieval basket (Boston Scientific) offers the same "side by side" approach, preventing retrograde ureteral stone migration [51]. These two devices are of particular interest in cases of entrapped ureteral or renal stones where laser lithotripsy prior to stone capture cannot be accomplished. Recently the Boston Scientific 1.3 Fr Optiflex basket has been released, and this is currently undergoing evaluations.

## Ureteral balloon dilators

Ureteral balloon dilation is utilized in approximately 5% of cases, when the UAS will not advance to the site of pathology due to ureteral stricture, spasm, or a tight ureteral orifice. Ideally a ureteral balloon would dilate to 100% of the expected diameter regardless of any amount of radial constrictive force. An *in vitro* study compared the dynamics of ureteral balloon expansion under varying extrinsic compressive forces and inflation pressures [52] and concluded that at inflation burst pressure, the Cook Ascend AQ (Cook Urological) was the most reliable balloon, achieving and maintaining over 100% of the expected inflation diameter with minimal pressure and a small coefficient of variation. Not evaluated in this study was the new Bard X-force balloon dilator, which is the only balloon rated to 30 atm inflation pressure.

## Flexible ureteroscopes

Current flexible ureteroscopes offer increased lower pole access through exaggerated active deflection compared to older passively deflecting scopes. Some achieve this by incorporating separate dual-lever primary and secondary active deflection that offers increased unidirectional downward deflections of 270° (Gyrus-ACMI DUR-8-Elite, Stryker Flexvision). Other endoscopes provide increased bidirectional primary deflection of up to 270° using one deflection lever (Gyrus-ACMI DUR-D, Olympus URF-P5, Karl Storz Flex-X2, Richard Wolf Viper). In addition, a dual-channel flexible ureteroscope has been developed which affords the opportunity to hold traction on soft tissue while transecting the tissue with a laser, or the ability to hold a stone in a basket while laser ablating through the second channel (Richard Wolf Cobra®). This endoscope offers superior deflection and irrigation characteristics in particular when larger 2.4 Fr accessory instruments are utilized [53].

A comparative study of the fiber-optic flexible ureteroscopes available in market showed that the Wolf Viper (Richard Wolf Endoscopy, Vernon Hills, IL, USA) provides superior irrigant flow, and better visualization through the unique fused quartz bundle compared to glass fiber-optic bundles [54]. Moreover, the Wolf Viper 7.5 Fr was shown to have twofold greater resolution than the other flexible fiber-optic ureteroscopes [55], and *in vitro* evaluations of scope manipulation have demonstrated that the Wolf Viper is superior at accessing all calyces in a hydronephrotic kidney model [56].

Another critical consideration is the durability of the flexible fiber-optic ureteroscope. It was first evaluated by Afane et al. who noted that despite flexible ureteroscopes being highly efficient in diagnosing and treating upper tract abnormalities, they needed to be repaired after only 6–15 uses, mostly due to problems in the deflection unit [57]. Subsequently, a randomized prospective multicenter study demonstrated that the Gyrus-ACMI DUR-8-Elite was the most durable flexible ureteroscope in 2005 [58]. Another randomized clinical study of the next generation of flexible ureteroscopes demonstrated that the Wolf Viper, Olympus URF-P5, and Stryker Flexvision U-500 flexible ureteroscopes appeared comparable with regard to durability, suggesting that some parity has been achieved between manufacturers [59].

Modern digital flexible ureteroscopes (Olympus URF-V, ACMI DUR-D) offer improved ease of handling and visibility as they have eliminated the light cord and improved optical resolution with complementary metal oxide semiconductor (CMOS) technology. Digital scopes employ light-emitting diode (LED) technology, a durable and cheap cool light, putting aside the traditional xenon light, an expensive and less durable heat-generating light source. The absence of optic fibers in the shaft of the flexible scope allows for better deflection and adds simplicity to the instrument, which may lower costs, improve maneuverability, and result in more durability [60]. However, Knudsen and Ferraro reported that the distal lens of a digital ureteroscope appears to be extremely fragile and prone to breakdown, different to what has been previously reported. The authors concluded that to improve reliability and cost-effectiveness refinements of digital scope design are still required [61]. Interestingly, opposite to the above-mentioned findings, a more recent study looked at the performance and durability of two digital scopes, Flex-Xc® (Karl Storz) and URF-Vo (Olympus), and found that the latest models of flexible digital ureteroscopes demonstrated good maneuverability and visibility, less deflection deficiency, and better visual quality when compared to the Wolf Cobra [62]. Additionally, a prospective randomized trial comparing two digital scopes, DUR-D (ACMI/Olympus) and URF-V (Olympus), showed that both had similar failure rates compared with the fiber-optic scopes, while providing better image quality [63].

## Disposable flexible ureteroscopes

A cost-effective technology is available for retrograde access to the upper urinary tract, and it is based on the premise of a single-use flexible endoscope, which eliminates the need for sterilization between cases.

The first design comprised a reusable fiber-optic cable attached to a handle with a deflection lever, a detachable light source, and an irrigation source. For every new case a sterile 8 Fr sheath is snuggly advanced over the fiber-optic shaft, keeping the latter from touching the patient. This sterile sheath contains a 3.3 Fr working channel and is capable of deflecting along with the fiber-optic cable. [64] It was reported by Boylu et al. that this new modality of endoscope has acceptable active tip deflection, field of view, and flow rate compared to six other flexible ureteroscopes on the market [64]; however, it is advised to use this type of disposable ureteroscope for simple clinical cases only, reserving traditional reusable flexible ureteroscopes for more complex cases.

More recently, the Boston Scientific LithoVue® single-use digital flexible ureteroscope (Boston Scientific) was launched. LithoVue reaches 270° deflection in both directions and has image quality comparable to reusable flexible digital scopes [65]. It has been tested in live porcine models and had demonstrated similar performance to the fiber-optic URF-P5 (Olympus) with better visual quality [66].

The concept of the single-use flexible ureteroscope relies on using always a brand new scope for each case, thus avoiding scope repairs, inconsistent performance, reprocessing, and degradation associated with reusable scopes.

## Endo-irrigation systems

The passage of instruments through the working channel of a flexible ureteroscope can significantly decrease irrigant flow and result in poor visualization. Gravity with or without the assistance of pressure-bag compression is commonly utilized. With the use of a UAS, intrarenal pressures can be maintained below 30 $cmH_2O$ even with systems pressurized to 200 $cmH_2O$ [67]. Alternatively, handheld, foot-pedal-controlled, or automated irrigation systems may be utilized.

An automated irrigation/suction system (Endo-FMS Urology, Future Medical Systems USA, Glen Burnie, MD, USA) incorporates an irrigation roller pump with a suction roller pump (functional during rigid ureteroscopy only) to provide continuous flow and controlled pressure. The Peditrol (EMS Medical Systems, Stroud, UK) is a foot-pedal syringe-based irrigation system that functions by two separate one-way valves, one attached to gravity or a pressure bag and the other attached to a 3 ml syringe secured to the Peditrol foot pedal. The Boston Scientific single-action pump is a 10 ml vacuum syringe that has one-way valves that provide automatic refill of the syringe for immediate access to irrigation fluid.

An *in vitro* study evaluated the impact of stone migration with each system as well as the efficiency of irrigation to clear the operative field of blood, as measured by number of pulses and duration of irrigation. The study demonstrated that, of the hand-held devices, the Boston Scientific single-action pump exerted the weakest impulse on a stone, decreasing the likelihood of dislocating the stone during endoscopic surgery [67]. Although pressurized saline bags were not as efficient at clearing the operative field, they did result in less migration than hand-held or foot-pedal devices.

Recently, a pressurized irrigation system that allows concurrent temperature control, FluidSmart® (Thermedx, Solon, OH, USA), was appraised in an *in vitro* study and shown to be a promising pressurized/warmed irrigation strategy [68].

## Future innovations

Future innovations may lead to higher stone-free rates. Investigators are developing iron oxide microparticles that bind to the calcium component of stones and provide the opportunity for expeditious extraction with a magnet-tipped retrieval device [69]. Alternatively, future innovations may lead to safer procedures. The addition of isoproteronol (a β-1,3-adrenoreceptor stimulant) to the irrigating solution during ureteroscopy relaxes the ureteral smooth muscle, leading to lower intrarenal pressures and may facilitate the passage of fragments, debris, or clots [70].

As technology advances, the scientific world witnesses the introduction of new minimally invasive treatment modalities for a broad scope of diseases. Flexible ureteroscopy is a good example of this, and it has become the standard of treatment for almost any kind of kidney stone. However, it demands training and practice in order to outrun the learning curve and acquire coordinated hand skills. Recently a robotic platform has been designed for flexible ureteroscopy to improve ergonomics, learning, and treatment outcome. To date, new studies have demonstrated encouraging results for robotic flexible ureteroscopy [71, 72].

These are a few futuristic concepts that may lead to better outcomes for the patient and facilitate the procedure for the endourologist. Driven by innovation, endourology will remain a dynamic field, with evolving improvements towards the best clinical practice.

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# 44

# Access to the Ureter: Rigid Ureteroscopy

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## Introduction

With ongoing technological advances in both minimally invasive and noninvasive techniques, there are increasing options for the evaluation and treatment of ureteral pathology. In particular, advances in the miniaturization and optics of flexible endoscopic equipment have dramatically improved the success of endoscopic treatment for proximal ureteral and renal collecting system pathology. Despite these innovations, rigid ureteroscopy demonstrates distinct advantages and retains a key role in the treatment of upper urinary tract pathology.

## Indications for semirigid and rigid ureteroscopy

With larger working channels that allow for enhanced irrigation and passage of larger endoscopic instruments such as biopsy forceps, rigid and semirigid ureteroscopes are the favored approach for access to the distal ureter and treatment of all distal ureteral conditions including ureteral calculi, tumors, and strictures [1, 2]. Classically, the ureter is divided into three segments: the mid ureter overlying the sacrum, and the proximal and distal ureter superior and inferior to the sacrum [3, 4]. In practice, rigid ureteroscopy was occasionally limited by the natural angulation of the ureter over the iliac vessels [5]. Semirigid ureteroscopes, which contain fiber-optic bundles rather than a solid lens, can overcome this limitation by affording a small degree of shaft flexion over the iliac vessels.

For distal ureteral calculi, rigid and semirigid ureteroscopy demonstrate superior stone-free rates compared to shock-wave lithotripsy (SWL) (90–97% vs. 75%, respectively) [2]. Rigid and semirigid ureteroscopy also appear to have stone-free rates comparable to endoscopy with flexible ureteroscopes only (90–97% vs. 93–97%, respectively) [2]. Recent data have also demonstrated that rigid and semirigid ureteroscopy can be used to successfully treat proximal ureteral stones [6]. Although flexible ureteroscopy demonstrates the highest stone-free rate for treating stones at any location in the ureter (95%), rigid and semirigid ureteroscopy demonstrate stone-free rates that are only somewhat lower (85–92%) [6]. This is in contrast to SWL, which demonstrates a stone-free rate for stones at any ureteral location of only 69% [1]. These data emphasize the fact that rigid and semirigid ureteroscopy can be used successfully throughout the ureter and that their use should not be dogmatically limited to the distal ureter. Because of their advantages and relative ease of use, rigid and semirigid ureteroscopy can be the initial modality for accessing the ureter as far proximally as the anatomy safely permits.

## Preoperative considerations

As with any surgical patient, a thorough history and physical examination are key to identifying conditions that may lead to potential intraoperative and perioperative complications [7]. The American Society of Anesthesiologists recommends against the routine ordering of preoperative laboratory studies in patients without risk factors, although this remains controversial [8]. According to guidelines from the American Urological Association, a complete blood count would not be necessary for ureteroscopy as the risk of hemorrhage is very low. Serum creatinine and electrolytes are

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Companion website: www.wiley.com/go/smith/textbookofendourology

necessary if there is suspicion for decreased renal function [1]. With any planned urinary tract instrumentation, preoperative urinalysis and culture should be obtained and culture-specific antibiotics should be prescribed to attempt to sterilize the urine prior to the procedure [1, 9]. In the absence of clinical indications, coagulation studies do not need to be routinely obtained prior to the endoscopic management of stone disease [1, 8]. Indeed, ureteroscopy with holmium:YAG lithotripsy has been shown to be safe and effective in patients on full therapeutic antiplatelet and anticoagulant therapy [10].

Although placing a ureteral stent prior to ureteroscopy to allow passive dilation of the ureter has been shown to lead to decreased operative time and higher stone-free rates [11–13], this is not recommended as a routine practice due to the added costs and diminished quality of life associated with stenting [1].

## Patient positioning

Two positions have been described for ureteroscopy: dorsal lithotomy and modified dorsal lithotomy in which the ipsilateral leg of the ureter being examined is slightly extended and abducted [14] (see Figure 44.1). Immediately after induction of anesthesia, the patient can be positioned according to surgeon preference. Extension of the leg and abduction of the hip minimizes the angle of the ureter over the psoas muscle and therefore facilitates the passage of the rigid or semirigid ureteroscope into the ureteral orifice and proximally into the ureter [15]. In a study by Korkes et al. the modified dorsal lithotomy position resulted in a significant decrease in operative time when compared to the dorsal lithotomy position [14]. Complication and success rates remained similar between both positions.

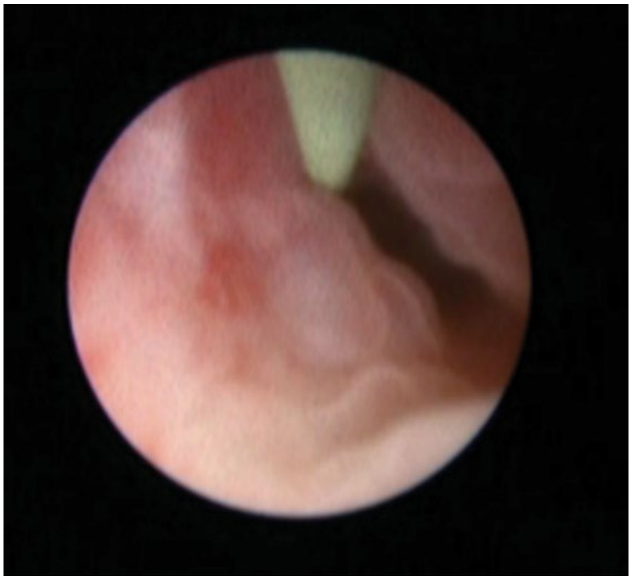

**Figure 44.1** Accessing the ureter with a single wire in place. The safety wire can be tented upwards to facilitate access of the ureter by the rigid ureteroscope inferiorly.

## Equipment for rigid and semirigid ureteroscopy

### Instruments

Although not absolutely required, a rigid or flexible cystoscope is frequently used to place guidewires to facilitate ureteroscopy. Less commonly, guidewires can be placed using the ureteroscope itself. On occasion, however, difficulties associated with an enlarged prostate or edema of the ureter may make cannulation of the ureteral orifice difficult without the wider view of the cystoscope. Difficulties encountered in bypassing an impacted stone can also frequently be overcome by using a rigid cystoscope with a sheath larger than 17 Fr that can accommodate an open-ended ureteral catheter through which multiple wire types can be exchanged prior to placement of the ureteroscope within the ureter.

Rigid and semirigid ureteroscopes are available in a variety of sizes that range from 4.5 to 12 Fr and have working channels that range from 2.3 to 6.4 Fr [16]. There are typically one or two working channels. With two working channels, a constant flow of irrigation can be maintained despite placement of working elements such as laser fibers or stone retrieval baskets.

### Guidewires

Initially developed for vascular procedures, guidewires have become an essential part of upper urinary tract endoscopy [17]. Guidewires are often used as the first means of accessing the ureter and the collecting system. A number of different guidewires are available with different core designs, diameters, and coatings. Selection of a particular guidewire depends upon its intended use.

Guidewires typically have soft, flexible tips to prevent tissue damage [18]. They are generally made up of two components: an outer polytetrafluoroethylene (PTFE) coating, which provides for a hydrophobic surface that is more easily handled, and an inner steel core which determines the rigidity and flexibility of the wire [18]. Nitinol (nickel-titanium) can be substituted for the inner core and allows resistance to kinking as opposed to the stainless steel core wire which can be permanently bent rather easily [17, 19]. Guidewires range in a diameter from 0.018 to 0.038 inches, with the majority of wires used in ureteroscopy being 0.035 and 0.038 inches. Larger-diameter wires provide increased stiffness at the potential cost of impaired irrigation flow should the wires need to be passed through a flexible ureteroscope. With the multiple larger diameter working channels of rigid and semirigid ureteroscopes, decreased flow is not typically a concern when flexible ureteroscopy is not contemplated.

Standard stainless steel/PTFE wires and nitinol/PTFE wires are well suited for obtaining and maintaining ureteral access during uncomplicated ureteroscopy. Hydrophilic wires have low-friction characteristics that are useful for negotiating beyond a ureteral obstruction such as that due to an impacted stone or a ureteral stricture. As hydrophilic wires typically lack the stiffness and friction required for easy handling, they are typically not used as safety wires and should be exchanged for a standard wire once an obstruction has been bypassed. Stiffer wires (Amplatz style) are useful for preventing buckling or kinking of wires while placing dilators and access sheaths [20].

### Irrigation devices

Pressure irrigation systems are necessary for visualization in the upper urinary tract as gravity irrigation is typically insufficient to distend the ureter and collecting system through the small working channels of ureteroscopes. Pressure irrigation also helps to clear the endoscopic field of stone fragments, blood, and debris [21]. Due to the risk of systemic absorption from pressure irrigation and/or ureteral perforation, normal saline is the irrigant of choice to prevent electrolyte disturbances [22, 23]

Commonly used commercial irrigation devices are syringe-style pumps (Single Action Pumping System, Boston Scientific), bulb-style pumps (Pathfinder, Utah Medical), and hands-free foot pumps (Flo-Assist, Nortech). Each of these systems provides pressure irrigation in a pulsatile manner. Bulb pumping appears to be associated with less operator hand fatigue compared to syringe irrigation while syringe irrigation appears to allow finer titration of irrigation flow [24]. All three systems have the disadvantage of requiring an assistant to provide the pressure irrigation. Furthermore, the quality of irrigation is dependent upon operator technique and operator fatigue.

Pressure irrigation can also be achieved with a simple pressure bag or a pressure irrigation system such as a Level 1 Normoflo irrigator (Smiths Medical). Such irrigation systems have the advantage of maintaining constant pressure and continuous flow without the need for an assistant. When such systems are used, the target irrigation pressure is 150 mmHg. Once the target pressure has been reached within the collecting system, a standing column of fluid is theoretically established such that retropulsion of stone fragments is diminished relative to manual, pulsatile irrigation. In addition, manual irrigation, in which pressures are not regulated, can generate potentially greater irrigation pressures that could lead to increased risk of sepsis in infected systems. It is also important to use warm irrigation to prevent hypothermia during prolonged endoscopic cases. The Level 1 irrigator has the added benefit of warming the irrigant as it passes through the device.

### Fluoroscopy

Intraoperative fluoroscopy is necessary to confirm appropriate placement of guidewires and stents. Fluoroscopy is also useful for mapping the upper urinary tract with pyelography, identifying calculi, and assessing progress during the procedure [25]. Fluoroscopy can be accomplished with a standard C-arm or a fixed fluoroscopy table. With the advent of video monitors, most urinary tract endoscopy is now performed in the standing position. A C-arm, which has its radiation source below the table, scatters radiation predominantly toward the floor, thereby reducing a standing surgeon's head and upper torso radiation exposure relative to a fixed fluoroscopy table that involves a radiation source above the table [26]. Regardless, personal protection including lead aprons, thyroid shields, and leaded eyewear should be worn when in close proximity to the fluoroscopy unit.

## Accessing the ureter

### Cystoscopy and placement of a safety wire

A rigid or flexible cystoscope is typically used for the initial placement of a safety wire into the ureter. Immediately prior to guidewire placement, a thorough assessment of the bladder for abnormal pathology should be done. Safety wire placement is recommended to allow for rapid re-access to the ureter or stent placement, particularly in the event of an iatrogenic ureteral injury such as ureteral perforation necessitating early termination of the procedure [1, 2, 27].

For placement of a safety guidewire, a 21 or 22 Fr rigid cystoscope with a 30° lens is placed as close to the ureteral orifice as possible to minimize deflection of the wire over the prostate and bladder neck. The cystoscope may be turned up to 180° to further minimize the angle of approach to the ureteral orifice. A 5 or 6 Fr open-ended ureteral catheter can be employed to further direct the floppy tip of the wire into the ureteral orifice. With an open-ended ureteral catheter, a retrograde pyelogram can be performed to identify the course of the ureter and any anatomic abnormalities such as tortuosities, stones, or strictures [28]. A retrograde pyelogram is not always necessary if a guidewire passes easily and coils uneventfully in the renal pelvis. If tortuosities or obstructing stones are encountered, a hydrophilic wire with an angled tip may be negotiated beyond this area and exchanged for a standard safety wire after advancing the open-ended ureteral catheter beyond the difficult area [29]. Should a safety wire not be able to be placed beyond a tortuosity or impacted stone, the wire may be left distally and a rigid ureteroscope passed into the ureter for direct visualization of wire placement and possible treatment of the obstruction to allow adequate safety wire placement. If purulent drainage from the ureter is noted after wire placement or cannulation of the ureter, the procedure should be aborted to prevent potentially serious infectious complications. A urine culture should be obtained and drainage of the renal unit with either a stent or nephrostomy tube should be performed [1]. The patient should subsequently be treated with culture-specific antibiotics and the procedure performed at a later date.

If the patient has been previously stented and the stent does not appear encrusted, the stent may be withdrawn and the safety wire passed through the stent. Should significant edema of the ureteral orifice be encountered, placement of a safety wire alongside the existing stent prior to its removal would be recommended to avoid the situation in which access to the ureter is lost and the ureter cannot be recannulated.

### Ureteroscope insertion

After appropriate placement of a safety guidewire, the bladder should be drained to reduce compression and angulation of the intramural ureter and to prevent over-distension of the bladder during ureteroscopy [28]. A rigid or semirigid ureteroscope may then be passed into the ureteral orifice. Typically, the ureteroscope is passed underneath the safety wire as this maneuver allows the ureteral orifice to be tented open. Occasionally, the ureteral orifice is too narrow to permit passage of the ureteroscope easily. In this situation, a second guidewire may be placed through the working channel of the ureteroscope into the ureter (see Figure 44.2). The ureteroscope is then advanced between the two wires, safely and gently dilating the ureteral orifice [28] (see Video 44.1)

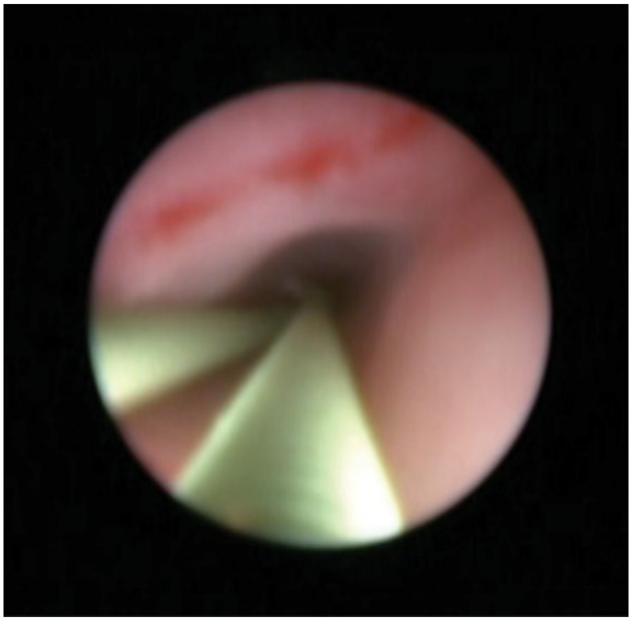

**Figure 44.2** Accessing the ureter with two wires in place. After previously placing a safety wire, a second wire can be placed through the working channel of the ureteroscope into the ureter. The ureteroscope can then be gently advanced between the two wires.

### Ureteral dilation

It is estimated that a difficult ureter will be encountered in 8–11% of patients who are undergoing ureteroscopy without prior stent placement [30]. If the ureteroscope does not pass easily between two wires, a stent may be placed and the procedure aborted to allow passive dilation of the ureter. Alternatively, a tight ureteral orifice and/or ureteral stricture can be dilated rapidly with a 5 mm balloon. The balloon dilator is passed over the safety wire and guided into a position where the balloon markers are above and below the area of narrowing. This can be done through the cystoscope or over a wire under fluoroscopic guidance only. The balloon is then inflated with contrast and the loss of "waisting" at the stricture is visualized fluoroscopically. A retrospective review of ureteral dilation with an 18 Fr balloon by Kuntz et al. demonstrated a 95% success rate for completion of ureteroscopy in a single stage with a low overall complication rate of 8% and a ureteral stricture rate of only 0.7% [31]. Another alternative is the use of coaxial ureteral dilators placed over a wire.

## Altered anatomy

On occasion, anatomical variants are encountered that may make ureteroscopy more challenging. These variants may be congenital, the result of prior treatment, or acute reaction to stone disease and typically involve the ureteral orifice.

### Ureterocele

A ureterocele may be found incidentally during attempted ureteroscopy, frequently in the setting of an obstructing ureterovesical junction calculus. Due to the pinpoint opening of most ureteroceles, balloon dilation or incision either with a cold knife or holmium laser may be required to gain access to the ureter. This is typically done after placing a safety wire to ensure that access to the ureter is not lost after incision. When incising, a low transverse horizontal incision is preferred to prevent subsequent vesicoureteral reflux [32, 33].

### Ureteral reimplantation

Ureteral reimplantation is often performed for the treatment of pediatric vesicoureteral reflux, ureteral stricture disease, and ureteral trauma. Such procedures have the potential to significantly alter trigonal anatomy making endoscopic procedures more challenging. With the Glenn–Anderson ureteral reimplant technique, the ureteral orifice is advanced distally toward the bladder neck [34]. This technique is associated with relative success in obtaining subsequent ureteroscopic access [35]. Of particular concern is the Cohen cross trigonal technique in which the ureteral orifice is relocated to the contralateral side of the trigone and results in an acute angle of approach to the ureteral orifice from the bladder neck [36]. The ureteral orifice in this case can be cannulated with an angled-tip hydrophilic guidewire and open-ended ureteral catheter. Once the open-ended catheter is passed beyond the distal ureter, the hydrophilic wire is exchanged for an extra-stiff wire in order to straighten out the distal ureteral tortuosity [37]. Even if access to the ureter is achieved, ureteroscopy for calculus disease may still be unsuccessful as stone fragments may be unable to pass through the tunneled portion of the ureter [35]. When ureteral access is unable to be achieved, a percutaneous antegrade approach may be necessary.

### Urinary diversion

Urinary diversion poses significant problems for ureteroscopy. These difficulties stem primarily from difficulty locating the ureteroenteric anastomoses [38]. For patients with neobladders or continent catheterizable reservoirs, the redundancy of the reservoir and the presence of an afferent limb typically preclude identification of the ureteroenteric anastomoses. Ileal conduit urinary diversions are somewhat easier to negotiate, with the ureteral orifices being identified at a conduit's most proximal point. Although rigid cystoscopy can be performed with a urinary diversion to place access wires, the additional degrees of movement afforded by flexible cystoscopes or flexible ureteroscopes are useful for identifying and accessing the ureteroenteric anastomoses [38]. Intravenous dyes such as fluorescein, indigo carmine, and methylene blue are also useful in identifying ureteroenteric anastomoses. However, these dyes may be less effective in the setting of an obstructive pathology for which ureteroscopy is being undertaken. Even when ureteral access is achieved, passage of a rigid ureteroscope through the tortuous course created by the urinary diversion is frequently not feasible and retrograde ureteroscopy with a flexible ureteroscope or antegrade ureteroscopy is necessary.

### Stone impaction at the ureterovesical junction

Occasionally, an obstructing stone at the ureterovesical junction can obscure the ureteral orifice and/or prevent placement of a safety wire. The ureterovesical junction and the intramural ureter can also present difficulties in fragmentation of a stone due to the decreased ability to distend this segment with pressure irrigation. If the stone is visible, an attempt to dislodge the stone proximally into a more dilated area of the ureter may be made with the rigid ureteroscope. If this is unsuccessful, laser fragmentation can be performed until the stone can be dislodged. If the ureteral orifice and stone cannot be visualized due to reactive edema, the laser fiber can be used to probe the expected location of the ureteral orifice overlying the calculus bulge. Where the hard calculus can be appreciated in this manner, an incision with the laser can be made to reveal the stone. In all situations, a safety wire should be placed as soon as the stone is dislodged proximally.

## Conclusions

Due to technical advantages unique to rigid ureteroscopy, rigid and semirigid ureteroscopy continue to be integral to the treatment of ureteral pathology, particularly in the distal ureter. While more proximal ureteral conditions may be more successfully treated with flexible ureteroscopy overall, rigid ureteroscopy is not precluded from the proximal ureter. Rigid ureteroscopy may be performed in the proximal ureter as long as the anatomy safely permits. Rigid ureteroscopy should therefore always be considered as complementary to flexible ureteroscopic techniques.

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# 45

# Access to the Ureter: Flexible Ureteroscopy

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## Introduction

Retrograde flexible ureteroscopy (URS) is a widely utilized technique for evaluation and treatment of upper urinary tract pathology, both benign and malignant. Technologic improvements (e.g. smaller-caliber ureteroscopes, greater active deflection) have expanded the role of flexible URS for the management of these processes, including urolithiasis, ureteral stricture disease, and upper tract urothelial or transitional cell carcinoma (TCC). Obtaining ureteral access for flexible URS is typically straightforward, but can be challenging depending on anatomic and disease factors.

In this chapter, we review the preoperative evaluation of patients undergoing flexible URS, preparation of the operating room, and techniques for standard and difficult access. We also review the role and technique for ureteral access sheath (UAS) placement to enable rapid and safe re-entry into the ureter, particularly in the management of stone disease.

## Preoperative evaluation

A thorough history and physical examination should be performed preoperatively. History details that may illuminate an increased risk of difficult access should be elicited. Advance knowledge of these risk factors allows for preoperative planning as well as appropriate counseling of patients regarding risks and the possibility of failed access.

Specific aspects of the past medical history should be emphasized. History of benign prostatic hyperplasia and/or bladder outlet obstruction should be elicited. A large occlusive prostate may impede bladder access and, if friable, may impair visualization secondary to bleeding. A large intravesical median lobe may obscure visualization of one or both ureteral orifices. Chronic bladder outlet obstruction may also cause bladder trabeculations or diverticula, which may distort intravesical anatomy and hinder the identification of the orifices. A history of pelvic or retroperitoneal radiation, or trauma, may increase the likelihood of scar tissue formation, leading to tissue or anatomic distortion. Additionally, history of prior abdominal or pelvic radiation can increase the risk for ureteral stricture formation following ureteroscopic intervention. Large abdominal masses (e.g. abdominal aortic aneurysms, or colorectal, uterine, or ovarian pathology) should be noted as they may cause extrinsic compression of the ureter and/or deviation from its normal course. Patients with retroperitoneal fibrosis, which may be secondary to numerous processes (e.g. trauma, medication-related, idiopathic), may also have narrowing of the ureter.

Surgical history pertaining to the urinary tract should be reviewed. Prior open or endoscopic interventions may increase the risk of ureteral stricture disease and thus make gaining access more difficult. Prior surgery may alter anatomy, including ureteral reimplantation. Reimplantation may also convey risk of vesicoureteral anastomotic stricture or reflux. Review of prior operative reports may guide access planning regarding location of the new orifice. Prior urinary diversion surgery similarly requires ureteral reimplantation, which can make a retrograde approach technically challenging and has a potential risk of ureterointestinal anastomotic stricture. Finally, prior abdominopelvic (e.g. colorectal surgery, hysterectomy/salpingo-oophorectomy) or retroperitoneal surgery (e.g. abdominal aortic aneurysm repair, retroperitoneal lymph node dissection) can lead to stricture disease from injury to or devascularization of the ureter.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

Other pertinent details of the patient history include use of anticoagulants or antiplatelet agents. Often these agents can be stopped in consultation with a cardiologist or internist; however, in certain instances patients cannot safely stop these medications and the procedure should be performed as atraumatically as possible. Ureteral dilation techniques should be avoided when operating on patients who are actively anticoagulated. If there is difficulty with access to the ureter, a ureteral stent should be placed to allow for passive dilation prior to definitive treatment. There is evidence that ureteroscopic interventions in patients taking these agents are safe, particularly in the management of stone disease [1–3].

Another important detail of the history is whether a patient demonstrates signs or symptoms of urinary tract infection, or risk factors for colonization of the urinary tract. Patients should be treated to clear an acute infection prior to surgery. Those with colonization should be placed on culture-specific antibiotics prior to surgery to minimize risk of urosepsis with instrumentation.

Informed consent is necessary prior to proceeding to the operating room. Risks and benefits of the proposed surgery should be discussed with the patient preoperatively; these include, but are not limited to, bleeding, infection, injury to the kidney, ureter, and adjacent structures, and ureteral stricture. Patients should be informed of the risk of failed access and the possible need for ureteral stent placement with abortion of the procedure and/or percutaneous nephrostomy tube placement. The more thoroughly patients are counseled preoperatively, the greater trust will persist postoperatively if these situations occur, and subsequent counseling of the patient will be facilitated.

## Preparation of the operating room

Prior to flexible URS, the operating room staff should confirm that all potential instruments and disposable equipment are available, and the surgeon should confirm that this equipment is correct (Table 45.1). The steps of the procedure should be anticipated and the scrub table organized to ensure a smooth succession of events. Additional equipment for difficult access cases may also be required at the discretion of the surgeon (Table 45.1) and should be readily available. If access fails, the patient may require a percutaneous approach or nephrostomy tube, which can be placed by the urologist or interventional radiologist.

Balloon dilators are useful for accessing anatomically tight or strictured segments of ureter. Dimensions of available standard ureteral balloon dilators vary by manufacturer and include balloon lengths of 4–10 cm, inflated balloon diameters of 12–18 Fr (4–6 mm), and dilation pressures up to 30 atm. We typically use 4, 6, or 10 cm dilators with 12–15 Fr balloons inflated to 12 atm under fluoroscopic guidance ideally until no significant "waisting" is noted.

**Table 45.1** Equipment for standard and difficult ureteral access for flexible URS.

| Type of access | Equipment |
|---|---|
| Standard access | Rigid cystoscope (30 and 70° lens) with light cord, camera, and irrigation fluid (Albarran bridge if desired)<br>Nitinol guidewires: 0.035 or 0.038 inch (hybrid guidewire if desired – polytetrafluoroethylene [PTFE]:nitinol with hydrophilic tip); at least two wires (working and safety)<br>Dual-lumen or coaxial catheter<br>Contrast medium (50:50 ratio with saline) for retrograde pyelography with syringe for injection<br>If retrograde pyelogram needed before access to upper tract performed → 5 or 6 Fr open-ended catheter or cone-tip catheter<br>UAS at the discretion of the surgeon<br>Flexible ureteroscope (tested to ensure clear lens and adequate deflection)<br>Ureteral stent (double-J or pigtail) with different calibers and lengths (or multi-length) |
| Difficult access | Flexible cystoscope<br>Semirigid ureteroscope<br>Angiographic catheters with an angled tip<br>Balloon dilators<br>Serial dilators<br>Angled-tip and straight hydrophilic guidewires (with torque device if needed)<br>Various sizes of wire (e.g. 0.025 inch) |

Fluoroscopy (C-arm or table) is required to guide positioning of wires, catheters, and UAS, and to enable retrograde pyelography. Placement of the flexible ureteroscope can be performed with fluoroscopic guidance over the working guidewire up to the level of disease, e.g. stone or stricture, or can be performed under direct vision. Fluoroscopy is also useful for identification of radiopaque stones and following the fragmentation of a stone during laser lithotripsy. The surgeon should confirm that fluoroscopy is correctly positioned and can be easily manipulated prior to surgery.

## Standard retrograde access for flexible ureteroscopy

Depending on institutional protocol, the surgical site (i.e. side for URS) should be marked by the operating surgeon. A time out should also be used that confirms all safety mechanisms are in place and all operating room staff are in agreement with the proposed procedure.

The type of anesthesia will depend on a detailed conversation between the anesthesiologist, surgeon, and patient, and may be influenced by numerous factors (e.g. cardiopulmonary status of the patient, need for apnea during the procedure, patient preference).

The patient is positioned in the dorsal lithotomy position, and prepared and draped in standard sterile fashion. A single dose of prophylactic antibiotic is administered prior to the procedure if the preoperative urine culture is negative. If the patient has a positive preoperative urine culture, they should be treated with a full course of culture-specific antibiotics prior to intervention. Sequential compression devices should be placed on the patient's lower extremities prior to induction of anesthesia whenever used. Alternatively, deep venous thrombosis prophylaxis can be given with subcutaneous heparin or low-molecular-weight heparin.

The bladder is initially entered with a rigid cystoscope. After cystoscopic evaluation of the bladder, the relevant ureteral orifice is identified and cannulated with a guidewire. The guidewire may advance through the end of the rigid cystoscope directly into the orifice, or a 5 Fr open-ended catheter may be required to provide the correct angle for intubation of the orifice. Keeping the camera stationary, the scope can be rotated to change the angle at which the wire advances. When advancing the wire into the orifice, it is important to ensure the end of the cystoscope sits directly at the orifice to prevent buckling or curling of the wire in the bladder. We prefer to use a 0.035 or 0.038 inch × 150 cm hybrid guidewire because its flexible, hydrophilic tip minimizes trauma to the upper urinary tract, it allows easy manipulation around upper urinary tract stones and obstruction, it is kink-resistant, and it has sufficient rigidity to act as a working wire. The wire is advanced gently under fluoroscopic guidance into the kidney (Figure 45.1), minimizing trauma to the collecting system which can lead to mucosal bleeding and obscure visualization. This is particularly important when URS is being performed for evaluation of upper tract TCC as wire trauma may confound evaluation of TCC or carcinoma *in situ*. Also, patients who are anticoagulated or have a bleeding diathesis may have significant bleeding from wire trauma; thus extra caution is necessary in these patients.

If the wire does not advance easily, a retrograde pyelogram should be performed with an open-ended catheter (or with the use of a dual-lumen catheter placed over the initial guidewire) to delineate the ureteral anatomy (e.g. evaluate for presence of ureteral tortuosity, narrowing/stricture, or obstruction). Methods of addressing an inability to advance the initial wire are discussed below.

With the first wire in the correct position, the bladder is emptied through the cystoscope (side port or sheath) to maximize the likelihood of successful passage of a catheter and/or ureteroscope through the intramural ureter. At this time, we typically recommend placement of a second wire as a safety wire. A safety wire allows for ureteral stent placement at any time should there be iatrogenic injury or an inability to proceed. It will also prevent loss of access to the upper urinary tract during the surgery. A dual-lumen or coaxial catheter can be placed over the initial wire into the distal ureter under fluoroscopic guidance and the second wire is advanced alongside the first wire to the renal pelvis (Figure 45.2). A retrograde pyelogram can be performed through the dual-lumen catheter prior to second wire placement if it has not been performed earlier. Alternatively, a second wire can also be placed under direct vision through the

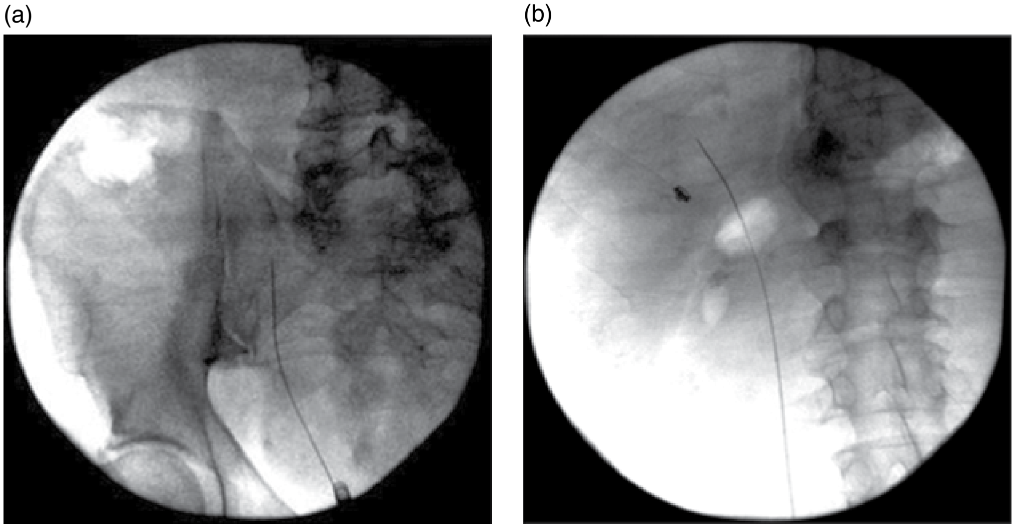

**Figure 45.1** Guidewire advanced to (a) mid ureter and (b) level of kidney.

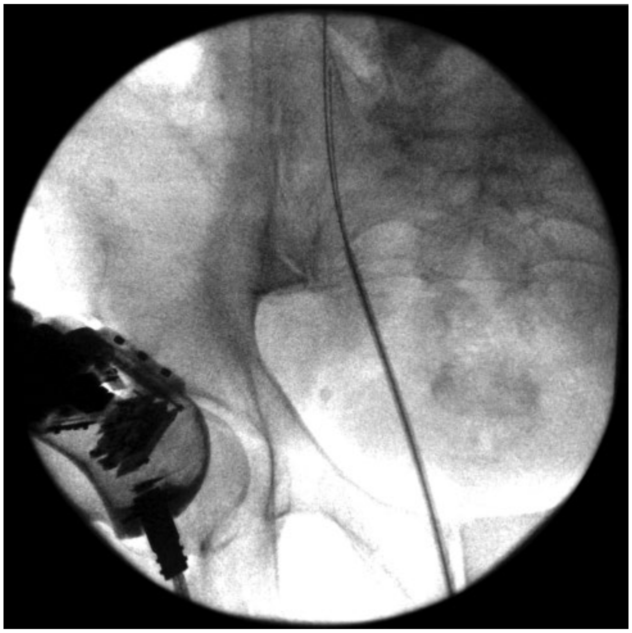

**Figure 45.2** Dual-lumen catheter with two wires advanced.

cystoscope adjacent to the first wire. The benefit of using a dual-lumen 10 Fr catheter or 8/10 Fr coaxial catheter is that either will gently dilate the distal ureter, allowing for easier passage of the flexible ureteroscope.

After the second wire is placed, the dual-lumen catheter is removed and one wire is secured to the drape as a safety wire. The safety wire should be secured away from the immediate surgical field to minimize risk of dislodgment. At this time, the flexible ureteroscope is placed over the working wire and advanced to the level of interest under fluoroscopic guidance.

## Difficult retrograde access for flexible ureteroscopy

Certain situations can confound efforts to obtain ureteral access. Below we discuss methods of troubleshooting these scenarios.

### Ureteral orifice(s) cannot be visualized

There are various reasons why ureteral orifices may not be readily visible on cystoscopic evaluation: distorted anatomy (e.g. bladder trabeculations, mucosal edema, neoplasm), obscured anatomy (e.g. intravesical median lobe), congenital anomalies (e.g. ureteral ectopia), or prior surgery (e.g. ureteral reimplantation, resection). If there is anatomic distortion, an ampule of indigo carmine or methylene blue can be administered intravenously and efflux of dye can be sought. It is important that patients are well hydrated, have adequate renal function, and do not have significant obstruction of the ipsilateral kidney to ensure the dye is rapidly excreted. Intravenous furosemide can be concomitantly administered to expedite excretion from the kidneys. If there is obscured anatomy from a large median lobe, a rigid cystoscope with a 70° lens may enable identification of the orifice. A flexible cystoscope can also be utilized to identify the orifice beneath the lobe and in patients with a very high-riding bladder neck, which prohibits bladder access with a rigid scope. Accessing the orifices with flexible cystoscopy can be technically challenging as irrigant flow and visibility are inferior to those with a rigid scope, and achieving the correct angle for access of the orifice may be difficult. Additionally, the use of an Albarran deflecting bridge or an angled-tip angiographic catheter (e.g. 5 Fr Berenstein catheter) can help deflect guidewires into a ureteral orifice that is at an acute angle or distorted secondary to bladder and prostate anatomy.

If the orifices cannot be found, there should be consideration of congenital anomalies or prior surgical history that may have altered their position. Preoperative imaging can be helpful in delineating upper tract anatomy, including ectopic ureters; urographic imaging is particularly helpful. Clinical history may reveal the possibility of variant or altered anatomy, e.g. history of vesicoureteral reflux disease, incontinence, or chronic pyelonephritis. Review of prior operative reports may provide guidance regarding location of ureteral orifices after ureteral reimplantation.

### Guidewire will not advance through the ureteral orifice

The tip of the cystoscope should be placed immediately at the ureteral orifice to prevent kinking of the wire. A 5 Fr open-ended catheter can be placed through the cystoscope and used as a guide and/or support for the wire, creating the desired angle for access and preventing kinking. An angiographic catheter can also be used for this purpose. Use of an open-ended catheter also allows for retrograde pyelography; the catheter can be placed at the orifice and contrast injected to determine if there is patency of the orifice and/or distal ureter. With the open-ended catheter at the orifice, either a straight or angled-tip guidewire (nitinol or hydrophilic) can be gently advanced and manipulated. If there is concern for a stricture at the orifice or an impacted stone, a rigid ureteroscope can be used to directly access the orifice and wire placement under vision can be attempted. If there is an impacted stone, it can be treated to expose and access the proximal ureteral lumen and enable wire placement; however, without a safety wire this should be done with great care. If wire access cannot be achieved and there is clinically significant obstruction, the procedure should be aborted and a percutaneous nephrostomy tube placement should be performed.

### Guidewire will not advance through the ureter to the kidney

If the wire has successfully accessed the ureteral orifice but will not advance past a level of the ureter, an open-ended catheter should be placed over the wire and a retrograde pyelogram performed to ensure there is no stricture, ureteral injury/false passage, obstructing lesion or stone, or severe tortuosity/J-hooking. This can also be performed with a dual-lumen catheter which can be advanced over the guidewire that has already been placed. If the open-ended catheter will not easily advance over the wire, it is possible that the wire has been placed submucosally, and it should be withdrawn and replaced into the true lumen. If there is a transition point for obstruction or severe tortuosity, the open-ended catheter can be placed to that level to prevent buckling of the wire as it is advanced. An angled-tip hydrophilic guidewire can be useful if there is a severe angle to negotiate. Surgeon experience is critical to understanding how much pressure can be safely applied while advancing the wire. If there is obstruction and concern for a pinpoint stricture, an experienced surgeon may place the ureteroscope over the wire to the level of interest and then attempt to advance the wire under vision. Also, if there is a severely impacted stone and inability to obtain proximal access with a wire, an experienced endourologic surgeon can attempt to treat the stone with caution to expose the proximal ureter and enable safety wire placement. Importantly, without a safety wire in place these maneuvers can worsen obstruction, cause damage to the ureter without an option for immediate stent placement, and necessitate percutaneous nephrostomy tube placement.

If a guidewire cannot eventually traverse the level of obstruction, the procedure should be aborted and nephrostomy tube placement should be considered. If access is achieved but traumatically, a retrograde pyelogram should be performed and ureteral stent placement with deferral of the procedure should be considered if there is extravasation.

### Initial guidewire placement was successful, but a coaxial/dual-lumen catheter or ureteroscope will not advance through the ureteral orifice

First ensure that the bladder is empty; it is not uncommon to neglect to empty the bladder before removing the cystoscope. Careful twisting and advancement of the dual-lumen catheter, which has a tapered tip, can often enable access into the distal ureter. While advancing the catheter over a wire, it is important that the wire remains stationary (secured by the surgeon or an assistant) to allow the catheter to advance without buckling. Inability to advance the catheter may indicate anatomic narrowing or stricture at the ureteral orifice. This necessitates a decision whether a ureteral stent should be placed and the procedure deferred for 5–7 days for passive dilation of the ureter, or whether ureteral dilation should be performed. Fuller et al. determined the failure rate of primary URS in the previously unstented ureter was 7.7% in their multi-institutional study; this rate decreased to approximately 4% when the distal ureter was dilated with balloon or serial dilators [4]. Young female patients and proximal ureteral stones were less likely to be able to be accessed primarily. Viers et al. showed a 16% incidence of access failure that required prestenting at the time of URS. They showed a 4.4% increased risk of requiring prestenting based on a preoperative computed tomography urogram finding of <50% ureteral opacification [5].

Our algorithm usually begins with retrograde pyelography with a dual-lumen catheter. If multiple areas of the ureter appear narrow in addition to the ureteral orifice, we place a ureteral stent and return to the operating room in approximately 1 week. If the ureteral orifice or intramural tunnel appears to be discretely narrow or strictured, several dilation techniques are available.

Ureteral balloon dilation can be performed by advancing a balloon dilator over the wire and ensuring the radiopaque markers span the orifice/intramural tunnel (Figure 45.3). The balloon is filled with contrast and held at 12 cm$H_2O$ for approximately 1 minute. The balloon is then deflated and removed. The dual-lumen catheter can then be advanced over the wire to allow for passage of the second working guidewire (if not already placed). The ideal balloon dilator for this region is 4 cm × 12 Fr, which minimizes trauma to the ureter and the risk of extravasation, and has not been shown to increase the risk of ureteral stricture formation [6, 7]. Active dilation can also be performed with serial dilators (e.g. Nottingham dilators). Finally, dilation can be performed under direct vision with a semirigid ureteroscope.

While dilation may enable access to the ureter, it can be traumatic and cause edema and/or urinary extravasation; thus, it is important to ensure a ureteral stent is placed at the end of the case if dilation is performed. When treating a stone, it is important to be aware that, if a distal stricture is present, residual fragments may not pass after stent removal, and risk of an obstructing fragment or steinstrasse may be increased. A ureteral stricture should be ideally treated prior to the treatment of a more proximal stone, and allowed to heal prior to lithotripsy. Concomitant treatment can increase the risk of submucosal stones or stone granuloma formation, which can lead to stricture disease.

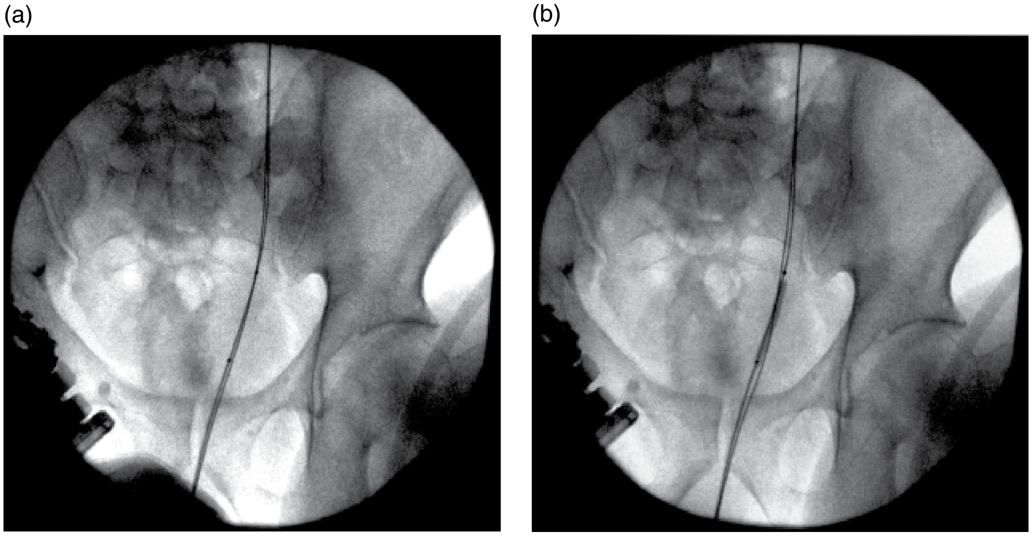

**Figure 45.3** Balloon dilator. (a) 4 cm × 12 Fr ureteral balloon dilator positioned in the intramural tunnel. (b) Balloon expanded to dilate distal ureter/intramural tunnel.

If a dual-lumen catheter will not advance despite balloon dilation, or if balloon dilation is contraindicated (e.g. bleeding diathesis), a ureteral stent should be placed to allow passive dilation of an anatomically tight ureteral orifice or healing of a dilated stricture, and/or to relieve acute obstruction. Without a safety wire it is typically not recommended to proceed with URS when an intervention is anticipated, except in the hands of experienced endourologists. With the newer generation flexible ureteroscopes, URS has been demonstrated to be safe without the use of a guidewire ("wireless") [8].

If a wire has passed but even a stent will not advance through the orifice, a small open-ended catheter can be advanced to the kidney and secured to the Foley catheter; this can allow for retrograde pyelography at the time of nephrostomy tube placement to facilitate placement of the tube, particularly if there is no severe dilation of the collecting system.

With safety and working wires in place, the flexible ureteroscope may not advance through the ureteral orifice or a segment of the ureter. The techniques discussed previously may apply here (e.g. emptying the bladder, holding the wire tautly, balloon or serial dilation). If the ureteroscope will not advance within the ureter, retrograde pyelography should be repeated to ensure there is no ureteral injury. If there is an obstructive lesion, the ureteroscope can be advanced to the level of the lesion and the area examined. With a safety wire in place, the lesion can be treated (e.g. laser lithotripsy of a ureteral stone, endoureterotomy). At any time, if the ureteroscope will not advance despite these efforts, ureteral stent placement can be performed and interval surgery planned.

If at any stage there is evidence of ureteral perforation with extravasation, a ureteral stent should be placed and the ureter should be allowed to heal before re-intervention. There may be new stricture formation from a ureteral injury, and this should be investigated at the time of follow-up surgery. If ureteral avulsion occurs, stent placement should be performed if possible, and the procedure should be aborted. Percutaneous nephrostomy tube placement will likely be necessary, and ureteral reconstruction may be considered in the same sitting if severe injury has occurred to a focal segment (e.g. ureteral reimplantation for an avulsion at the level of the bladder). If more complex reconstruction is required in delayed fashion, percutaneous nephrostomy tube placement should be performed.

During manipulation of multiple wires and catheters, patients can develop bleeding from the upper tract that may obscure visualization. If visualization is significantly compromised, the procedure should be aborted and a ureteral stent placed. Bleeding from the upper tract will typically tamponade, and a stent will allow continued drainage of the kidney. Any uncorrected coagulopathy should be addressed. Severe persistent bleeding with clot retention and/or hemodynamic instability may require continuous bladder irrigation, blood transfusion, and consideration of angioembolization.

Finally, instrumentation of the urinary tract may cause urosepsis in a patient with active infection or colonization. This may occur despite the administration of prophylactic antibiotics, and in particular may occur in patients with infected stones. If a patient develops hemodynamic instability during the procedure and there is consideration for urosepsis, a stent should be rapidly placed along with bladder drainage, and broad-spectrum antibiotics administered until culture results return. If there are signs of purulent urine when accessing the upper urinary tract, cultures should be obtained and the procedure should be aborted until cultures are negative. If this occurs, a ureteral stent (+Foley catheter) should be placed to allow for drainage of the infected urine from obstructed renal moiety.

## Ureteral stenting prior to ureteroscopy

Ureteral stents are most commonly used preoperatively in the setting of infection, presence of a solitary kidney, or compromised renal function, or when other attempts to gain access to the kidney have failed. The most recent American Urological Association and European Urology Association guidelines do not mandate the need for preoperative ureteral stenting in routine patients [9, 10]. However, their use in the pediatric population to passively dilate the ureter has been illustrated [11]. The use of preoperative stenting in the adult population had not been fully elucidated. The Clinical Research Office of the Endourological Society (CROES) recently published their work on the use of preoperative ureteral stenting prior to ureteroscopy. In their population, 11.9% (978 patients) had a ureteral stent placed prior to ureteroscopic intervention. They showed an increased stone-free and decreased complication rate in patients with renal stones. There was no significant difference in measurable outcomes for patients with ureteral stones [12]. In addition to improving clinical outcomes, Averch et al. showed in a retrospective review of 104 patients that the use of preoperative double-J stenting decreased the median cost, reduced operative time, and decreased the reoperative rates for patients with stone burden >1 cm, but no significant difference in patients with stone burden <1 cm [13, 14].

### Ureteral access in patients with urinary diversion

Retrograde ureteral access in patients with prior urinary diversion surgery has been shown to be feasible and safe, although altered anatomy may increase the complexity of these procedures [15–17]. Success of retrograde access may vary depending on the type of diversion and the indication for URS (ureteroanastomotic stricture disease vs surveillance or stone treatment), as well as the experience of the surgeon. In one retrospective study of these patients, 21 renal units underwent attempted retrograde access for diverse indications, and 75% of attempts were successful [15]. The success rate by type of diversion was 90% (9 of 10) for orthotopic neobladders, 73% (11 of 15) for ileal conduits, and 33% (1 of 3) for Indiana pouches. All attempts to access renal units for management of suspected upper tract malignancy were successful (13 of 13 patients, 100%), while attempts were less successful in patients with anastomotic stricture disease (5 of 10, 50%).

Prior to attempted retrograde access in these patients, operative reports should be reviewed to confirm the type of diversion, type of anastomosis (e.g. Bricker vs. Wallace), and likely location of the orifices. A loopogram or cystogram can be performed prior to attempted access to determine patency and location of the orifices, though we do not believe this is routinely necessary. The bladder should be initially accessed with flexible cystoscopy, particularly for pouches or conduits; rigid cystoscopy can be considered in neobladders for direct access to the orifice, particularly in cases of ureteroanastomotic stricture. If a neobladder with a Studer limb has been performed, the afferent limb should be cannulated with a flexible cystoscope and the orifices sought. If the orifices cannot be readily identified, methylene blue or indigo carmine can be administered intravenously to view efflux of dye. Cannulation of the orifice with a flexible guidewire is then attempted (Figure 45.4). If there is difficulty with cannulation because of the location or angle of the orifice, a 5 Fr open-ended or Bernstein angiographic catheter with a straight or angled-tip hydrophilic guidewire can be used. We recommend routine placement of a safety wire in these patients as the initial access may be challenging.

### Ureteral access sheath

UAS are used to facilitate access to the ureter during flexible URS. They are used primarily for flexible URS/holmium laser lithotripsy to enable repeated entry into the ureter with extraction of fragments or to allow for passive egress of fragments. They may also be used for repeated biopsies and treatment of suspicious upper tract lesions (e.g. upper tract TCC). UAS have become standard practice in many institutions for treatment of stone disease in particular; however, routine use of a UAS is still controversial based on concern for ureteral ischemia, ureteral perforation/injury, and questions regarding the ultimate benefit of a UAS for clinical outcomes. Dimensions of UAS include 9.5/11.5, 10/12, 11/13, 12/14, or 13/15 Fr diameter, and 20–55 cm length depending on the manufacturer.

Advantages of using a UAS are both theoretical and practical. They have been shown to decrease intrarenal pressure and may decrease pyelovenous and pyelolymphatic backflow, thus decreasing absorption of irrigant and possibly decreasing the risk of infectious complications, particularly in previously infected patients [18, 19].

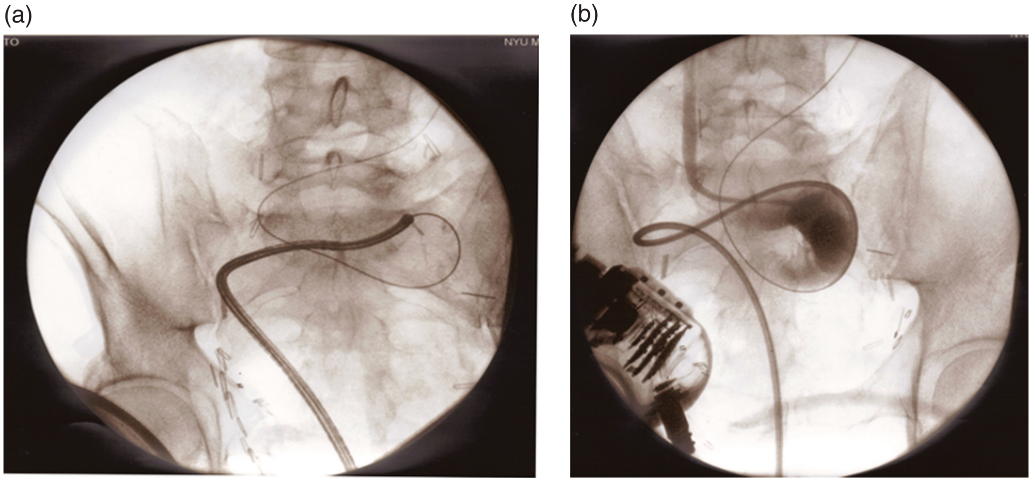

**Figure 45.4** (a) Orthotopic neobladder with Studer limb: access into the left ureter with guidewire. (b) Orthotopic neobladder with Studer limb: cystogram reveals right ureteral reflux. Reproduced from [15] with permission of Elsevier.

UAS improve irrigant flow, which may improve visibility and help to flush out small stone fragments, as well as decrease the need for emptying of the bladder during a protracted procedure. Additionally, Pietrow et al. showed the use of UAS increased the average life span of the ureteroscope prior to being sent out for a repair [20]. There is conflicting evidence regarding the impact of UAS on stone-free rates [21–26] (Table 45.2). There is also evidence that UAS decrease the cost and operative time for treatment of renal stones, but these studies have not been rigorously designed [22].

There have also been objections to routine use of UAS, including risk of acute injury to the ureter and unknown long-term risk of stricture formation [27, 28]. The latter appears low and consistent with standard URS; however, there have been no studies with long-term follow-up [23]. Traxer et al. showed, in 1490 patients undergoing URS with a UAS, an intraoperative complication of 5.9% which included bleeding and perforation as the two most common complications. This was shown to be nonsignificant when compared to patients undergoing URS without UAS (5.6%) [26]. Nonetheless, there is *in vivo* evidence of transient ureteral ischemia with UAS use [29]. Similarly, Razvi et al. showed in farm pigs that prolonged indwelling time and resistance to insertion of a UAS was associated in the short-term formation of ureteral stirctures [30]. Whether this information from a porcine study can be extrapolated to humans is yet to be determined. Furthermore, placement of a UAS may be impeded by a tight ureteral orifice, which may require balloon dilation to accommodate the access sheath; this may increase the risk of extravasation in addition to the time and cost of the procedure. Ultimately, the use of a UAS is at the discretion of the surgeon, and it may be beneficial on either a selective or routine basis.

Placement of a UAS is safest when performed over a working guidewire in the presence of a safety wire. The two components of an access sheath include an inner dilator and an outer sheath. Placement is facilitated by use of a working nitinol guidewire or Amplatz super-stiff wire (not a hydrophilic guidewire), and the access sheath is placed as a unit to the desired level within the ureter, at which point the inner component is withdrawn (Figure 45.5). It is important that all components of the access sheath are wet as the surfaces are hydrophilic. The access sheath may be secured to the drape to ensure it does not dislodge. The level of placement depends on the clinical scenario; for a renal stone, placement in the proximal ureter is typical to protect as much ureter as possible during entry and re-entry. Newer versions of access sheaths have also been created that allow passage of the sheath over only one wire, and when the inner dilator is removed, the guidewire is left on the outside of the sheath to serve as a safety guidewire.

Placement of a UAS can be compromised by an anatomically tight ureter or ureteral stricture disease. If the UAS cannot be placed through the orifice, balloon dilation may be performed. While some surgeons dilate the orifice on a regular basis for UAS placement, others will simply abort use of the sheath and continue without it. It has not been rigorously studied whether one approach is superior to the other from the standpoints of safety or stone clearance. Kuntz et al. looked at the risks of ureteral balloon dilation and found in 151 patients a failure of balloon dilation in 5% and an intraoperative ureteral perforation in 5%. Patient who experienced ureteral perforation were managed with either immediate ureteral stenting or percutaneous nephrostomy tube. The determined postoperative complication arte was 8% and a single ureteral stricture (0.6%) was attributed to balloon dilation [31].

**Table 45.2** Series of UAS use for treatment of upper tract calculi.

| Study | Number of patients | Size of sheath | Number of balloon dilations (%) | Mean size of stone (mm) | Successful placement (%) | Stone-free rate | Complications |
|---|---|---|---|---|---|---|---|
| Traxer et al. 2015 [26][a] | 1494 | Not mentioned | Not mentioned | 10.8 | 99.2 | 73.9 | Perforation (17), converted (3), sepsis (7), acute abdomen (2) |
| Berquet et al. 2014 [25] | 157 | 12/14 Fr | Not mentioned | 15.15 | 100 | At 3 months: 86% | Four major complications, not elaborated upon |
| Portis et al. 2006 [24] | 58 | 14 Fr | Not mentioned | 9.4 | 100 | 54% 0 mm;<br>84% <2 mm; 95% <4 mm | Ureteral perforation (3) |
| Delvecchio et al. 2003 [23] | 71 | 10/12 Fr (8), 12/14 Fr (56), 14/16 Fr (7) × 20, 28, 35, 55 cm | 6 (8.4) | 10.7 | 100 | 77.4% 0 mm;<br>90.3% <4 mm | Asymptomatic stricture (1) |
| Kourambas et al. 2001 [22][b] | 23 | 12/14 Fr × 20, 28, 35 cm | 1 (4.3) | 13.7 | 91 | 78.9% | Ureteral obstruction secondary to edema requiring stent placement (1), deep vein thrombosis (1) |
| L'Esperance et al. 2005 [21][c] | 173 | 12/15 Fr, 35 cm | Not mentioned | 8.7 | 100 | 79% | None |

[a] Propsective, observational, international, multicenter study of UAS (1494) versus no UAS (745); there was a statistically higher stone-free rate in non-UAS (73.9% vs. 82.8%, $P < 0.01$).

[b] Prospective randomized study of UAS (23) versus no UAS (21); there was no difference in stone-free rate (78.9% vs. 85.7%; $P = 0.78$).

[c] Retrospective comparative cohort study of UAS (173) versus no UAS (83); stone-free rate was improved overall by use of a UAS (79% vs. 67%; $P = 0.04$).

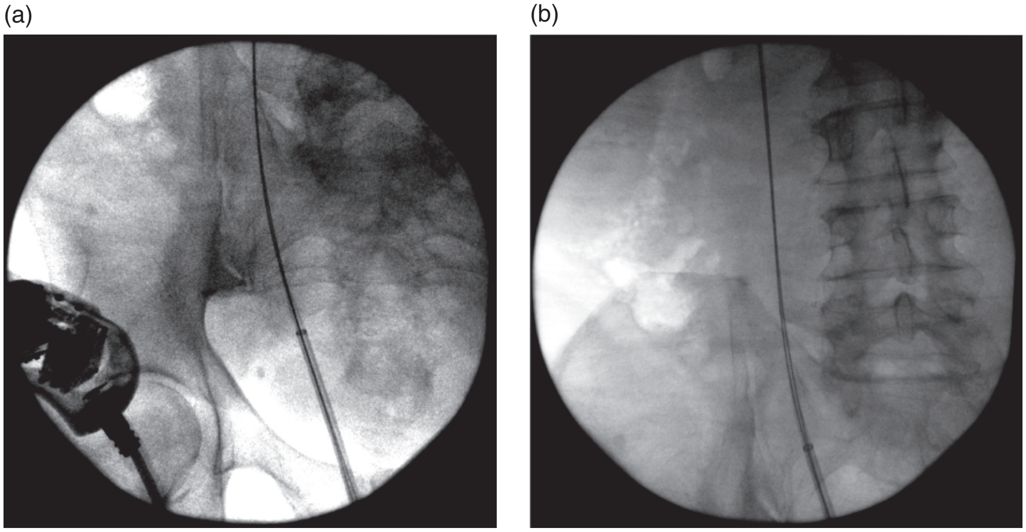

**Figure 45.5** UAS placed in (a) distal ureter and (b) mid ureter.

Finally, when placing an UAS, it important to be aware of small ureteral stone fragments that can be trapped alongside the sheath and are at risk for being pushed submucosally. If unrecognized this can lead to an impacted stone, or possibly a submucosal stone that can cause ureteral obstruction secondary to stricture formation.

We recommend placing a ureteral stent at the end of any procedure in which a UAS is used, although there is some evidence that this may not be necessary in previously stented patients [32]. Rapoport et al. retrospectively reviewed a series of consecutive patients who underwent URS for renal and ureteral stones, and found that use of a UAS without postoperative stenting significantly increased the risk of unplanned emergency room visits with increased emergency computed tomography scans, hospital readmission, and need for urgent decompression [33].

## Conclusions

Access to the ureter for flexible URS is typically straightforward, but can be complicated by both anatomic and disease factors. Anticipation of the "next step" and planning for difficult access can maximize the likelihood of success in these cases. Repeated entry to the ureter for flexible URS can be facilitated by use of a UAS, although the precise risk-to-benefit ratio of UAS is not known.

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## 46

# Ureteroscopy Energy Sources

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## Introduction

With endoscopic technology allowing excellent access to urinary stones, ureteroscopic treatment of nephrolithiasis has become a primary option in many cases. According to the 2016 American Urological Association and Endourological Society Guidelines for Surgical Management of Stones, ureteroscopic treatment is first-line for all ureteral calculi, as well as for intrarenal stones less than 20 mm [1, 2].

While smaller stones can be extracted intact, urinary calculi frequently require fragmentation prior to removal. As flexible and semirigid ureteroscopic technology provides better access to stones, adjunctive tools, including stone manipulation devices and lithotripters, have similarly become more advanced. In addition to efficiency and safety of intracorporeal lithotrites, newer fragmentation devices require reduced size and increased flexibility to allow for use with third-generation ureteroscopes.

Given the wide array of intracorporeal lithotrites, the endourologist must be familiar with each device, including mechanism of action, to appropriately choose the treatment for stones of various sizes, compositions, and locations (Figure 46.1). In this chapter, techniques for ureteroscopic lithotripsy will be discussed, with focus on the differences between each method, including their advantages and disadvantages in various clinical situations.

## Electrohydraulic lithotripsy

### Overview

Electrohydraulic lithotripsy (EHL) was the first method for intracorporeal lithotripsy utilized in clinical applications. The technology, first invented by Yutkin in 1955 at the University of Kiev, was used for upper tract stones during an open nephrolithotomy in 1975 [3, 4]. Since that time, EHL probes have been miniaturized for use in rigid and flexible ureteroscopes for treatment of ureteral stones [5, 6]. Despite its effectiveness and low cost, it is rarely used because of the high risk of ureteral injury. Yet, its low cost still makes EHL an option in certain situations.

### Technology

The mechanism for EHL fragmentation involves discharge of electrical energy in a liquid medium. The probe is composed of two electrodes of different polarities; a current passes between the electrodes and the energy release forms a plasma channel and vaporization of nearby water. This vaporization creates a shock wave and cavitation bubble, whose collapse creates secondary shock waves or high-speed microjets, all of which cause stone fragmentation.

### Advantages/disadvantages

The advantage of EHL is the low cost of components. The EHL generator and probes are currently less expensive than other intracorporeal lithotripters, with one or two probes used per procedure depending on stone composition [7, 8]. Additionally, modern EHL probes are small and flexible, allowing for treatment of stones through all types of ureteroscopes.

The main disadvantage of EHL is high risk of intraoperative injury. Initial experience of EHL reported high complication rates, as the lithotripsy was performed with large probes (9 Fr) and without endoscopic guidance [4, 9]. With improvement in endoscopic visualization, decrease in probe size (to 1.6 Fr), and improved control of energy output, EHL has become safer, although the

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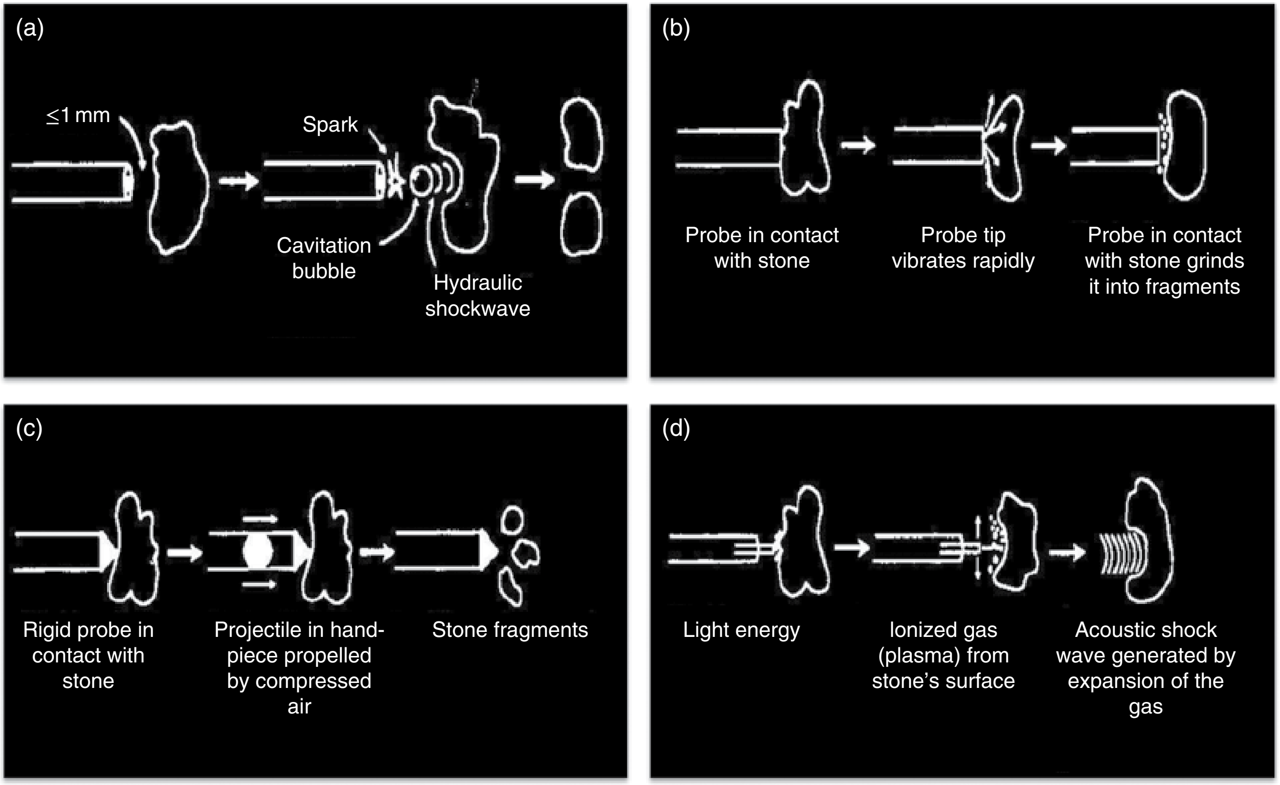
(a)
≤1 mm
Spark
Cavitation bubble
Hydraulic shockwave
(b)
Probe in contact with stone
Probe tip vibrates rapidly
Probe in contact with stone grinds it into fragments
(c)
Rigid probe in contact with stone
Projectile in hand-piece propelled by compressed air
Stone fragments
(d)
Light energy
Ionized gas (plasma) from stone's surface
Acoustic shock wave generated by expansion of the gas

**Figure 46.1** Mechanisms of lithotripsy. (a) Electrohydraulic lithotripsy, (b) ultrasonic, (c) pneumatic/ballistic, (d) laser.

complication rate remains high, between 6 and 17.6% [6, 10–12]. Complications of EHL range from ureteral perforation and hemorrhage to mucosal erosion, inflammation, and ureteral stricture.

Studies have been performed to understand the mechanisms by which EHL causes ureteral injury. In addition to direct injury to the ureteral wall from firing of the probe onto mucosa, expansion of the cavitation bubble may induce a burst effect on the ureter [11]. With energy of more than 1300 mJ, the cavitation bubble can reach 1.5 cm in size; thus, decreasing the energy can reduce capacity for injury. One *in vitro* study demonstrated that 24 pulses to the ureteral wall were sufficient for perforation from 0.5 mm, highlighting the care needed while using EHL [13].

The stone fragmentation and clearance rates are not significantly higher for EHL than for newer lithotripters. In addition to fragment retropulsion, which appears more common than with other methods, EHL produces more and larger fragments, reducing stone clearance [14]. EHL is less effective with harder and larger stones (>1.5 cm) and the stone-free rates range widely from 67 to 98% [7].

### Technical tips

Given its risks, EHL should be performed under careful attention and with the lowest power settings that can produce fragmentation. Smaller probes (1.6–1.9 Fr) should be used to decrease perforation risk and to improve irrigation. Prior to use of the lithotripter, insulation layers of the probe should be examined to ensure they are intact. The distal tip of the probe should be placed 2–5 mm from the end of the ureteroscope to reduce damage to the lens, while the probe should be kept 1 mm from the stone to improve shock-wave interaction [15].

Visualization of the stone must be maintained, along with adequate irrigation to distend the ureter away from the probe, to reduce risk of injury. Lithotripsy should begin with low voltage (50–60 V) and single pulses with a slow increase in generator output until the fragments are small enough for basket removal. After 60 seconds of firing, the probe should be examined for loss of insulation, as a new probe may be required. Care must be taken to avoid firing upon any safety wire or retrieval device, as these are damaged by EHL energy.

## Ballistic/pneumatic lithotripsy

### Overview

Similar to EHL, ballistic and pneumatic lithotripsy is an older method of fragmentation. These lithotripters come in many sizes and types of energy production and all necessitate a straight probe during use. The rigid probes decrease the practicality of this technology for upper tract stones requiring flexible ureteroscopy. Still, ballistic and pneumatic lithotripsy remains safe and effective when used in the proper setting.

### Technology

Ballistic and pneumatic lithotrites pass energy from a projectile to the probe (0.8–3.0 mm) and then directly to the stone with a "jackhammer" effect. When fired repeatedly (on the order of 12 Hz with automatic lithotripters), this production of 2–30 atm at the stone surface causes cracking and fragmentation.

Production of this ballistic energy varies between lithotripters, with use of large-scale compressed air (Lithoclast, Electromedical Systems/Boston Scientific), handheld high-pressure $CO_2$ cartridges (StoneBreaker, LMA Urology/Cook Medical), or electromagnetic acceleration of a magnetic core (LithoBreaker electrokinetic probe, Electromedical Systems). In each case, the probe is held in contact with the stone to transmit the ballistic energy. This method requires energy transfer through a rigid probe; bowing of the device reduces power transmission, limiting the utility of this method to unflexed endoscopes.

### Advantages/disadvantages

Ballistic lithotripsy is a low-cost option. Disposable costs are minimal, as probes have a long life span, unlike laser and EHL [10]. While free-standing pneumatic lithotripters require more expensive consoles compared to EHL, there is minimal maintenance and no disposable costs. The handheld pneumatic lithotripter is less expensive and the disposable $CO_2$ cartridges, which deliver approximately 80 shocks each, add minimal cost to the device.

Ballistic and pneumatic lithotripsy, utilizing direct mechanical energy transfer, are safe compared to other technologies. In contrast to EHL, ultrasonic lithotripsy, and holmium laser, ballistic lithotripsy causes less injury and has lower risk of ureteral perforation [16]. After 6 minutes of direct application of pneumatic lithotripsy to a ureteral wall *in vitro*, no perforation was seen [13]. Additionally, thermal injury is unlikely as minimal heat is produced. Compared to the relatively slow comminution of laser fragmentation (which is discussed later), ballistic lithotripsy has a more rapid stone clearance time [17, 18].

Despite its safety and low cost, ballistic lithotripsy has slightly lower success than other methods, likely secondary to its inability to fragment stones when torqued and the high risk of stone retropulsion. Stone-free rates after ballistic or pneumatic lithotripsy range from 70 to >90%, although the lower rates occur in settings of probe deflection and retropulsion [19–21]. Through a flexible ureteroscope, deflection of more than 24° will significantly reduce energy transmission; distal semirigid ureteroscopy allows for decreased need for flexion and decreased power loss [22]. Thus ballistic lithotripsy is very effective through a semirigid ureteroscope for mid/distal ureteral stones.

The other disadvantage of ballistic lithotripsy is its retropulsion rate, which has been reported in 2–17% of ureteroscopic treatments. Due to this high rate of retropulsion, especially given the rigid lithotripter, migration into the proximal ureter or kidney can render stone fragments untreatable with this method alone. Many tools have been developed to prevent stone migration, including stone-trapping devices (such as stone baskets, gel polymeric plugs, and ureteral balloons) and suction devices to be used alongside the lithotripter [23, 24]. These methods reduce the risk of retropulsion and improve fragmentation efficiency and stone-free rates, although careful use of the lithotripter may preclude the need for such techniques [25, 26].

### Technical tips

As with all lithotripters, endoscopic visualization of the stone is a prerequisite for treatment. The stone should be pinned in place for fragmentation and to decrease retropulsion, whether held against urothelium or using a trapping mechanism. Bending of the endoscope or probe should be avoided in order to maintain power during lithotripsy. The probe must be in contact with the stone and it is recommended to work from the periphery to separate fragments small enough for spontaneous passage. Given the minimal flexibility of this device, if larger fragments migrate proximally, chasing and treating such pieces becomes problematic.

## Ultrasonic lithotripsy

### Overview

Ultrasonic lithotripsy was described by Mulvaney in 1953, with the first ureteral applications in the 1970s and 1980s [27, 28]. This method uses ultrasonic vibrations to fragment calculi; many ultrasonic lithotripter probes include a suction channel to allow simultaneous fragment removal. Similar to ballistic lithotripsy, this requires a rigid device, reducing the utility of ultrasonic lithotripsy during ureteroscopy. Smaller probes (2.5 and 4.5 Fr), with or without suction capabilities, can be used through a semirigid ureteroscope with success and safety.

### Technology

The ultrasonic method of lithotripsy utilizes an electrically charged piezoceramic plate within the transducer that resonates at high frequency (23 000–25 000 Hz) and generates ultrasonic waves. These longitudinal and transverse waves are passed along a hollow steel probe, which makes contact with and fragments the stone. Fragmentation occurs as noncompliant stone material is vibrated at a high frequency such that the stone breaks; compliant tissue (e.g. urothelium) does not resonate in this manner and inadvertent damage is minimal [3, 29].

Due to vibration of the ultrasonic probe, heat development is a concern, but most probes allow for concurrent suction through their core, which enables irrigation flow and heat dispersion. With adequate irrigation/suction and intermittent probe firing, temperature increase can be minimized [30]. The probes are reusable but will incur damage: periodic replacement is required.

Of note, combination lithotripters exist that allow for ultrasonic and ballistic fragmentation (Lithoclast Ultra/Select, Electromedical Systems/Boston Scientific) or dual-probe ultrasonic lithotripsy (CyberWand, Gyrus ACMI/Olympus). These technologies allow for improved fragmentation and suction, but are only available in the percutaneous setting given their size and rigidity [31, 32].

### Advantages/disadvantages

The advantages of ultrasonic lithotripsy are rapid fragmentation along with concomitant fragment removal. Studies report stone-free rates from 88 to 98%, making this an effective method [33–35]. These success rates are seen throughout the literature using ureteroscopic probes of 4.5 Fr (hollow probe with suction) or 2.5 Fr (solid probe without suction). Still, the capability for simultaneous removal of small fragments during lithotripsy is beneficial. This suction ability is particularly useful in a setting of steinstrasse, as the stone debris can be continuously evacuated.

An advantage discussed previously is the relative safety of the ultrasonic mechanism. Due to the method of vibrational energy transmission, flexible material – such as ureteral tissue – is not damaged easily. *In vitro*, the ultrasonic device has the longest average time to urothelial perforation, with injury occurring at 118 seconds of continuous firing in direct wall contact [29]. Probe temperature rise is a concern, but is managed with adequate irrigation.

Despite these advantages, this method is only utilized in semirigid ureteroscopy. If suction is necessary, a ureteroscope with a large working channel is required for passage of the 4.5 Fr probe. While the 2.5 Fr solid probe is smaller, semirigid ureteroscopy is still required for use of this device. Given its inability to be used with a flexible ureteroscope, this technology is typically restricted to percutaneous surgery, where rigid nephroscopes allow passage of larger and more powerful ultrasonic probes.

### Technical tips

Endoscopes with minimal flexion and large working channel are required for rigid probe use. Gentle pressure against the stone is required, although suction capabilities or simultaneous use of a stone-trapping device can reduce the need for pressure and decrease the risk of urothelial injury. With larger ureteroscopic probes, suction allows for concurrent removal of small stone fragments during lithotripsy. Fragmentation is most efficient when performed along the stone periphery to produce smaller pieces that are suctioned away. To reduce heat production, continuous high-flow irrigation is recommended along with intermittent probe firing.

## Nanosecond electropulse lithotripsy

### Overview

Nanosecond electropulse lithotripsy (NEPL) is the newest method of intracorporeal lithotripsy, described in 2007 [36]. It utilizes similar technology to EHL, although due to different characteristics of energy discharge it has a better safety profile. Early data show similar ease of access and flexibility compared to laser/EHL, along with excellent fragmentation, making this a promising new method for lithotripsy.

### Technology

While EHL and NEPL probes contain two distal electrodes across which current is applied, the NEPL probe differs due to the voltage and time over which energy is released. In contrast to EHL discharge time of hundreds of microseconds at low voltages, NEPL releases higher voltages in less than 50 nanoseconds. This method of energy release, when the probe is touching a non-conducting material such as urinary calculi, produces spontaneous conduction and direct electrical breakdown of the target. In the absence of a solid target, the probe performs similarly to EHL and releases energy into the surrounding fluid, creating a shock wave and cavitation bubble. The focus of electrical energy into the target (instead of the surrounding fluid) is what provides the proposed safety of NEPL.

### Advantages/disadvantages

NEPL has become the focus of recent studies given the potential for improvement over previous technology.

*In vitro* studies have shown improved energy and time efficiency compared to EHL and laser lithotripsy [37–39]. Stone-free rates are comparable to other methods, with 91–100% success depending on the stone location (mid ureter with better success than upper ureter) [36]. This high success rate is likely related to the efficiency of the treatment as well as the ease of access allowed with the small, flexible probes (2.7 or 3.6 Fr) along the upper urinary tract.

The safety profile of NEPL is generally favorable, although more data are needed. *In vitro* studies have documented nonperforating injury isolated to the submucosal or muscular layers after 10 pulses of 1.0 J [40]. Additionally, in a study of 799 patients with ureteral stones undergoing NEPL, 18 ureteral perforations occurred (2.1%), although most perforations were related to torque of the semirigid ureteroscope, not energy dispersal [36].

The disadvantages of this technology are the potential for retropulsion and lack of information about this new lithotripsy method. Rates of retropulsion are approximately 5%, although this is less of a concern than with rigid lithotripters, as access to the kidney is more feasible with the flexible NEPL probes [36]. While the mechanism of action and safety have been studied, this technology is still in its infancy. Additional studies are needed to document its utility and safety before widespread use. Still, the advantages give this technology a chance to become a strong addition to the endourologists' arsenal.

### Technical tips

As NEPL use is not widespread and there are few recommendations on use, although it is expected that treating this method similarly to EHL would produce safe and effective results. As such, ureteroscopic visualization of the stone is of paramount importance to ensure probe contact throughout treatment. By maintaining contact with the stone, risk of shock-wave formation is theoretically decreased, preventing complications seen with EHL. Higher power is required for electrical breakdown of the stone; therefore, care must be taken with probe placement prior to firing. Additional studies will better evaluate the risk for retropulsion, but preliminary data suggest that standard methods to reduce retropulsion may be beneficial.

## Laser lithotripsy

### Overview

Laser lithotripsy is the most commonly used method of intracorporeal stone fragmentation. Laser, which is an acronym for **l**ight **a**mplification by **s**timulated **e**mission of **r**adiation, involves transmission of energy to the target in a directed, collimated beam of photons of a single wavelength. Depending on the wavelength, power, pulse length/frequency, and method for beam delivery, the mechanism and efficacy of stone fragmentation differs wildly. Still, urologic lasers have excellent safety and probe flexibility and, despite slower fragmentation, they are widely utilized for ureteroscopic lithotripsy.

Clinical laser technology was developed in 1960 by Theodore H. Maiman, while 6 years later Parsons was first to experiment with this device in urology, testing a pulsed-ruby laser in canine bladders [41, 42]. In 1968, Mulvaney and Beck reported this ruby laser could fragment urinary calculi, although it was clinically unsafe given excessive heat generation [43]. Since that time, there has been improvement within the field of laser physics to allow for safer and more efficient tools for treatment of urinary stones.

### Technology

Laser energy is produced when a material – gas, liquid, or solid – known as gain medium, is stimulated by an energy source; photons are released as excited electrons return to their normal state. Photons released in this manner contain a large amount of energy as the beam is in-phase, collimated, and of a single wavelength. Amplification occurs as mirrors refocus the beam, producing further excitation and emission. The beam is then released as a continuous wave, or a mechanism induces an intermittent or pulsed quality, which has profound effects on the physics of energy transfer. The laser is then carried along a fiber where it is released upon the target.

Many types of gain medium have been used, from $CO_2$ gas (which produces a continuous beam of 10 600 nm wavelength light) to organic liquid dye (e.g. coumarin, which generates a tunable short-pulse laser) and solid crystals (e.g. ionically doped yttrium aluminum garnet; YAG). Each laser is named for the medium used; the choice will affect the characteristics of the laser generated. Additionally, these characteristics will produce different responses in the target, as these variations lead to differing methods of energy transfer.

Laser energy transfer in lithotripsy is described in two forms: photomechanical and photothermal. Photomechanical ablation occurs when a short-pulse laser produces transient stress waves in the surrounding medium, leading to formation of shock waves from plasma or cavitation bubble formation and collapse [44]. Since the shock wave from bubble collapse propagates in all directions, the fiber can be placed anywhere near the stone, although distance is required for bubble expansion [45]. Photothermal ablation, on the other hand, involves direct absorption of longer-pulse laser energy into the stone crystal lattice or water molecules within the crystal. In this method, direct transfer of energy to the stone produces fragmentation and contact is needed between the fiber and target for lithotripsy to occur. In photothermal ablation, laser energy is highly absorbed by water and, when fiber and stone are not in contact, energy is lost in vaporization of a water channel before it reaches the stone ("Moses effect") [46]. Compared to creation of shock waves in photomechanical fragmentation, which leads to large stone fragments, the direct energy transfer of photothermal fragmentation typically produces smaller dust-like debris [47].

The laser fiber allows for direction and delivery of the photon beam to the target and an ideal fiber should be small, flexible, durable, and able to transmit energy with efficiency. The basic fiber design consists of core material (typically silica) surrounded by two or three layers of cladding and protective coating. Since laser output is not ideal and perfectly collimated, there is frequent delivery of off-axis rays that undergo internal reflection during passage of the beam along the fiber; with large amounts of fiber flexion and beam divergence, energy can be transmitted through the cladding and cause fiber, ureteroscope, and patient injury [48]. The fiber tip also has a strong effect on the output, although this has mostly been studied in the holmium:YAG (Ho:YAG) setting. Tip degradation is typical over the course of a procedure, and multiple stripping/cleaving techniques are thought to prolong the use of the fiber [49, 50]. Despite this manipulation being common practice, latest data call into question the efficacy of these maneuvers, showing that stripped fibers have a lower power output and increased tip degradation [49, 51].

Recently, ball-tip fibers have been developed to allow smoother passage through deflected ureteroscopes with hopes of minimizing damage to the working channel. While these delicate tips degrade rapidly at higher energy settings, comminution efficiency of the ball-tip fiber is comparable to standard fibers. Moreover, in low-energy, high-frequency laser settings the ball tip remains intact. Most importantly, the ball tip appears to be protective of the working channel as a decreased force is required for insertion in deflected ureteroscopes [52, 53].

## Laser types

The pulsed-dye laser was one of the first used for clinical treatment of urinary stones. It used a coumarin green dye as laser medium and produced a short-pulse beam with 504 nm wavelength. This wavelength of light is well absorbed by hemoglobin, utilizing the bloodstream as a heat sink and making the laser safe *in vivo* [45]. Pulsed-dye lasers utilize the photomechanical effect and, therefore, are not effective at fragmenting harder stones such as calcium oxalate monohydrate, brushite, and cystine [54]. Given this disadvantage, along with the toxicity of the dye, this laser has fallen out of favor and is rarely used.

Neodymium-doped YAG crystal is used as the medium for the frequency-doubled double pulse Nd:YAG (FREDDY) laser, within which a potassium titanyl phosphate (KTP) crystal is placed to create pulses of two different wavelengths (532 and 1064 nm). This dual-wavelength laser creates a plasma bubble on the surface of the stone, and collapse of this bubble induces fragmentation through photomechanical effects. Similarly to the pulsed-dye laser, this energy must be delivered within a 3 mm distance, is absorbed by the bloodstream and has a very low risk of ureteral perforation [13, 55]. This laser has excellent efficiency – even compared to Ho:YAG – but with a significantly increased risk of retropulsion, inability to fragment harder stones, and similar costs, it is no longer commonly utilized clinically [56].

The Ho:YAG laser is currently the workhorse of ureteroscopic lithotripsy [57]. This laser uses a holmium-doped YAG crystal to create a 2140 nm wavelength pulsed beam. The pulses of this laser are longer (250–350 microseconds) than the dye lasers, leading to a largely photothermal effect on the target. Many studies have been done to evaluate the energy transfer in holmium laser lithotripsy and have noted minimal photomechanical effects. A weak shock wave is noted during holmium lithotripsy and fragmentation begins before cavitation bubble collapse and shock-wave formation [58]. Additionally, holmium laser lithotripsy is improved with warmed stones, with dry stones fragmented in air rather than irrigation, and when the laser is discharged with minimal incident angle, all pointing towards a direct transfer of energy and photothermal mechanism of action [59].

The Ho:YAG laser has many advantages that allow widespread use. There are multiple fiber sizes (200, 365, 550, and 1000 μm) utilized for ureteroscopic lithotripsy, but the 200 μm fiber allows for excellent flexibility and irrigation flow compared to other lithotripters, improving ureteroscopic access to the entire collecting system [60]. The 365 μm fiber is used primarily during semirigid ureteroscopy. In contrast to older lasers, the photothermal mechanism of action allows for fragmentation of all stone compositions, including cystine and calcium oxalate monohydrate. Additionally, with maximum penetration of approximately 1 mm and minimal shock-wave formation, the holmium laser is very safe for use in the urinary tract, even in patients with bleeding diatheses [13, 57, 61]. The modest shock wave also reduces risk of retropulsion, although increasing pulse energy can induce a more significant shock wave and increase retropulsion risk [56, 62]. In combination with – and because of – these advantages, holmium laser lithotripsy enjoys an excellent success rate, with current stone clearance rates typically between 86 and 98% [19, 20, 63].

Despite these advantages, Ho:YAG laser does have shortcomings. The drilling mechanism of lithotripsy that this laser utilizes produces relatively small fragments, which leads to longer procedures and less efficient lithotripsy [64]. Still, while occasionally inefficient, this allows for the "dusting" method of lithotripsy discussed in a following section. Despite its excellent safety profile, holmium laser does have the capability to injure the urothelium and endoscopes – as well as adjunctive devices such as basket and antiretropulsion devices – if not carefully directed, with an approximate risk of 1%. Retropulsion is not a large concern with this laser, although it can still occur during ureteroscopy and pulse energy must be managed accordingly. Lastly, holmium laser requires a relatively expensive laser generator and the majority of fibers are nonreusable, requiring comparatively high costs (Table 46.1).

## Technical tips

Given that Ho:YAG laser is most frequently used, recommendations within this section will focus on its use. Similar to other methods of ureteroscopic lithotripsy, adequate visualization of the stone is required. The laser fiber should be placed against the stone with care taken to avoid firing upon the urothelium or other endourologic equipment as they can be damaged by the laser. Additionally, the fiber should be extended at least 2 mm from the tip of the ureteroscope to prevent damage to the fiberoptics or digital chip.

A variety of power settings are utilized for ureteroscopic lithotripsy with the Ho:YAG laser, depending on the method of fragmentation planned. A high-energy, low-frequency setting (e.g. 1.2 J and 5 Hz) will produce deeper and wider fissures than a low-energy, high-frequency setting at the same power, suggesting that this type of fragmentation is most energy-efficient [65]. This method produces larger fragments, increased risk of retropulsion, and leads to quicker degrading of the fiber, thus it is not always the most useful setting [52]. A low-energy, high-frequency method of laser discharge (e.g. 0.2 J and 50 Hz) reduces the risk of retropulsion and allows for the "dusting" technique for stone fragmentation. In this technique, the laser fiber is "danced" across the surface of softer stones, producing submillimeter particles that are easily passed; this method reduces the number of fragments that require removal at the conclusion of the fragmentation. There are not sufficient data to evaluate whether dusting or fragment removal is more efficient, although studies are underway.

**Table 46.1** Comparative costs of ureteroscopic lithotripter devices.

| | EHL | Pneumatic | Ultrasonic | NEPL | Laser |
|---|---|---|---|---|---|
| Probe | $ | $$ | $$ | $ | $$$$$ |
| Generator | $ | $$ | $$ | $ | $$$$$ |

"Popcorning" is another technique where stone fragments are isolated within a calyx and high-energy, high-frequency settings (such as 1.0 J and 20 Hz) are used to agitate the stones; this method intermittently brings the fragments into contact with the fiber and further fractures the pieces [66]. Given all possible settings and minimal research comparing the options, it is recommended to start with relatively low energy settings and increase the energy and/or frequency depending on the planned method of fragmentation and clinical situation.

The overall power output of the laser generator is also of clinical significance, as it determines the maximum values of laser energy and frequency possible. The typical Ho:YAG generator produces 80 W of power and this generator has been the most commonly studied and used for intracorporeal lithotripsy. Given the cost of this generator, low-power and cheaper Ho:YAG generators have been evaluated for similar outcomes. While they do not allow for higher power settings (such as 1.5 J and 30 Hz), low-power lasers (10–30 W) are useful in all urologic procedures – except for prostatic ablation or enucleation – and are capable of intracorporeal lithotripsy [63, 67]. Conversely, new high-power lasers (120 W) are being utilized in certain situations, primarily for managing benign prostatic hyperplasia, although data are currently lacking regarding the improvement over standard power generators for stone fragmentation.

A final technical recommendation regarding use of Ho:YAG laser involves changes in pulse duration, which was recently evaluated with regards to fragmentation efficiency and risk of retropulsion. At a set power level, shorter pulse duration allows for a more concentrated discharge of energy, which produces more significant retropulsion and fiber damage compared to a longer pulse [68, 69]. Conversely, a shorter pulse may lead to increased fragmentation efficiency, thus the advantages and disadvantages of different pulse lengths must be taken into account [70]. Newer laser generators allow for alteration of pulse duration, as well as energy and frequency, giving the surgeon an additional layer of refinement regarding laser use.

While Ho:YAG laser is the most commonly used method for intracorporeal lithotripsy, advances are being made to bring newer and more efficacious laser technologies to clinical use. The erbium:YAG (Er:YAG) laser, which is used in dentistry and ophthalmology, has a significant increase in lithotripsy efficiency compared to Ho:YAG

**Table 46.2** Overall advantages and disadvantages of ureteroscopic lithotrites.

| | Advantages | Disadvantages |
|---|---|---|
| EHL | Inexpensive, versatile, deflectable | Low safety, poor visibility |
| Pneumatic/ballistic | Efficient, inexpensive/reusable probe, safe | Rigid probe, retropulsion |
| Ultrasonic | Reusable probe with suction capability, efficient, safe | Large, rigid probe |
| NEPL | Efficient, deflectable | Minimal clinical data |
| Laser | Multipurpose, fragments all stones, deflectable, safe | Inefficient, expensive |

*in vitro*. Lee et al. tested stones of multiple compositions and, likely due to high absorption of energy at its wavelength of 2.9 μm, the Er:YAG laser outperformed the Ho:YAG by two to three times [64]. This laser requires stronger and larger fibers for transmission of the beam, and while sapphire or fluoride fibers may become a feasible option, at this time this laser is excluded from clinical use in urology [71]. Similarly, the tunable thulium laser is a newer technology that, with a wavelength of 1908 nm, may have improved efficiency over Ho:YAG laser. This low-energy, high-frequency laser, which fires at speeds up to 1000 Hz, produces comparable ablation along with lower risk of retropulsion and ureteral injury [72, 73].

## Conclusions

There is a variety of ureteroscopic lithotripter options available to the urologist. Given the range of techniques, an understanding of each lithotripter is required to choose the proper tool for each clinical situation and to safely use each technology (Table 46.2). The endourologist must factor in stone type, stone location, patient anatomy, and desired method of fragmentation before finalizing the treatment plan. As endoscopic technology improves, fragmentation devices will advance, but the basic tenets of safe and effective ureteroscopic lithotripsy will remain constant.

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# 47

# Ureteroscopic Management of Ureteral Calculi

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## Introduction

Improvements in technology over the last 15–20 years have led to an increased ability to successfully manage ureteral calculi using a variety of methods. Although extracorporeal shock-wave lithotripsy, antegrade percutaneous approaches, and laparoscopic ureterolithotomy are options, the mainstay in the treatment of patients with ureteral calculi continues to be retrograde ureteroscopic stone removal [1]. Refinements in ureteroscopic technology, as well as the development of improved laser techniques and advances in ancillary equipment, such as baskets, graspers, and others, have led to a situation in which almost all ureteral calculi can be successfully managed in a single procedure using ureteroscopy (URS).

Despite these advances, the selection of the single best approach to treat patients with ureteral stones remains controversial, especially given the complexity of today's changing healthcare environment. As there is increasing public focus on less invasive treatment strategies, it should be kept in mind that such approaches may in some cases lead to higher treatment failure rates with the need for secondary procedures. Additionally, a variety of economic factors have increased in importance in all areas of healthcare, and ultimately the most cost-effective approach to ureteral stones may be deemed best for all patients.

In this chapter, we will review the use of URS in relation to other treatment options for patients with ureteral calculi and discuss the wide variety of equipment and instruments that can be used with this procedure.

## Treatment options

There are several management options for patients presenting with ureteral calculi and a multitude of factors that guide clinical decision-making in this setting. Carefully selected patients can be managed conservatively with observation during a trial of spontaneous passage. These are patients with mild-to-moderate symptoms that can be controlled with oral analgesics, and those who do not have any factors that would warrant immediate intervention. These factors include urine infection – especially in an immunocompromised patient – compromised renal function, obstructed solitary kidney, intractable nausea and vomiting preventing adequate hydration, and inadequate pain control. The likelihood of stone passage also has an important impact on the decision to proceed with intervention versus observation. Stone size (measured in the transverse dimension) is an important factor to consider. Based on meta-analysis performed by the 2007 European Association of Urology (EAU)/American Urological Association (AUA) Nephrolithiasis panel, stones measuring 5 mm had a spontaneous passage rate of 68% (95% confidence interval [CI] 46–85%) and stones measuring between 5 and 10 mm yielded a spontaneous passage rate of 47% (95% CI 36–59%) [2]. The use of medications to promote spontaneous stone passage – so-called medical expulsive therapy (MET) – has come into favor over the last several decades. The goal of MET is to reduce time to stone passage, decrease pain/colic episodes, decrease pain medication requirements, and decrease need for procedural intervention. The pathophysiology of ureteral obstruction involves increased ureteral pressures and decreased frequency of ureteral contraction. Given this, it has been hypothesized that relaxation of the ureter and decreasing pressure should promote stone passage. Several classes of medications have been studied, including alpha-blockers, calcium channel blockers, nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, and others; however, the evidence for the use of MET remains controversial [3].

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Seitz et al. conducted a meta-analysis of published literature concerning the use of MET in patients with ureteral stones [4]. For 47 randomized controlled trials they assessed the use of alpha-blockers and calcium channel blockers in patients with untreated ureteral calculi of varying sizes. Their results demonstrated that the use of either medication led to a higher and faster stone expulsion rate compared to the control groups. In addition, treated patients had lower analgesia requirements, fewer episodes of colic, and fewer hospitalizations. In contrast, other recent work has called these and other similar findings into question. A study of emergency room patients with small ureteral stones (mean 3.6 mm) examined the rates of spontaneous stone passage at 14 days. Patients were randomized to ibuprofen, oxycodone, and tamsulosin, or ibuprofen and oxycodone alone. There was no difference in their primary outcomes nor pain scores, unscheduled emergency room or primary care visits, days out of work, analgesic use, or adverse events [5].

The largest multicenter, randomized, placebo-controlled trial (SUSPEND trial) included 1167 patients randomized to tamsulosin, nifedipine, or placebo and examined outcomes including rate of spontaneous passage by 4 weeks and cost measures [6]. The results of this study showed no difference in rates of spontaneous stone passage between treatment arms and placebo and between the two treatment arms. In addition, there was no increase in cost-effectiveness of MET versus placebo. Despite the controversial evidence, the practice of MET remains accepted and is still endorsed by the most recent AUA Nephrolithiasis Clinical Guideline Panel [7].

The decision to proceed with a trial of spontaneous stone passage as the initial management approach is often largely based on patient preference. With the exception of the indications for immediate intervention listed above, most patients can at least be offered the opportunity to pass the stone spontaneously. In our experience, some patients with ureteral calculi who have well-controlled symptoms react negatively if a urologist is perceived to be "too aggressive" in recommending an immediate procedure, and may lose confidence in this urologist and end up seeking an alternative medical opinion. On the other hand, a frank discussion of the relative likelihood of stone passage is important in helping the patient decide whether immediate intervention is appropriate. Since an accurate prediction of the time to spontaneous stone passage is very difficult, patients must understand that the quoted statistics on stone passage are largely based on trial periods of up to 4–6 weeks. In many cases, due to work and personal considerations and the uncertain nature of when a stone will pass, patients may opt for immediate definitive stone removal rather than a period of observation.

## Ureteroscopy

In performing URS, there are two basic choices of endoscopes: semirigid and flexible (see Chapters 39 and 40 and other chapters in this section). Semirigid instruments have fiber-optic bundles, range in size (external diameter) from 6.9 to 10 Fr, and may have single or dual working channels. There are several advantages associated with the use of semirigid ureteroscopes. In most cases, visualization is superior and it is easier for the operating urologist to control the instrument and manipulate accessory equipment such as baskets, graspers, etc. The diameters of the working channels of semirigid ureteroscopes are usually wider than those seen with flexible instruments, which allows for easier use of accessory equipment and improved irrigant flow. When removing stone fragments, repeated passage of the scope into the ureter is generally easier than when using a flexible instrument. In addition, semirigid instruments are often more durable than flexible instruments, leading to less breakage and lower cost associated with long-term use. Semirigid ureteroscopes are best suited for stones in the distal ureter (see Video 47.1) below the crossing iliac vessels and may be more difficult to pass proximally, especially in men with large prostates. Over the last few decades, these scopes have been made with narrower calibers and greater lengths to allow access to the proximal ureter, renal pelvis, and even parts of the calyceal system. Nevertheless, further technologic advancement of these rigid instruments (aside from incorporation of digital imaging systems) has slowed in recent years, as the utility of these scopes has reached a plateau [8]. The semirigid instrument is often easier for a single operating surgeon to use and usually allows for better visualization and irrigant flow. The semirigid scope is particularly well suited for patients who have an indwelling stent prior to URS as this leads to passive dilation of the ureter, thus making passage of the instrument easier. However, if resistance is encountered, the semirigid instrument should never be forced more proximally in the ureter and instead switching to a flexible instrument is advisable.

The greatest technologic advances in URS over the last several years have come in the area of flexible instruments. Initially, lack of durability of flexible ureteroscopes was a significant problem, and expensive and frequent need for repair was the norm in most busy endourologic practices [9]. However, improvements have been made and today's flexible instruments are generally less prone to breakage than earlier generations of scopes [10]. In addition, the degree of deflection (less important when treating ureteral stones than those in the kidney), size of the working channel, and overall visualization have also been significantly improved (see Video 47.2). A significant advance has been the development of fourth-generation digital flexible ureteroscopes [11]. Multescu et al. compared an Olympus digital ureteroscope and a standard Storz instrument and found that the digital scope had significantly greater maneuverability and visibility [11]. There was also less deflection loss with the digital scope when an accessory instrument was present in the working channel and irrigant flow was also superior. Furthermore, the light source for these digital scopes is dual light-emitting diodes (LEDs) at the tip, which essentially eliminates the risk of drape fire or patient burns in addition to lasting 10–20 times longer than the traditional fiber-optic scopes [12]. These digital scopes do have a slightly larger distal tip which houses "chip-on-the-tip" sensors to create improved imaging quality. A notable benefit of this is that an endoscope is no longer needed to attach to the scope on the proximal end, making the entire system lighter and easier to maneuver [13]. The digital scope's wider, and often more blunt, distal tip presents a potential disadvantage. Access to the ureter and passage through narrow segments of the upper urinary tract may be more difficult. In most cases, we have found that it is necessary to have a ureteral access sheath in place in order to pass the digital ureteroscope into the ureter, whereas the standard flexible scope can be passed, if desired, without this sheath. This observation is corroborated in a study of 157 ureteroscopies performed with either analogue fiber-optic scope or digital scope, which demonstrated significantly more cases performed with a digital scope that required ureteral access sheath (25 vs. 7.5%, $P = 0.0042$) [14].

In reality, semirigid and flexible ureteroscopes maintain complimentary roles in the treatment of ureteral stone disease: rigid instruments are better suited for distal ureteral stones while flexible scopes allow better access to the proximal ureter and intrarenal collecting system [15].

## Patient preparation and preoperative evaluation

Radiographic evaluation of the urinary tract is essential prior to URS and most patients will have undergone a noninfused computed tomography scan of the abdomen and pelvis [7]. Although no contrast is used with this study, the ureteral anatomy can usually be well defined. Additional information can be obtained at the time of the procedure by performing a retrograde pyelogram if necessary.

Some patients will initially present with urinary tract infection or urosepsis secondary to the obstructing ureteral calculus. This situation may be more commonly seen in patients with diabetes or those who are immunocompromised [16]. In this circumstance it is best to simply decompress the upper urinary tract with either ureteral stent placement or percutaneous nephrostomy tube insertion. Attempts to perform URS in the face of untreated or inadequately treated infection may lead to significant bacteremia with potentially disastrous complications. Even in patients without overt signs of infection or sepsis, clinicians should always perform urinalysis and consider urine culture to ensure any infection is adequately treated prior to URS [7].

Informed consent prior to URS should include a discussion of the risks of ureteral injury or perforation, as well as the risk of retreatment if the patient is not rendered stone-free. Although most injuries can be managed simply with stent placement alone, there are rare circumstances in which more extensive treatment may be necessary. In addition, the risks of ureteral stricture and the need for treatment of this complication should also be discussed.

## Surgical technique

URS is performed in most cases using general anesthesia. However, intravenous sedation alone or regional anesthetic techniques may be appropriate as clinical circumstances dictate. Allowance for adequate fluoroscopic visualization of the entire urinary tract is critical and provisions for radiographic monitoring should be made in all cases. In general, patients are placed in a dorsal lithotomy position with the contralateral lower extremity maximally abducted to facilitate access to the involved ureter. Patients without a urinary tract infection should be provided with 24 hours of antimicrobial prophylaxis per AUA best practice recommendations [17], with first-line treatment consisting of a fluoroquinolone or trimethoprim/sulfamethoxazole; alternative options include an aminoglycoside with or without ampicillin, a first- or second-generation cephalosporin, or amoxicillin/clavulanate. Patients with a history of urinary tract infection with organisms resistant to these first-line treatments should be offered culture-direct prophylaxis.

Increasingly, issues related to the use of anticoagulant medications prior to urologic surgical procedures have arisen. If such medications can be temporarily discontinued perioperatively with minimal risk to the patient, it is reasonable to do so if there is concern for potential bleeding. However, URS can be safely performed if necessary while patients remain anticoagulated so these medications should typically not be discontinued if nonurologic complications, such as to the cardiovascular system, could result from withholding them. Turna et al. retrospectively analyzed 37 patients undergoing flexible URS while on warfarin, clopidogrel, or aspirin, and compared them with a matched cohort of patients treated without anticoagulation [18]. No procedure had to be terminated due to poor visibility from bleeding and there was no significant difference in intraoperative or postoperative complications in the two groups.

All URS procedures should begin with surveillance of the bladder with particular attention paid to the location and configuration of the ureteral orifices. If the ureteral stone is readily visible at the expected location on initial fluoroscopic imaging, we generally do not perform a retrograde pyelogram initially since the injected contrast may obscure visualization of the stone or change its location. However, if the stone is not easily seen or there is a question regarding the ureteral anatomy, then it is best to perform a retrograde pyelogram to define the anatomy of the involved collecting system and ureter. The next step is passage of a wire past the stone and into the renal pelvis. A variety of guidewires are available, although we generally prefer a hydrophilic wire with a curved tip as this usually is the easiest to manipulate around the stone with minimal trauma to the ureter. Alternative wires with polytetrafluoroethylene (PTFE) coating allow more friction [19]. Once the wire is confirmed to be in the renal pelvis, a second guidewire may be placed as a safety wire. In the less common situation in which a wire cannot be passed proximal to the stone, the ureteroscope can be passed to the stone and then a wire can often be manipulated by the stone under direct visualization. If this is not possible, then careful fragmentation of the stone can be performed to free some space in the ureter alongside the stone and then the wire can be placed as early as possible. If a semirigid instrument is to be used, which is often preferable in the distal ureter, this can often be placed alongside the initial wire without the need for a second wire. If a flexible ureteroscope is to be used, this is generally passed over a wire or through a ureteral access sheath. In this case, the wire is usually removed after the scope is in position, so it is best to initially place a second wire as well that can be maintained throughout the procedure as a safety wire.

When passing the semirigid ureteroscope, it is important never to try to advance the instrument if visualization is limited or there is significant resistance, even if going over a guidewire. In most cases, active dilation of the ureter is not needed as the instruments are small enough to pass. However, in the presence of a stricture or in selected other cases, active dilation using a balloon dilation catheter or progressive dilators can be considered. Irrigation by an assistant using a hand-held syringe or other pumping device is often helpful to improve visualization; however, it is important to use this judiciously to avoid displacement of the stone more proximally. Pressure pumps are also available, although we prefer to use a hand-held syringe, which allows better control of the force with which the irrigant is delivered. Similar issues exist for the flexible ureteroscope, which is almost always passed initially over a wire to the level of the stone or through a ureteral sheath. As mentioned above, ureteral sheaths are available and are very helpful, particularly with flexible endoscopy, as they often facilitate passage of the instrument and allow for multiple insertions of the scope to remove fragments, etc. If difficulty is encountered in safely performing the procedure, it is always best to simply place a ureteral stent and allow for passive ureteral dilation, which generally makes a secondary URS procedure much easier to perform at a later date.

## Stone fragmentation and removal (see Video 47.1)

Once the ureteroscope has been successfully advanced to the level of a ureteral stone, a decision needs to be made whether to try and remove it intact or fragment the calculus. In previous years, when larger instruments were routinely used and the ureter was frequently dilated with a balloon or by another method, it was more common to remove stones intact. However, the advent of smaller scopes that may be passed without active dilation has made it more difficult to directly extract larger stones without risking damage to the ureter. As a general rule, when in doubt about whether a stone can be successfully removed without fragmentation, it is best to err on the side of caution and break it into pieces prior to removal. The two most commonly used methods to fragment ureteral stones are laser lithotripsy and pneumatic lithotripsy. The holmium:YAG end-fire laser is used commonly and offers several advantages in stone fragmentation. First, it can be used to fragment all stones irrespective of composition or hardness using narrow fibers of 200–365 μm in diameter. Second, the smaller fibers can be easily passed through flexible endoscopes with limited effect on the ability to provide irrigation to ensure adequate visualization. When working in the ureter, there is no significant concern about limitations in the ability to deflect the instrument as may occur when dealing with renal stones, particularly those in the lower calyces. Another advantage is the ability to ablate the stone, converting it to dust particles that do not have to be actively removed. The main disadvantage of the holmium:YAG laser is the associated cost of the instrument itself and of the disposable fibers.

Pneumatic lithotripsy most commonly involves the use of the Lithoclast device. This instrument is also highly effective in fragmenting stones and is generally associated with lower costs than those seen with the holmium:YAG laser as nondisposable probes are available. Disadvantages of pneumatic lithotripsy include the rigid probes which cannot be used with a flexible ureteroscope and the increased risk of retrograde stone propulsion. Garg et al. compared laser and pneumatic lithotripsy for ureteral stones in a randomized, prospective study and found that both methods were safe and effective [20]. However, the immediate stone clearance rate was significantly better in the laser group and stone migration occurred in 16% of cases using the pneumatic device. Similar results when comparing laser and pneumatic lithotripsy in treating ureteral stones were reported by Maghsoudi et al. [21].

Once the stone has been adequately fragmented, or if it is to be removed intact, a variety of devices can be used for stone retrieval. Stone baskets are available in a variety of shapes and configurations, and personal preference and experience are important in selecting which to use. In most cases, our preference is a tipless, nitinol basket when using the flexible instrument, and stone graspers with a rigid instrument. The advantage of the graspers is that the stone can be more easily disengaged if it is too large to remove and it will generally fall out of the graspers before significant damage to the ureter can occur. The baskets hold the stones more securely, but if the size of the calculus has been misjudged, it may be more difficult to disengage the stone from the basket for further fragmentation. In addition, the ureter can be damaged as the stone and basket are pulled distally if too much force is applied.

Another decision that needs to be made after the stone has been fragmented in the ureter is whether to try and remove all the fragments during the procedure or to allow them to pass later. It is generally our practice to remove all fragments from the ureter and this approach is supported by the literature [22, 23]. Schatloff et al. randomized 60 patients undergoing URS with laser lithotripsy to intraoperative fragment retrieval or spontaneous fragment expulsion, and found a significantly higher rate of unplanned medical visits in the group with incomplete fragment extraction. In addition, there was a trend towards higher rates of rehospitalization, residual stones, and the need for ancillary procedures in this group [22]. A report by the EDGE Consortium [23] found that residual fragments larger than 4 mm in size were independently associated with re-intervention compared to smaller residual fragments when controlling for other patient and operative factors. When directly comparing dusting versus basketing techniques, dusting resulted in a shorter median time to re-intervention. However, the technique was not independently associated with re-intervention on multivariable analysis.

The role of postoperative stenting after ureteroscopic stone removal is controversial and will be addressed in Chapter 55.

When performing ureteroscopic stone removal, prevention of inadvertent retrograde calculus migration is important in achieving a successful outcome. This is particularly true when using a semirigid instrument since it may not be possible to advance the scope further proximally in the ureter or renal pelvis to reach the stone if it has been displaced. In some situations, a flexible ureteroscope may not be available and some surgeons may not be comfortable performing flexible endoscopy. A variety of approaches are available to help avoid stone retropulsion. First, when using the holmium:YAG laser to fragment the stone, we try to place the fiber on top of the stone rather than on the most distal portion, so that the energy delivered to the calculus is less likely to push it more proximally. Second, some semirigid instruments have two working channels which allow the stone to be engaged in a basket placed through one channel while the laser fiber or pneumatic probe is placed through the other channel. In addition, baskets that can accommodate a laser fiber to be placed through them are also available. Third, instillation of lidocaine jelly proximal to the stone appears to help prevent retropulsion [24]. Zehri et al. used a 5 Fr ureteral catheter advanced beyond the stone to instill 2 ml of lidocaine jelly. Semirigid URS was then performed and the stones were fragmented using a pneumatic lithotripsy device. When comparing groups using lidocaine jelly and a randomized control group treated without, there was significantly less proximal stone migration and a better stone-free rate at 2 weeks in those receiving lidocaine [24]. Finally, a variety of antiretropulsion disposable devices are available [25–29]. In general, these devices are placed proximal to the stone and are then deployed in a configuration that prevents stone migration as fragmentation occurs. They may also help in removal of stone fragments as they are pulled distally after fragmentation is completed. Reduction in stone retropulsion using these devices has been demonstrated both *in vitro* and in clinical assessments [25–29]. The primary disadvantage of these antiretropulsion devices are the associated cost. One study estimated that antiretropulsion devices are cost-effective if the rate of retropulsion is above 6.3% [30]. Overall, when a flexible ureteroscope is available and the operating surgeon is comfortable and experienced with its use in the proximal ureter and kidney, stone migration is a minor concern and can usually be avoided with simple measures as described above. However, if semirigid URS is the only available option, then retropulsion is a greater concern since there is a risk that the procedure will not be completed successfully, leading to the need for secondary approaches, such as extracorporeal shock-wave lithotripsy, if the stone moves into the proximal ureter or kidney before it is adequately fragmented. In such circumstances, extra efforts to avoid stone migration, such as the use of retropulsion devices, may be appropriate.

## Complications

Advances in fiber-optic technology and the availability of smaller and flexible instruments have led to an overall improvement in the safety of ureteroscopic stone removal. However, complications may still occur due to mucosal injury from the endoscope itself or from the use of lithotripters to fragment stones within the ureter. The most common complication is ureteral perforation or the development of a false passage in the ureter. In general, this should be easily recognized at the time of the occurrence or when a retrograde pyelogram is performed at the completion of the procedure. As long as a safety wire is left in place, minor perforations generally are easily managed by the placement of a ureteral stent which is left in place for up to 4–6 weeks depending upon the extent of the injury. There is an increased risk for the development of ureteral strictures after perforation has occurred, so imaging 6–12 weeks after the stent is removed is essential in these cases, even if the patient is asymptomatic [31]. If a stent cannot be placed or if the injury is more extensive, then a percutaneous nephrostomy tube may be placed.

Overall, the incidence of strictures following ureteroscopic stone removal is 1–2% [31, 32]. In addition to ureteral injury, the extent and duration of stone impaction may increase the risk of stricture formation. Some authors have recommended routine imaging following stone removal since silent obstruction may occur. Weizer et al. reported that seven of 459 patients undergoing ureteroscopic stone removal were asymptomatic despite the development of ureteral strictures [32]. Therefore, they recommended that all patients undergo imaging of the upper urinary tract within 3 months after stone removal. Adiyat et al. investigated the need for routine postoperative imaging in 253 patients undergoing ureteroscopic stone removal [31]. While the overall incidence of stricture formation in this group was 1.4%, none of 158 patients with uncomplicated procedures developed strictures. Patients with complications were defined as those with ureteral perforation, stone impaction, or the need for balloon dilation of the ureter. Therefore, these investigators concluded that routine follow-up imaging is not essential after uncomplicated URS.

The most serious complication of ureteroscopic stone removal is ureteral avulsion, which fortunately is a rare occurrence. Ureteral avulsion most often results from trying to pull a stone that is too large to be removed intact down the ureter in a basket. The treatment of ureteral avulsion depends on the extent and location of the injury. If the distal ureter is the site of injury, avulsion can be managed by ureteral reimplantation with the use of a psoas hitch or Boari flap. For injuries that occur in the mid or proximal ureter, management can be quite challenging and may require ureteral substitution, autotransplantation of the kidney, or even nephrectomy. Surgery is best performed immediately to avoid the development of edema and inflammation, which can hamper a successful outcome. If a delay in treatment is necessary, then a nephrostomy tube should be placed.

## Conclusions

Ureteroscopic stone removal has become the procedure of choice for most patients with ureteral stones. With modern fiber-optic technology, the availability of effective lithotripsy devices, such as the holmium:YAG laser and pneumatic devices, and flexible endoscopes, the success rate in removing ureteral stones at all levels of the ureter is excellent. Issues related to stone migration can be effectively managed using a variety of techniques and disposable devices that are readily available, allowing for a minimal risk of the need for secondary procedures to remove stones. Overall, ureteroscopic stone removal is highly effective, with a low risk of complications, and it can be performed successfully and safely by most urologists.

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# 48

# Ureteroscopic Management of Renal Calculi

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## Introduction

During the past three decades, the surgical management of kidney stones has undergone many technological advances and one is the development of the flexible ureteroscopy (fURS). The development of this technique as well as ancillary equipment such as baskets, graspers, and others, and improvements in lithotripsy with holmium:YAG lasers, have led to the expansion of its indications to diagnostic and therapeutic management of medical issues of the upper urinary tract such as urolithiasis and urothelial tumors.

First described in 1964 by Marshall, the flexible ureteroscope did not gain popularity since it was only passively deflectable and did not include a working channel. Although the first successful procedure using fURS with active deflection in humans was reported by Takayasu, it was not until 1987 that Demetrius Bagley introduced fURS as we know it today [1–5]. At this time, the fURS suffered from poor resolution, low angle of deflection, difficult ureteral insertion, and, until 1974, lack of irrigation [3]. But this instrument benefited from many advancements in the 1980s, including fiber-optic bundles for light transmission and image relay, reduction of the outer diameter, passive and active deflection in upward and downward directions, and addition of a working channel. One of the latest developments was the introduction of a digital imaging system which has improved the image quality substantially. Currently, we can distinguish two types of fURS: fiber-optic and digital fURS. The difference between these two endoscopes is the light transmission and image relay. In fiber-optic scopes, light and image are transmitted in analogue format through fiber-optic cable whereas the illumination in digital scopes is produced made by fiber-optics or by a light-emitting diode (LED) and image capture is via a digital sensor located at the distal end of the endoscope: either a complementary metal oxide semiconductor (CMOS) or charge-coupled device (CCD). In both cases, most manufacturers have models with a working channel of 3.6 Fr (for irrigation and the use of accessory instruments) and at least one 270° active deflection of the tip. The most recent development in fURS was the introduction of single-use digital fURS [6, 7].

Due to these technological advances, fURS has gained in popularity and has become the treatment of choice for kidney stones.

## Indications

The different treatment modalities offered to patients with kidney stones are:

- extracorporeal shock-wave lithotripsy (ESWL),
- fURS,
- percutaneous nephrolithotomy (PCNL): conventional and miniaturized PCNL (mini-PCNL, ultramini-PCNL, micro-PCNL),
- open surgical and laparoscopic removal.

In case of suspected cystine or uric acid stones, ESWL is not an option because cystine stones are often only faintly radiopaque and pure uric acid stones are typically radiolucent. Furthermore, cystine stones are typically resistant to ESWL fragmentation.

According to the European Association of Urology (EAU) guidelines, the indications for active stone removal of renal stones are stone growth, stones in high-risk patients for stone formation, obstruction caused by stones, infection, symptomatic stones (e.g. pain or hematuria), stones

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

>15 mm, stones <15 mm if observation is not the option of choice, patient preference, comorbidity, social situation of the patient (e.g. profession or traveling), and choice of treatment [8].

Once the choice of stone removal is taken, the choice of the treatment modality depends on several stone characteristics, such as size, location, composition (if available), collecting system anatomy. Other factors include complication rate, patient comorbidities, patient preference, available technical equipment, and economic aspects.

Both the American Urological Association (AUA) and EAU provide recommendations for the selection of procedure for active removal of kidney stones [8–10].

## AUA guidelines

The latest recommendations of the AUA about the surgical treatment of kidney stones were published in 2016 [9, 10]. ESWL, fURS, and PCNL are the treatment options for symptomatic patients with <20 mm non-lower pole renal stones. AUA guidelines recommend ESWL or fURS as first-line treatment for such stones because their stone-free rates are acceptable and have lower morbidity than PCNL.

For symptomatic ≤10 mm lower pole kidney stones, ESWL or fURS are the two options that urologists should offer. However, patients with a skin-to-stone distance greater than 9–10 cm or stone attenuation greater than 900–1000 Hounsfield units have less successful results with ESWL. An endoscopic approach (fURS or PCNL) is recommended for 10–20 mm lower pole renal stones because they appear to be less affected by stone burden than ESWL.

For stones >20 mm, PCNL is recommended as first-line option because it offers a higher stone-free rate than ESWL or fURS and is less invasive than open surgery or laparoscopic/robot-assisted procedures. PCNL should also be the first treatment utilized for most patients with staghorn calculi.

fURS should be offered as first-line therapy in most patients who require active stone removal with uncorrected bleeding diatheses or who require continuous anticoagulation/antiplatelet therapy.

The recommendations are summarized in Tables 48.1 and 48.2.

**Table 48.1** AUA treatment algorithm for renal calculi (<20 mm lower pole renal calculi excluded).

| Kidney stone (<20 mm lower pole stone excluded) | |
|---|---|
| <20 mm | ESWL or fURS |
| >20 mm | PCNL |

## EAU guidelines

The latest recommendations of the EAU about the surgical treatment of kidney stones were published in 2018 [8]. ESWL and fURS are the first-line treatment for renal stones <10 mm. For 10–20 mm non-lower pole renal stones, ESWL, fURS, and PCNL are the treatment modalities that clinicians should offer. For 10–20 mm lower pole renal stones, PCNL or fURS is recommended in cases of unfavorable factors for ESWL, because then its efficacy is limited. With favorable factors for ESWL, ESWL or an endoscopic approach (fURS or PCNL) should be offered. Unfavourable factors for ESWL are shock-wave-resistant stones (calcium oxalate monohydrate, brushite, or cystine), steep infundibular-pelvic angle, long lower pole calyx (>10 mm), and narrow infundibulum (<5 mm).

Kidney stones greater than 20 mm should be treated by PCNL as a first-line option because it offers a higher stone-free rate than ESWL or fURS. In cases where PCNL is not an option or contraindicated, renal stones >20 mm may be treated with fURS. However, in such cases there is a higher risk of staged procedures and placement of a ureteral stent may be needed.

In case of an uncorrected bleeding disorder or continued antithrombotic therapy, fURS, in contrast to ESWL and PCNL, might offer an alternative approach since it is associated with lower morbidity.

The recommendations are summarized in Tables 48.3 and 48.4.

**Table 48.2** AUA treatment algorithm for <20 mm lower pole renal calculi.

| Lower pole renal stone <20 mm | |
|---|---|
| ≤10 mm | ESWL or fURS |
| 10–20 mm | Endourology (fURS or PCNL) |

**Table 48.3** EAU treatment algorithm for renal calculi (10–20 mm lower pole renal calculi excluded).

| Kidney stone (10–20 mm lower pole renal stone excluded) | |
|---|---|
| <10 mm | 1) ESWL or fURS<br>2) PCNL |
| 10–20 mm | ESWL or endourology (fURS or PCNL) |
| >20 mm | 1) PCNL<br>2) fURS or ESWL |

**Table 48.4** EAU treatment algorithm for 10–20 mm lower pole renal calculi (>20 mm and <10 mm as in Table 48.3).

| Lower pole renal stone 10–20 mm | |
|---|---|
| **Unfavourable factors for ESWL** | **Options for treatment** |
| Yes | 1) Endourology (fURS or PCNL)<br>2) ESWL |
| No | ESWL or endourology (fURS or PCNL) |

## Contraindications

There are no specific contraindications to performing fURS apart from general problems such as general anesthesia or untreated preoperative positive urinalysis.

## Technique

### Patient positioning, anesthesia

The patient is placed in lithotomy position. Although local, spinal anesthesia and intravenous sedation are feasible, fURS is mostly performed under general anesthesia. General anesthesia is suggested because it offers some advantages: renal movement caused by respiration may affect renal navigation and lithotripsy whereas with mechanical ventilation the use of apnea stops this problem temporarily [11–13].

### Access to the upper urinary tract and ureteral access sheath placement

The procedure begins with rigid cystoscopy to look for the location and configuration of the ureteral orifices. The next step is the placement of a guidewire into the renal pelvis. The choice of guidewire depends on surgeon preference; however, we prefer to use a stiff hydrophilic guidewire. Some authors have reported the feasibility of performing fURS in the absence of a working or a safety guidewire without intraoperative complications [14–18]. However, we think the use of a safety guidewire is still useful as it does not increase morbidity, ensures access to the collecting system, and facilitates the placement of a stent in cases of ureteric or collecting system injury such as ureteral perforation or excessive bleeding. Alternatively, the procedure may begin directly with first-look semirigid ureteroscopy, always using a safety guidewire, which has the advantage of passively dilating the whole ureter in order to choose the most appropriate ureteral access sheath (UAS) size [19]. Once the guidewire has been placed – with or without performing semirigid ureteroscopy – the flexible ureteroscope may be passed up to the kidney alongside this safety guidewire or over a second guidewire (inserted using a dual-lumen catheter) under fluoroscopic guidance. The other option is to place a UAS under fluoroscopic control and insert the flexible ureteroscope through the UAS. These different options for endoscope insertion depend on stone burden, upper urinary tract anatomy, and the surgeon's preference.

The goals of using a UAS are to facilitate multiple passages for stone fragment removal, to protect the endoscope, and, most importantly, to provide irrigation with better fluid outflow, thereby decreasing the intrarenal pressure [2, 20–23]. The choice of the UAS, its size, and its diameter depend on patient anatomy, the endoscope used, and surgeon preference [24, 25]. Instead of using two guidewires, some new designs of UAS use only one guidewire, meaning that the working guidewire turns into safety guidewire [26, 27] (Figure 48.1). Attention has to be paid to the force applied during UAS placement because ureteral lesions may be the consequence of forced maneuvers. Furthermore, in cases that require a second procedure, any stone fragments that may have migrated into the ureter have to be removed

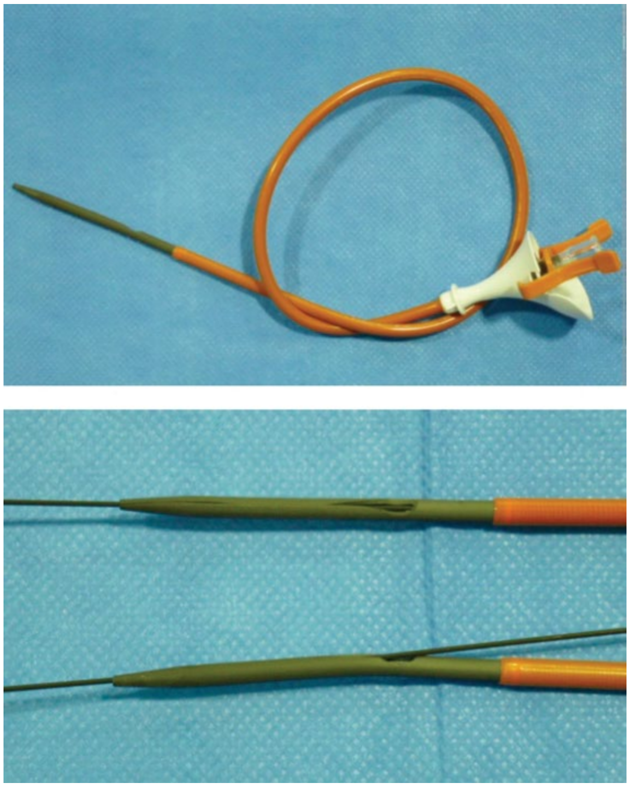


**Figure 48.1** Ureteral access sheath. The removal of the inner tip automatically converts the working guidewire as a safety guidewire lateral to the sheath.

before UAS insertion. If any resistance is encountered during UAS placement, it latter should be stopped and the endoscope introduced to explore the ureter. If not possible, it is safer to place a ureteral stent for passive ureteral dilation, making a secondary fURS procedure much easier to perform at a later date. The best position for the UAS is with its tip in the proximal ureter or just below the ureteropelvic junction but not through it, since this is the portion of the ureter at greatest risk of avulsion because it has the least muscular tissue support.

Once the flexible ureteroscope is placed in the kidney, the collecting system is explored starting with the upper calices followed by the middle and lower calices. In the right kidney, the calyces are seen on the left of the endoscope screen. Thus, supination is the essential movement for exploring the right renal cavities. Conversely, the left renal calyces are seen on the right of the endoscope screen, meaning that pronation is essential when exploring the left kidney (Figure 48.2).

## Lithotripsy and fragment extraction

Laser lithotripsy, using holmium:yttrium-aluminum-garnet (Ho:YAG) laser and a laser fiber, has become the standard for stone lithotripsy during fURS procedures as it has proven efficacy and safety [28]. It delivers a pulsatile energy and operates at a wavelength of 2100 nm, which is in the infrared spectrum and invisible to the human eye. The holmium laser is effective for all types of stone composition. Stones are ablated by a photothermal effect whereby long laser pulses (100–1000 microseconds) induce a temperature rise inside the stone. Laser radiation is absorbed by residual water in the stone, creating a vapour pressure that breaks the stone [29–31].

The majority of laser lithotripters allow the urologist to control two parameters: the pulse energy and pulse frequency (Figure 48.3). The total power output results from the product of these two parameters: total power (W) = pulse energy (J) × pulse frequency (Hz). By adjusting these parameters, the urologist decides the energy intensity that is delivered at the tip of the laser fiber to ablate the stone. In the new generation of laser lithotripters, a third parameter can be set: pulse duration. The laser machine allows a choice between short-pulse and long-pulse modes (Figure 48.3). The difference between these two modes is that, for a same amount of energy, its distribution is over a short (180–330 microseconds) or a longer period of time (650–1215 microseconds) [32]. At the same power level, high-frequency/low-pulse-energy is less efficient than low-frequency/high-pulse-energy lithotripsy. Stone ablation volume directly correlates with pulse energy, whereas frequency, especially high frequency, and total power setting play more minor roles [33]. An *in vitro* study showed that the short-pulse mode is 25.0 and 9.9% more ablative than the long-pulse mode

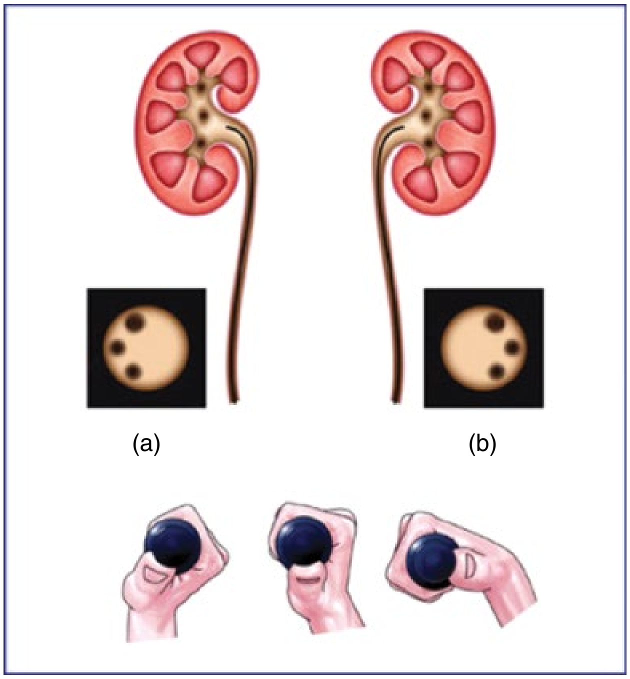
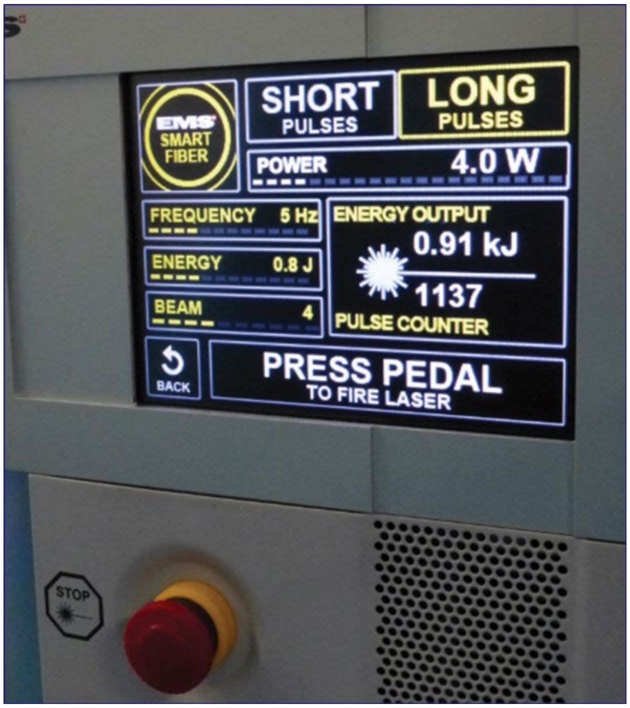


Figure 48.2 Dominant-hand pronation and supination to change the direction of the distal tip of the scope. (a) Supination is essential when the scope is in the right renal cavities and (b) pronation is essential when the flexible ureteroscope is in the left renal cavities.



POWER 4.0 W
FREQUENCY 5 Hz
ENERGY 0.8 J
BEAM 4
ENERGY OUTPUT 0.91 kJ
1137 PULSE COUNTER
PRESS PEDAL TO FIRE LASER

Figure 48.3 Laser parameters.

when associated with low frequency/high pulse energy and high frequency/low pulse energy, respectively [32–34]. Low pulse energy, like high-frequency/low-pulse-energy settings, produces smaller stone fragments (also called the "dusting effect") than high-pulse energy, such as low-frequency/high-pulse-energy settings [35–37].

Thus, there are two options for stone laser lithotripsy. The first is dusting, where the stone is reduced to fine dust and to small fragments of 2 mm or less in diameter which are supposed to pass spontaneously, avoiding the use of a basket. Second, stone fragmentation produces stone pieces that subsequently have to be removed individually with a basket [35–38] (Figure 48.4). Dusting lithotripsy requires the surgeon to work over the stone's surface and avoid always being in contact at the same place by "painting" with the laser fiber [38]. If fragmentation is performed and a 10/12 Fr UAS is used, for example, the stones have to be reduced to 3 mm fragments, which is the maximum stone size that can be removed through this type of sheath. The removal of such fragments is time-consuming and may require a specific laser lithotripsy technique called the "popcorn effect" to reduce the stone burden, thereby avoiding numerous back-and-forth movements with the basket [33, 39]. Each method has its advantages and disadvantages, but surgeon preference, stone size, composition, location, and intrarenal anatomy determine which ablative technique is the most appropriate. Furthermore, the two techniques can be combined by starting with dusting and finishing with fragmentation to obtain stone pieces for stone analysis. For large stones, fragmentation alone will produce a multitude of small fragments the removal of which may be time-consuming. Conversely, complete dusting of such stones may also increase operative time. Thus, both techniques may be used for large stones as well as utilizing the popcorn effect when significant stone pieces are remaining at the end of the procedure to avoid the extraction by basket of all the fragments.

The different laser settings for stone lithotripsy are:

- fragmentation: high energy (1–2 J), low frequency (3–5 Hz), and, if needed, short pulse duration,
- dusting: low energy (0.2–0.5 J), high frequency (10–20 Hz), and, if needed, long pulse duration,
- popcorn effect: high energy (1 J), high frequency (10–20 Hz), and, if needed, long pulse duration.

Another parameter that may facilitate laser lithotripsy is the influence of the working channel position. Most flexible ureteroscopes have a 3 or 9 o'clock working channel position. When performing laser lithotripsy in a

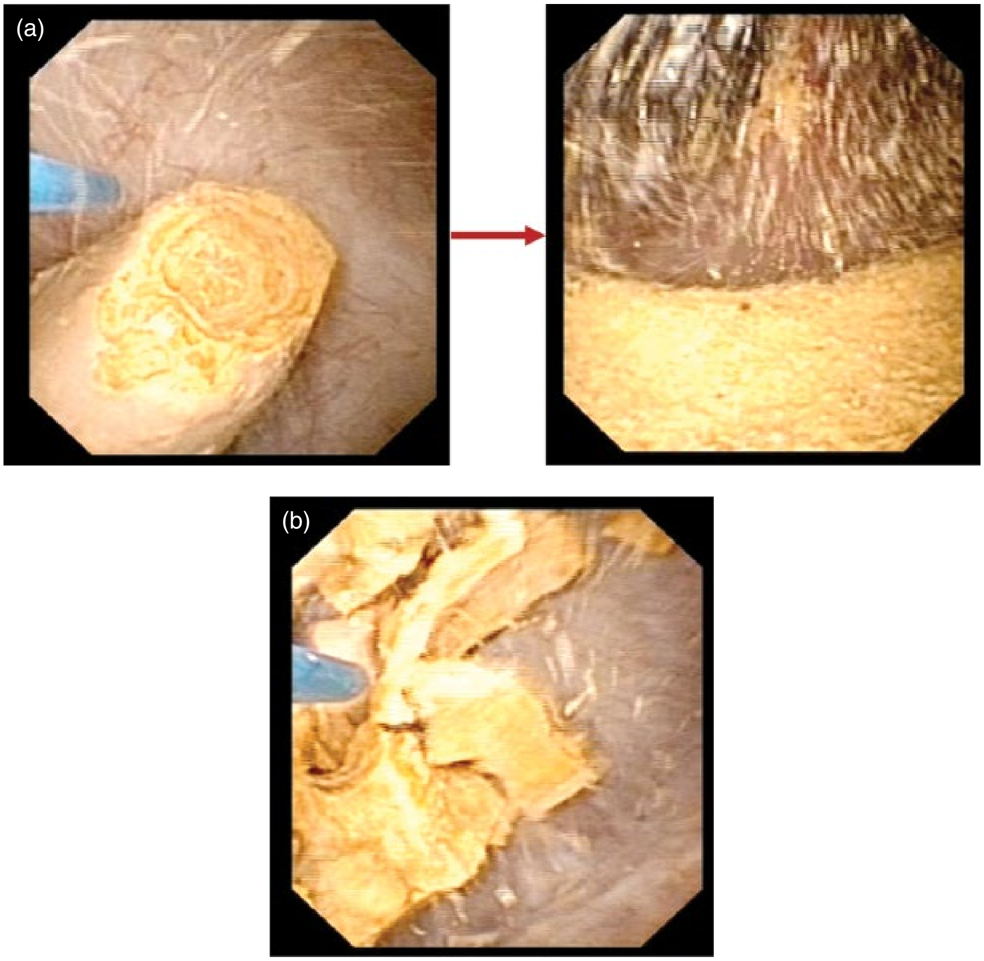


**Figure 48.4** Laser lithotripsy. (a) Dusting effect; (b) fragmentation.

right kidney, a 3 o'clock position is better to ablate stones. However, to better fragment stones located in right anterior calyces, a 9 o'clock working channel position is advised. Conversely, a 9 o'clock working channel is advised for left renal stones except for posterior calyces where a 3 o'clock working channel is preferable (Figure 48.5).

The last parameter to take into account is the laser fiber diameter. Large fibers (550 μm) produce wider fissures, while small fibers (200 μm) create deep fissures, but neither surpasses the other in terms of ablation volume [33, 34]. Although large-diameter laser fibers are more resistant to fiber-tip degradation or the "burn-back" effect, their stiffness reduces ureteroscope maximal deflection and their diameter decreases irrigation flow. Conversely, small-diameter laser fibers are more fragile and prone to fiber-tip degradation, but this is compensated for by better irrigation, better endoscope deflection, and less retropulsion [33, 40, 41].

Finally, when stone removal has to be performed, tipless nitinol baskets have become the standard devices and many designs are available on the market (Figure 48.6). The advantages of nitinol baskets are their flexibility and ability to not damage the scope and intrarenal cavities during fragment extraction. A diameter smaller than 2.2 Fr allows maximum irrigation flow and deflection of the endoscope, whereby all parts of the collecting system can be reached [41]. Using a basket blind has to be avoided as it may increase the risk of ureteral avulsion. Thus, stone retrieval with baskets, even if a UAS is used, has to be guided endoscopically. The stone and basket have to be kept under direct vision as they are removed; the size of the stone is continually compared with the size of the ureteral lumen until entry into the

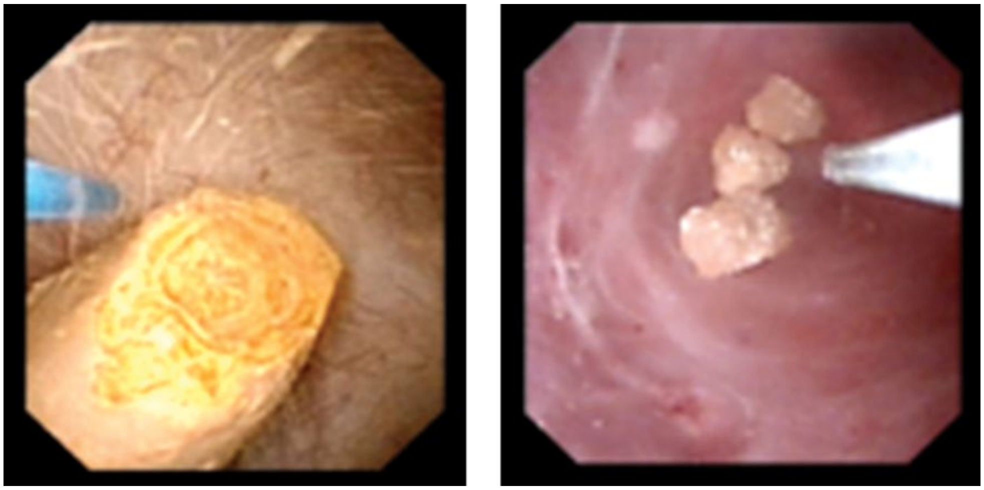


**Figure 48.5** Working channel position. Left: 9 o'clock working channel, Right: 3 o'clock working channel.

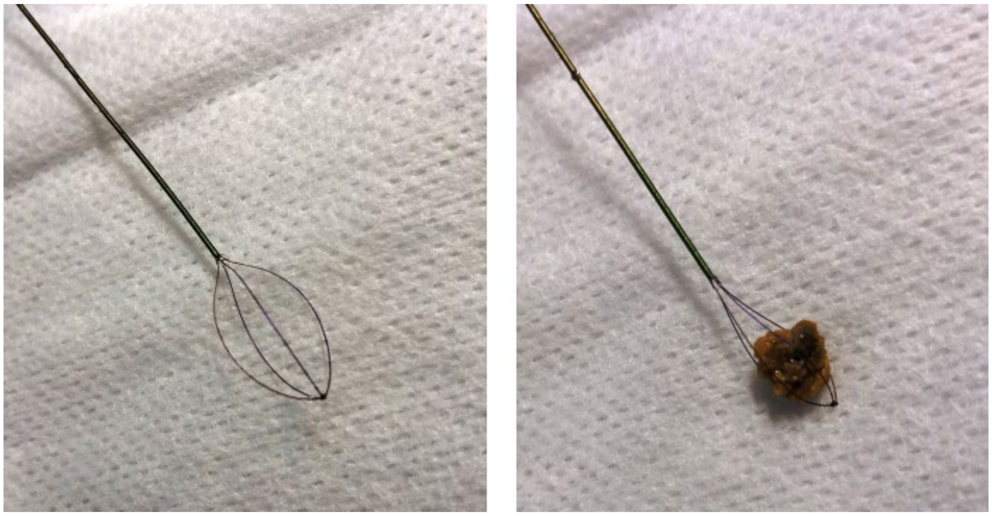


**Figure 48.6** Examples of nitinol baskets.

sheath, if used. If the stone appears to be too large to be removed intact, it should be fragmented into smaller pieces that may subsequently be removed [42].

Although fURS is often performed with continuous saline irrigation through the working channel, an additional device such as a syringe or manual hand pump may be needed to improve visibility when an instrument is inserted into the working channel, while dusting a stone, or of minor venous bleeding occurs. Furthermore, these devices may be helpful to flush stone fragments to facilitate basketing in difficult cases. However, although irrigation pressure devices are helpful and often used, there is a risk of increased intrarenal pressure. While working in the renal cavities for a long time, placing a UAS may prevent the elevation of pressure (Figure 48.7).

## Lower pole stones

When considering lower pole stones, the surgeon should attempt to relocate the stone with a nitinol basket to a more favorable position (upper pole or renal pelvis) [43] (Figure 48.8). This practice reduces the risk of damage to the ureteroscope and makes stone targeting during laser lithotripsy easier and more effective. Furthermore, according to the stone lithotripsy technique used, the stone fragments produced will be easier to grasp with the basket or able to pass spontaneously through the ureter instead of accumulating in the lower pole. However, stones larger than 10 mm may not be possible to grasp and relocate, necessitating laser treatment *in situ*, with the ureteroscope maximally deflected, potentially increasing the risk of laser fiber failure and ureteroscope damage [44]. In that case, it is recommended to insert the laser fiber with the minimal deflection of the endoscope to avoid any working channel damage and subsequently access the lower pole to treat the stone *in situ*. However, once the laser fiber is in place, this results in a loss of the flexible ureteroscope's maximal angle of deflection and access to the lower pole may be difficult [41, 45].

For this reason a new design of laser fibers with a ball-tip shape has been developed, which reduce friction within the working channel in a completely deflected ureteroscope, thereby reducing the likelihood of endoscope damage [46]. However, after the first minute of laser emission, the ball-shaped tip fibers lose their special feature due to fiber-tip degradation, especially at high pulse energies [47]. Thus, this allows the insertion of a ball-tip fiber only once in a fully deflected flexible ureteroscope. A recent study reported that cleaving the tip of standard laser fibers with metal scissors results in

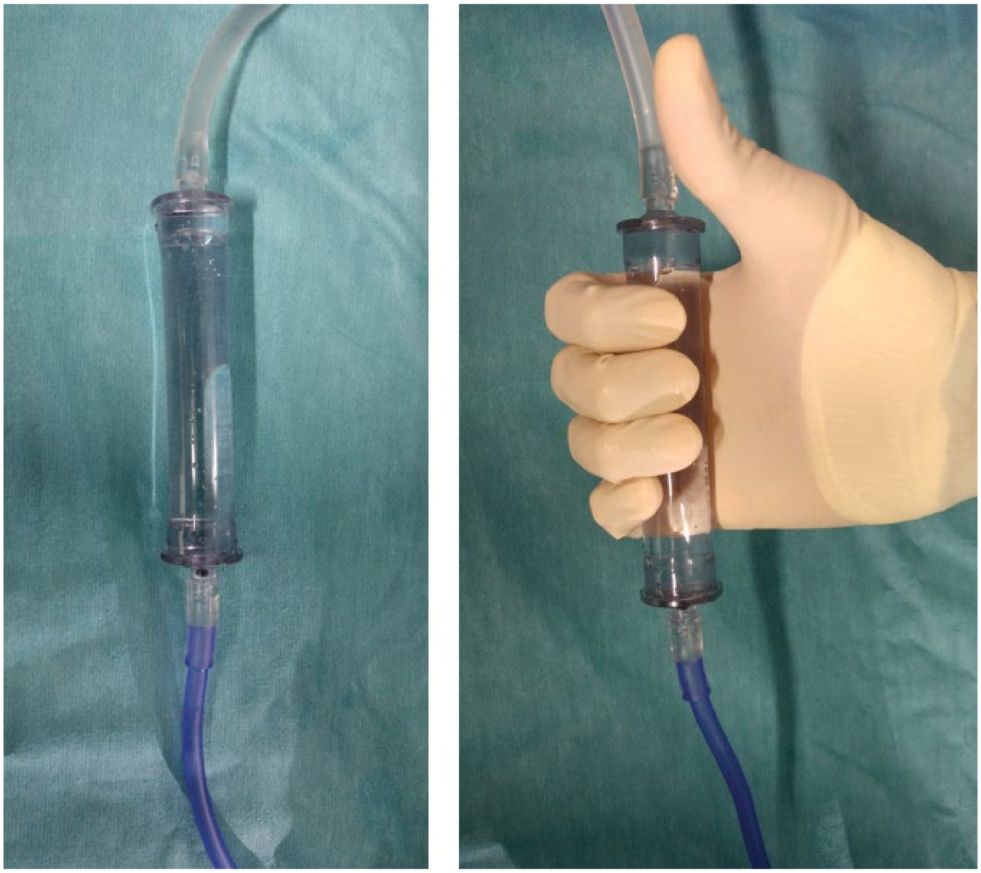


**Figure 48.7** Hand-assisted irrigation device.

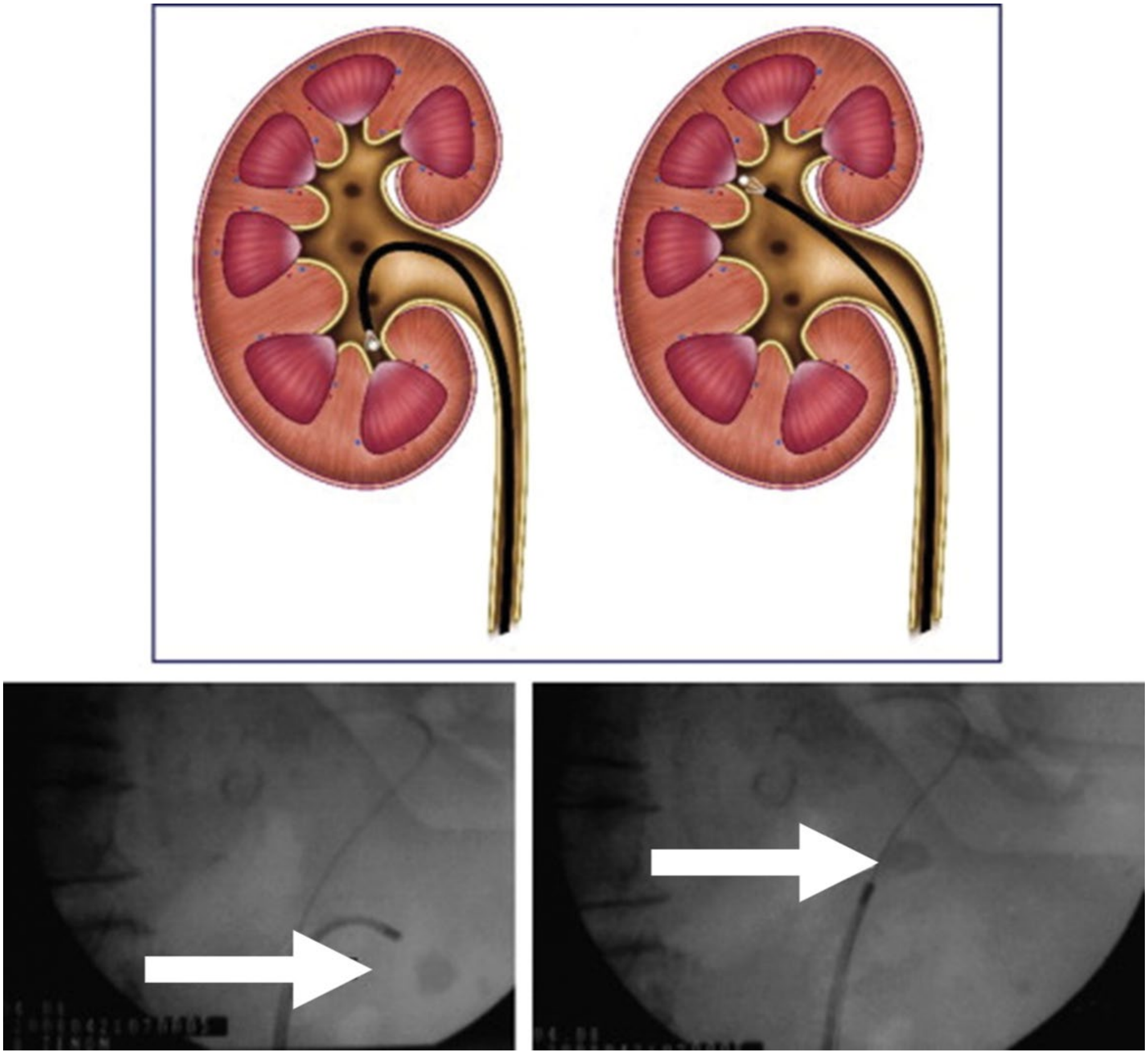
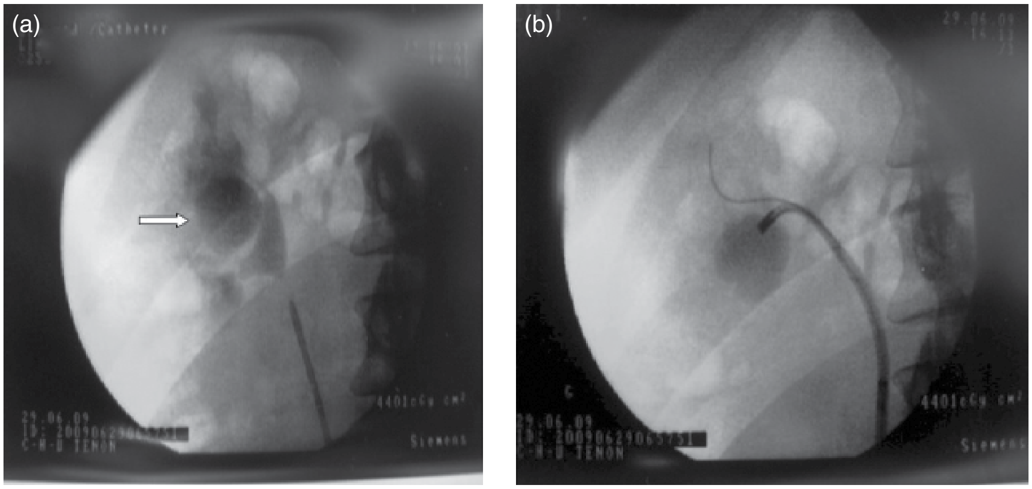


**Figure 48.8** Relocation of a lower pole renal stone.

equivalent passage capabilities through a deflected endoscope to ball-tip-shaped fibers [45]. Recent work also showed that laser fiber diameter and curve as well as laser settings are parameters to take into account when treating a lower pole renal stone *in situ* [48]. The 272 μm fibers broke at the curve diameter of 9 mm and below when using dusting parameters (high frequency and low energy) and at 12 mm when using fragmentation parameters (low frequency and high energy). The 365 μm fibers broke at 9 mm for dusting and required a smaller curve (15 mm) to break under fragmentation parameters. Thus, to prevent laser fiber breakage, it is advised to use small 272 μm fibers, with dusting parameters, to reduce the stone diameter. It can then be relocated as soon as possible.

## Calyceal diverticulum

In cases of calyceal diverticulum the procedure begins as standard fURS. Once the endoscope is placed into the renal cavities, the principle consists of injecting contrast through the working channel to identify the diverticular neck with the assistance of fluoroscopic guidance (Figure 48.9a,b). In difficult cases, the blue test technique has been suggested (Figure 48.9c). Instead of injecting contrast alone, a mix of contrast and methylene blue or indigo carmin is injected. If opacification of the diverticulum is obtained, this means that its neck is patent. Then, the collecting system has to be washed out using the saline irrigant through a manual irrigation device.



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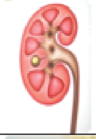
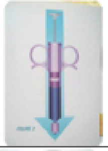
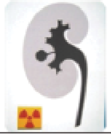
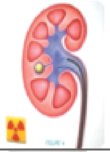
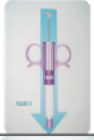
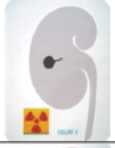
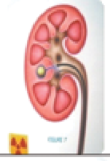
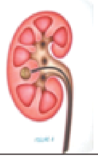
| step 1 |  | Installation, cystoscopy<br>Introduction of the guide wire |
| step 2 |  | UPR with methylene blue or the indigo carmin by ureteral catheter or dual-lumen catheter |
| step 3 |  | Fluoroscopy<br>Site and permeability of the diverticula |
| step 4 |  | Second guidewire (safety)<br>Introduction of the fURS |
| step 5 |  | Injection of the normal saline and washing of the renal cavities |
| step 6 |  | Fluoroscopy<br>Disappearance of the calyceal cavities<br>Persistence of diverticula |
| step 7 |  | Exploration of the cavities and identification of the leakage of the indigo carmin by diverticular neck |
| step 8 |  | Introduction of the laser and incision of the neck<br>Local fragmentation of the calculi and marsupialization |

**Figure 48.9** (a) Diverticulum at the middle portion (arrow). (b) Flexible ureteroscope at the diverticulum. (c) Blue test technique. Retrograde pyelography.

Once the cavities are clear, a leakage of blue by the diverticular neck is identifiable. The next step is laser incision of the diverticular neck and subsequent treatment of the stone burden [49].

### The use of apnea during laser lithotripsy

Laser lithotripsy of renal stones and precise laser ablation (upper tract urothelial carcinomas, endopyelotomy, incision of diverticular neck, stone in narrow calyx) are made challenging by the renal movement caused by respiration and diaphragmatic excursion. The surgeon has to treat a moving target without injuring the urothelium or papillae. For these reasons, apnea may be needed during fURS to facilitate treatment. A recent report described a protocol to perform apnea during fURS, allowing its maintenance for approximately 5 minutes. This illustrates the role of the collaboration between anesthesiologists and surgeons in order to achieve optimum treatment [13].

### Ureteral stenting

Careful ureteral exploration should be performed at the end of the procedure to retrieve the scope and the UAS while keeping the scope's tip a few centimeters out of the sheath to detect eventual ureteral lesions due to UAS placement and stone fragments [50].

To prevent the incidence of postoperative ureteric obstruction and renal colic secondary to ureteral edema, a ureteral stent may be placed. This stent placement has also been advocated to facilitate the passage of stone fragments secondary to passive ureteric dilation [51–55]. Although this common practice is still debated, it has been reported in large series that approximately 80% of urologists place a ureteric stent after uncomplicated ureteroscopy for stone disease [56–64]. The last AUA guidelines recommended ureteral stenting among patients with ureteric injury during URS, those with evidence of ureteral stricture or other anatomical impediments to stone fragment clearance, such as ureteral wall edema, a large stone burden (>15 mm), those who have an anatomically or functionally solitary kidney or renal functional impairment, and in those in whom another ipsilateral URS is planned [9, 10].

## Outcomes

The assessment of outcomes after renal stone treatment is always challenging because many parameters are variable. First of all the technique employed may vary. Secondly, the definition of the stone-free status depends on the imaging modality used, which is often evaluated in a different way in each study, and the cut-off used for insignificant fragments. And finally, most of the studies have a retrospective design, which may limit their strength.

A recent retrospective study compared the stone-free rates, defined as residual fragments up to a maximum of 2 mm in diameter detected on ultrasound or computed tomography scan at 1 month follow-up, between four stone size categories: ≤10 mm, >10 and ≤20 mm, >20 and ≤30 mm, and >30 mm. The authors found 90.4%, 79.8%, 70.5%, and 55% stone-free rates after one fURS procedure for the ≤10 mm, >10 and ≤20 mm, >20 and ≤30 mm, and >30 mm groups, respectively [19].

### Renal stones (<20 mm)

For <20 mm non-lower pole renal stones, PCNL stone-free rates are the least affected by stone size, while stone-free rates of ESWL and fURS decline with increasing stone burden [9, 10, 65]. However, stone-free rates of ESWL and fURS are acceptable and show less morbidity than PCNL. Compared to ESWL, fURS is associated with a lower likelihood of repeat procedure; therefore, the patient will become stone-free quicker than with ESWL [9, 10, 66]. No meta-analysis for renal stones has been published yet due to the lack of randomized control trials, except for lower pole renal stones.

### Large renal stones (>20 mm)

Although PCNL remains the first-line treatment for renal stones >20 mm, fURS as an option has emerged in some studies, pushing the limits of this technique. Recent publications have reported successful treatment of large stones using single or staged ureteroscopic procedures [67–69]. A meta-analysis published in 2015 found that PCNL provides a significantly higher stone-free rate (odds ratio [OR], 2.19; 95% confidence interval [CI], 1.53–3.13; $P < 0.001$) and higher complication rates (OR, 1.61; 95% CI, 1.11–2.35; $P < 0.001$) compared to single-session fURS for stone burden >10 mm [69]. Another meta-analysis assessing the outcomes of fURS for stones >20 mm found a mean of 1.46 ± 0.2 procedures per patient with 20–30 mm renal stones compared with 1.85 ± 0.02 for those with renal stones >30 mm. Stone-free rates after treatment completion were 95.7 and 84.6%, respectively [69]. Large stone burden can be treated by fURS but the patient has to be informed that a staged procedure may be required.

### Lower pole renal stones

A recent meta-analysis comparing ESWL, fURS, and PCNL for the treatment of lower pole renal stones reported a stone-free rate of 89.5% versus 70.5% for fURS and ESWL, respectively. Subgroup analyses revealed that fURS was more effective than ESWL for 10–20 mm stones (85.5 vs. 57%) but this benefit was markedly less for ≤10 mm stones (90% for fURS vs. 79.9% for ESWL) [70]. A preleminary study reported no significant difference in stone-free rates between PCNL and fURS for 11–25 mm lower pole renal stones (45.6% for fURS vs. 66.7% for PCNL) [70].

## Complications

A recent study including 11 885 patients who underwent an ureteroscopic procedure found an overall complication rate of 7.4%. The intraoperative and postoperative complication rates were 4.2 and 2.6%, respectively, and a total of five deaths were reported between January 2010 and October 2012. However, these rates do not distinguish the complications associated with fURS or semirigid URS. The location of the stones was ureteric and renal in 73 and 15.6%, respectively [71]. (See also Chapter 56.)

## Conclusions

fURS has become widely used due to the technical advancements and refinements made in the endourologic armamentarium over the last three decades. The high efficacy and low morbidity in the treatment of renal stones up to 20 mm have made it a treatment of choice for the management of renal calculi.

See accompanying Video 48.1.

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# 49

# Diagnostic Ureteroscopy

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## Indications

From the advent of ureteroscopy (URS) the procedure has been used for diagnostic purposes [1–3]. As the early instruments lacked a working channel, diagnosis was actually its initial primary function. The equipment has experienced significant innovation ever since, broadening indications and refining results. Diagnostic URS is still not perfect and should only be seen as one step in a suite of investigations along with ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI), and urine-based diagnostics, when looking at the upper urinary tract.

The main purpose of diagnostic URS has always been the detection of upper urinary tract urothelial cancer (UTUC). Established indications are hence derived from surrogate markers of this disease. Every patient presenting with visible hematuria or persistent nonvisible hematuria warrants a urological workup. Besides urine dipstick and culture, cystoscopy is performed to evaluate the lower urinary tract. The upper tract is usually primarily assessed with radiological techniques: ultrasound, CT kidney–ureter–bladder (KUB), and CT urogram, and – in select cases – intravenous pyelogram (IVP). Stones as a source of hematuria can be reliably identified this way. If any of these investigations shows abnormalities suspicious of a tumor, diagnostic URS is recommended prior to any treatment. However, as all these investigations have limited sensitivity, a diagnostic URS should still be considered in the absence of radiological abnormalities if there is a strong clinical suspicion of UTUC (e.g. persistent hematuria in a patient with a history of bladder tumors or positive urine cytology with normal cystoscopy) or in situations where early diagnostic accuracy is paramount (e.g. solitary kidney).

Classical findings suggestive of UTUC are hydronephrosis in the absence of ureteric calculi (differential diagnoses: ureteric stricture, pelviureteric junction [PUJ] obstruction, compression of the ureter) on CT KUB and contrast-filling defects on CT or IVP. Only tumors of a certain size are directly visualized on CT or ultrasound at which stage they are often invasive. This is the case for 60% of UTUC at primary diagnosis [4].

Other indications for diagnostic URS are follow-up after organ-sparing treatment of UTUC and in individual cases after radical cystectomy for transitional cell carcinoma (TCC) of the bladder, for example if a cutaneous ureterostomy has been established.

The procedure may also be used to investigate ureteric strictures, cases of suspected ureteric endometriosis, and other rare changes of the upper urinary tract (e.g. amyloidosis).

## Patient preparation

The preparation for diagnostic ureteroscopy should be even more vigorous than for other endourological procedures due to its delicate nature and susceptibility to confounding factors. All patients must have their urine cultured prior to the intervention and any urinary tract infection should be treated with antibiotics. Indwelling ureteric stents should be removed at least 3 weeks ahead if possible as they can provoke inflammatory changes rendering an endoscopic diagnosis of smaller lesions impossible.

The consenting process should include injuries to the lower urinary tract and ureter requiring open surgical repair, formation of strictures, hydronephrosis, and the necessity to insert a ureteric stent. Any intended simultaneous therapeutic procedure must also be addressed.

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All patients with suspected UTUC should be assessed with CT urogram (or MRI urogram in cases of impaired kidney function or allergy to iodine-containing contrast agents) prior to endoscopy in keeping with the European guidelines, whereas the American National Comprehensive Cancer Network guidelines do not make specific recommendations on the sequence [4, 5]. If a tumor is detected, a diagnostic URS should be performed prior to nephroureterectomy. Not only should a histological diagnosis be obtained but there is also a cohort of patients with small low-grade lesions who might benefit from organ-sparing treatment. Up to 42% of patients would receive unnecessary over treatment without diagnostic URS [6].

Diagnostic URS should not be considered for atrophic kidneys as this is an indication for nephrectomy. If the radiological findings are suggestive of a nonfunctioning kidney, a MAG3 or $^{99m}$Tc-labeled dimercaptosuccinic acid (DMSA) renogram should be considered for confirmation.

Single-shot antibiotic prophylaxis for diagnostic URS is currently a point of discussion. In the absence of risk factors, it can be omitted as the incidence of sepsis is very low [7].

## Instruments

It is important to use as little equipment as possible in order to visualize the ureter and collecting system in its original state, avoiding artificial injuries interfering with the inspection. Semirigid and flexible ureteroscopes are available, typically with a diameter between 6 and 10 Fr. They have either one or two working channels.

Due to the high maintenance costs and frequent need for repair of flexible ureteroscopes, disposable instruments have been introduced to the market recently. Furthermore, although fibre-optics have traditionally been used for flexible ureteroscopy, the advancements in digital optics ("chip on the tip") offer better image quality. Their use has systematically been validated in URS for stone removal. While stone-free rates and complications are comparable to fibre-optic scopes, the duration of procedures has significantly been reduced [8, 9]. Despite a lack of literature, it may be expected that the diagnostic accuracy of the new digital instruments is superior thanks to their enhanced image quality.

A plethora of auxiliary equipment is available for ureteroscopy: guidewires of variable stiffness both hydrophilic and nonhydrophilic, ureteric catheters, balloon dilatation catheters and other devices to facilitate entrance into and passage through the ureter, as well as therapeutic devices which may be applied during diagnostic URS, including baskets, biopsy forceps, and laser fibres. Balloon dilatation catheters bear a significant risk of injury to the ureter and can even result in tumor spillage if a perforation arises, so their application needs to be considered very carefully in diagnostic URS. If no access to the ureter can be obtained, it might be the better option to insert a ureteric stent and bring back the patient for a second look after 1 or 2 weeks.

## Technique

Every diagnostic URS begins with a close inspection of the urethra and bladder to rule out concomitant lower urinary tract lesions such as bladder tumors or prominent vessels in the prostatic urethra. Subsequently, the ureteric orifices (UOs) are identified and closely monitored for uni- or bilateral hematuric urine ejaculation. After exclusion of tumors, bilateral upper tract hematuria is suggestive of a glomerular cause which should be evaluated by a nephrologist.

If the UOs cannot be identified due to inflammatory changes to the mucosa, bleeding, or a large prostate, a rigid cystoscope with an angulated optic should be used. It might be sufficient to fill up the bladder in order to bring the UOs into view. The use of intravenous methylene blue should be omitted as it will impair the diagnostic quality upon entry into the ureter.

A semirigid ureteroscope should be used for inspection of the ureter to the PUJ. An experienced surgeon is often able to intubate the UO without using a guidewire. This has the advantage of omitting mucosal lacerations by the wire but bears an increased risk of injury to the ureteric wall. The risks and benefits in the individual situation must be outweighed against each other. The authors advocate using a hydrophilic guidewire routinely.

Due to the shape of the ureteroscope's tip it is advisable to twist the instrument by 180° (clockwise for a right-handed surgeon) to obtain an atraumatic intubation with fully opened irrigation. In this position, by lowering the tip, the UO can be widened slightly. Once the tip of the scope is passed into the distal ureter, it is twisted back into its original orientation.

If the UO is too tight to allow direct entrance, a hydrophilic guidewire should be used in the same technique. In case this is not sufficient, a ureteric catheter can be used instead as it has the advantage of higher rigidity. Any dilating devices such as balloon catheters or access sheaths can potentially injure the ureter and should be avoided wherever possible during diagnostic URS. If any of these devices is used, a guidewire should always be placed into the mid ureter. Hydrophilic guidewires are preferential as they are less traumatic. A guidewire with a hydrophilic tip and a more rigid body is a good compromise between preserving the mucosa and assisting with the passage of the instrument. Fluoroscopy for orientation is highly recommended. Any forced movements must strictly be avoided as they can result in a discontinuing injury of the ureter already in its intramural portion.

If a bladder tumor occludes the UO or if there is a stenosis following a transurethral resection, it may be necessary to perform another resection first before obtaining access to the ureter. This maneuver has a risk of ongoing vesicoureteric reflux and perforation. In almost all cases however, the UO can be intubated without problems, even with a flexible ureteroscope [10, 11].

With the scope in the distal ureter, a retrograde ureteropyelogram should be performed. Air bubbles in the syringe must be avoided. Any filling defects are noted. The images help during the navigation, especially inside the kidney. It is important to inject the adequate amount of contrast agent, allowing complete visualization of the ureter and collecting system but avoiding extravasation and bleeding of small vessels.

To improve the diagnostic quality when looking for UTUC, several urine cytologies should be taken, usually from the bladder, on three levels of the ureter, and subsequently in all portions of the kidney as well as targeted on any suspicious lesions. Cytology has limited sensitivity, particularly for low-grade tumors, but high specificity.

When advancing the ureteroscope, the ureteric lumen must remain central in the field of view so that the entire circumference of the wall can be inspected. Any obstacles such as kinks can usually be passed with the help of a (hydrophilic) wire or if necessary a ureteric catheter. Major kinks in a chronically ectatic ureter can sometimes be resolved by positioning the patient head down for a short while. Increasing the irrigation pressure can also be helpful but should be used sparingly to avoid overdistension with subsequent urothelial bleeding.

Extrinsic filling defects can often be determined visually with the appearance of compression of the ureter in the absence of any intrinsic mass in the ureteral lumen. When the ureter is extrinsically compressed by a venous structure, the ureteral lumen is distensible during ureteroscopic inspection, whereas extrinsic compression from an artery often results in visible pulsations. Ureteral strictures and PUJ obstructions also may be visually confirmed.

The semirigid ureteroscope can be used until gaining entrance to the renal pelvis. The instrument of choice for inspection of the proximal ureter and the collecting system is the flexible ureteroscope. Thus, a hydrophilic guidewire is placed through the semirigid instrument into the renal pelvis under vision. The ureter can usually be inspected more effectively when slowly drawing back the scope, rather than during the advancement. After removing the semirigid scope, a flexible instrument is inserted via the guidewire which can subsequently be removed. Using the previously performed retrograde pyelogram for guidance, the entire collecting system is carefully inspected. Again, urine cytologies should be obtained from several sites in the kidney.

Towards the end of the procedure, the flexible ureteroscope is removed, allowing for a final inspection of the ureter. After an uneventful diagnostic URS, a ureteric stent is usually not required. If there is a risk of obstruction or significant bleeding, a stent may be inserted.

## Diagnosis of upper tract urothelial cancer

Some 5% of TCCs are localized in the upper tract, more commonly in the ureter than in the collecting system, in keeping with the relative amount of urothelial surface. Tumors in the upper tract have an appearance similar to bladder tumors: they are mostly exophytic and papillary but there can also be flat reddish lesions, especially when carcinoma *in situ* is present. These are easily missed on inspection, especially with older instruments and optics. Many patients with TCC have multifocal disease. After nephroureterectomy, further lesions are reported after histology that were not detected on URS in 25% of patients [12]. Figures 49.1 and 49.2 show examples of TCC in the renal pelvis.

Fibroepithelial polyps, while often long and papillary, can be distinguished from upper urinary tract TCC as they frequently have a smooth, normal-appearing urothelial surface whereas TCC often show hypervascularization and in later stages can be necrotic.

The location of any tumor should be documented as exactly as possible to optimize further treatment planning. Every suspicious lesion should be biopsied. As every diagnostic component for UTUC has its own flaws, only the combination of imaging, endoscopic inspection, cytology, and biopsy is adequate. The presence of hydronephrosis, positive cytology, and high-grade tumor on biopsy correlate with ≥ pT3 disease [13].

Biopsies can be obtained with forceps or stone baskets. Forceps are useful for flat lesions whereas baskets can be helpful for exophytic tumors which can be completely removed if the basket is placed around the stem. If forceps are used, multiple biopsies should be taken as the volume with each biopsy is very small. The histological sample should include muscular tissue but, at the same time, a perforation should be avoided as it can lead to tumor spillage. If reasonable, a basket should be used as it harvests better results in terms of successfully obtaining a representative tissue sample and correctly grading a tumor [14]. Video 49.1 shows an example of a basket biopsy of TCC recurrence in the renal pelvis of a patient with ileal conduit.

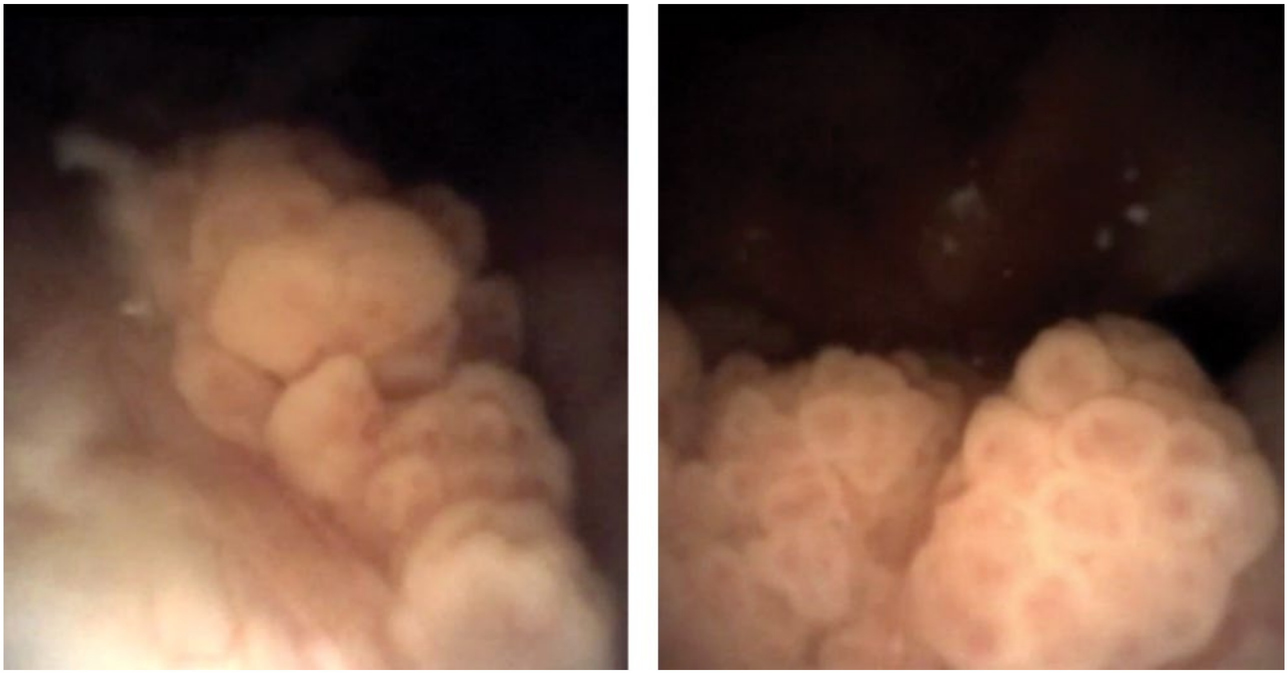

**Figure 49.1** Ureteroscopic impression of exophytic TCC in the renal pelvis. Images courtesy of Mr Oliver Wiseman, Cambridge, UK.

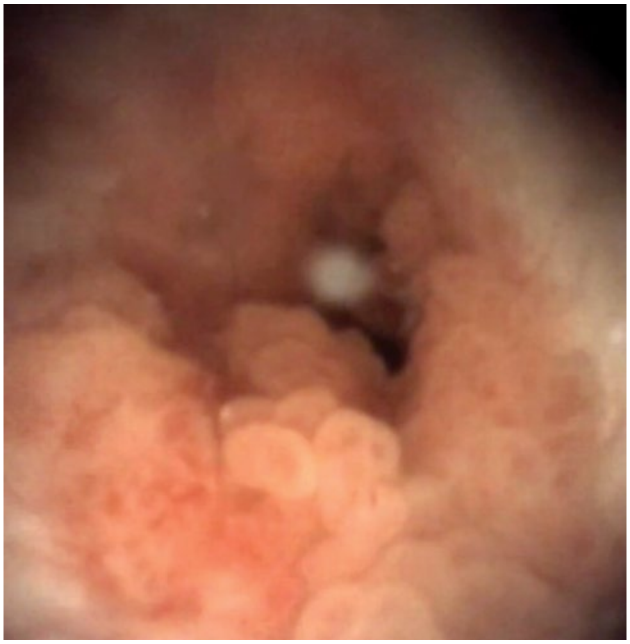

**Figure 49.2** Further tumor material in the same patient. Image courtesy of Mr Oliver Wiseman, Cambridge, UK.

While tumor grading with biopsies is 79–93% accurate, assessing the local stage is problematic [15–18]. Many tumors are upstaged following nephroureterectomy. High-grade tumors on biopsy are suggestive of invasive stages (≥pT2), which are found in around 60% of cases.

## Endoscopic treatment of upper tract urinary cancer

Upper tract TCC can be treated endoscopically with either diathermy resection using a special ureteric resectoscope or preferably a holmium laser. Nephroureterectomy remains the gold-standard therapy but in select patients an organ-preserving treatment regimen may be selected. This is the case in patients with low-grade and low-stage disease, a solitary kidney, severely impaired kidney function, bilateral tumors in the upper tract, and patients unfit for major surgery.

For tumors of the renal collecting system, a percutaneous approach is feasible, however this bears the risk of tumor cell spillage. Thus, ureteroscopic treatment is often preferred.

If nephroureterectomy is indicated, ureteroscopic management should only be offered to patients with small, low-grade tumors. The patient must be informed about the potential undergrading and understaging through biopsy (see above) and that a purely endoscopic treatment requires a rigid follow-up with semi-annual ureteroscopies as there are higher recurrence rates than with radical surgery. Adjuvant treatment with mitomycin and BCG has been described but is not the standard of care.

For an adequately selected patient group, the rate of secondary nephroureterectomy has been reported to be around 20% [19].

The use of a holmium:YAG laser for tumor ablation is the option of choice as its penetration into tissue is only 0.4 mm, thus the risk for perforation is comparatively low. Papillary tumors can be removed and subsequently the surface is coagulated for hemostasis. Neodymium:YAG lasers may also be used for larger tumors. They penetrate deeper (2–5 mm) and have a larger extent of thermic tissue destruction.

## Other causes for hematuria

If tumors and stones are ruled out, other causes for hematuria have to be considered. Bilateral ureteric hematuria is usually a glomerular problem. Other benign causes of hematuria are hemangioma and arteriovenous malformations. The term “nutcracker syndrome” describes a compression of the renal vein by other structures resulting in a rising intravenous pressure that subsequently leads to glomerular hematuria. Angiography with measurement of the intravasal pressure may be necessary for its diagnosis.

## New technologies and perspectives

Due to the limitations of diagnostic ureteroscopy that have already been described in this chapter there is an increasing number of auxiliary technologies on trial to enhance the diagnostic value.

- *Photodynamic diagnosis (PDD)* has been established for the diagnosis of bladder TCC for years. Hexaaminolaevulinic acid (5-ALA) is instillated into the bladder prior to endoscopy. It intercalates with replicating DNA and thus accumulates in malignant (and inflammatory) tissue. Light waves with a length of 400 nm excite the electrovibrational state of the fluorochrome. Upon relaxation to the ground state, a photon is emitted (wavelength 590–700 nm), permitting optical diagnosis of tumors. For the purpose of upper tract diagnostics, 5-ALA can be administered through a ureteric catheter or orally. Episodes of hypotension have been described as a side effect. Some authors describe enhanced sensitivity but the technique has limitations. PDD works best with a perpendicular view onto the tissue. On tangential visualization as in ureteroscopy, it can lead to false-positive results [20, 21].
- *Optical coherence tomography (OCT)* has first been employed in ophthalmology. It employs a similar principle to ultrasound but uses light waves and covers a depth of up to 2 mm. The measurement of the attenuation coefficient $\mu_{\mathrm{OCT}}$ allows for differentiation of tissues. Only few data on its use in diagnostic URS is available yet [22].
- *Confocal laser endomicroscopy (CLE)* is another technique using fluorescence, in this case by injecting fluorescein intravenously. It allows ultra-high-resolution imaging of tissue microarchitecture but only has a depth of up to 400 μm. A drawback is the susceptibility to motion artefacts. Further studies are needed to prove an enhanced diagnostic value [20, 23].
- *Narrow-band imaging (NBI)* relies on the absorption of light at specific wavelengths by hemoglobin; hence microvessels are better visualized. Apparently, this improves sensitivity up to 23%, but again, further studies are required [20, 24].
- *SPIES® (Storz professional image enhancement system)* uses spectral separation by digital filters in order to enhance contrast. There is no literature on its application in the upper tract available yet [20].

In conclusion, diagnostic URS is an important step in the workup for UTUC and other pathologies of the upper urinary tract. The current technological advancements in optics, endoluminal imaging, and image processing offer promising enhancements to further the sensitivity and specificity of upper urinary tract endoscopy.

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# 50

# Ureteroscopic Diagnosis and Treatment of Upper Urinary Tract Neoplasms

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Ureteroscopy is an essential technique in the diagnosis, treatment, and surveillance of upper tract neoplasms. The introduction of fiber-optic illumination, imaging, and small rigid and flexible ureteroscopes in the early 1980s provided access to the entire upper collecting system. This combination with devices for tissue sampling and ablation has made accurate diagnosis and treatment possible. Other diagnostic studies including radiologic, cytologic, and molecular techniques can provide initial or supportive diagnostic information, yet remain secondary to endoscopy as the definitive study.

Upper tract neoplasms are rare and upper tract urothelial carcinoma (UTUC) accounts for 5% of all urothelial carcinomas [1]. UTUC is more common in patients with a previous history of carcinoma of the bladder [2, 3]. The most common presentation is hematuria, either gross or microscopic, in approximately 80% of patients [1, 4, 5]. UTUC is an incidental finding in 10–15% of patients but flank pain can be seen in up to 30% of patients. Physical findings are rare, unless the patient has metastatic tumor or hydronephrosis secondary to obstruction.

Radical nephroureterectomy (RNU) with removal of a bladder cuff has been considered the standard for treatment of UTUC [6]. The application of endoscopic techniques to these lesions initially in patients with a solitary kidney or compromised contralateral kidney, which have been considered imperative indications, have shown the feasibility of this treatment. Consequently, it has been performed increasingly in patients with a normal contralateral kidney [7, 8]. Evidence of progressive functional renal loss in patients undergoing nephrectomy for renal cell carcinoma can also be expected in patients losing their kidney to nephroureterectomy and is a stimulus for nephron-sparing surgery [9].

## Noninvasive diagnosis

Radiologic studies, including intravenous contrast studies to outline the collecting system with excretory urography or computed tomography (CT) urography are the most useful noninvasive diagnostic techniques. A filling defect is the most common finding, which may indicate an upper tract urothelial neoplasm. The differential diagnosis includes blood clot, lucent calculus, air bubble, fungus ball, sloughed papilla, external compression with a crossing vessel, or benign inflammatory or neoplastic lesion. One series using a multidetector CT scanner for CT urography in patients with gross hematuria demonstrated a very high sensitivity, specificity, and accuracy [10]. In some patients with a severe contrast allergy with nonvisualization of the collecting system, retrograde ureteropyelography may be indicated. However, this suffers from low accuracy [4, 11].

Renal ultrasound can define intrarenal calculi, hydronephrosis, and renal masses accurately but is less useful to define small intraluminal soft tissue masses. In contrast, CT can accurately distinguish calculi from soft tissue masses. It is also helpful in demonstrating masses extending beyond the collecting system or enlarged lymph nodes. Inclusion of a pyelographic phase with reconstruction of the excretory system or an abdominal radiograph taken after the administration of contrast as an anteroposterior ureteropyelogram may be most useful in demonstrating intraluminal lesions [10, 12]. Magnetic resonance imaging has similar limitations, especially in the cross-sectional mode [13]. The magnetic resonance urogram designed to image the fluid of a distended collecting system may be helpful in some patients with nonfunctioning kidneys or severe contrast allergies.

Cytologic study of voided urinary samples is of limited value because of the frequent equivocal and false negative

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findings. It can be useful in detecting high-grade tumors, which shed obviously malignant cells in the urine. The sensitivity of voided urinary cytology increases with an increasing grade, ranging from 11% for Grade 1 to 83% for Grade 4 lesions [14]. Elective ureteral catheterization for a specific and localized upper tract urinary sample for cytologic study is occasionally indicated in patients with positive cytology without radiographic findings and with normal cystoscopy and bladder biopsy. However, routine ureteral catheterization to collect urine from a radiographically abnormal area is no longer indicated if ureteroscopy can be performed. Similarly, fluoroscopic guided brush biopsy is rarely indicated when ureteroscopy is available.

Fluorescence *in situ* hybridization (FISH) has been used to detect genetic aberrations in chromosomes 3, 7, 9, and 17 and improves the sensitivity of voided urine cytology for all bladder lesions, including low grade, from 25 to 53% [15, 16]. The appeal of FISH would be to utilize it in voided urine specimens to detect UTUC without the invasiveness of ureteroscopy. The largest published reports of FISH in UTUC detection using voided urine specimens demonstrate increased sensitivity compared to voided cytology but it is still not sensitive enough to forgo ureteroscopic visualization for diagnosis [17–19].

## Endoscopic diagnostic techniques

Endoscopic evaluation of an abnormality in the upper urinary tract suspicious for a neoplasm includes inspection of the entire bladder and involved collecting system. Cystoscopy is an essential evaluation of the patient with hematuria and/or filling defects because of the risk of associated bladder tumors and to provide access to the ureter for retrograde pyelography and ureteroscopy. A retrograde ureteropyelogram may give more information regarding the extent of the filling defect or suspicious lesion or ureteral abnormalities, which might affect access for treatment. A cone-tipped retrograde injection most efficiently outlines the entire collecting system without traumatizing the ureter itself. Care should be taken to prevent overfilling of the collecting system, which can obscure filling defects. Initial ureteral catheterization without contrast study should be avoided since it can traumatize the specific lesion of interest and the otherwise normal ureteral mucosa.

A "no-touch technique" should be employed to examine the involved upper collecting system. The distal ureter is first inspected either with a small rigid endoscope, preferably one small enough to pass into the orifice without other dilation, or with a flexible ureteroscope that can be passed into the ureter without dilation [20]. In this way, the ureter can be inspected without prior instrument trauma. When using a semirigid ureteroscope, it is passed as far as possible into the lumen before leaving a guidewire in place as the endoscope is removed. The guidewire is passed only to the level of the ureter that has been inspected with the semirigid ureteroscope and should not be passed into the intrarenal collecting system where the tip of the wire can traumatize the calyx or the renal pelvis and obscure subsequent visual inspection. The smallest flexible ureteroscope is then passed over the guidewire into the ureter. If a small flexible ureteroscope can be passed directly into the ureter, then the steps of semirigid ureteroscopy and wire placement can be avoided.

The flexible ureteroscope is used to inspect the more proximal portions of the ureter not previously seen and the intrarenal collecting system. Inspection at that level should be systematic going from the renal pelvis to the upper infundibula and calyces to the mid and then the lower pole. In this way, the risk of trauma to the mucosa with the endoscope is minimized.

Continuous irrigation with saline is maintained through the working channel of the ureteroscope to clear the field of view. Iodinated contrast medium can be used in the irrigant to outline the collecting system for fluoroscopic monitoring. Positioning of the flexible ureteroscope throughout the collecting system can then be confirmed fluoroscopically. Care must be taken to avoid overfilling the collecting system, since this can induce submucosal hemorrhage and rupture of the fornices. When adding contrast through the endoscope within the collecting system, the irrigant present should be removed. Lines of refraction will be visible as fluids of two different densities mix. This can be avoided by minimizing the mixing.

If there is a specific lesion to be examined, such as a filling defect or a point of obstruction, then the distal portion of the urinary tract should be inspected first, followed by the lesion itself in order to inspect it within a clear visual field without other manipulation that may cause bleeding and obscure the field of view. In many cases, visual inspection alone can provide a diagnosis [21–24]. For example, the appearance of a calculus will readily distinguish it from a low-grade papillary tumor. Irrigant with contrast should be used so that fluoroscopy can demonstrate the tip of the ureteroscope at the filling defect. In this way, correct visualization and identification of the lesion can be confirmed.

Epithelial neoplasms may have totally different appearances. Low-grade UTUC has a typical papillary appearance, similar to the same lesions in the bladder (see Videos 50.1, 50.2a,c, and 50.3). High-grade UTUC may be more sessile and less papillary, often with necrotic or inflammatory debris on the surface. However, these differences are not consistent. El-Hakim and colleagues [25] found an accuracy of only 70% in determining the grade of an upper tract neoplasm by appearance alone.

Benign lesions can often be diagnosed endoscopically. Fibroepithelial polyps located within the pelvis and inverted papillomas throughout the upper collecting system have been seen to have a smooth, rounded surface [26]. There may be an impression of an intact epithelial layer in the appearance. These differences have not been prominent enough to allow visual identification, but they have been strongly suggestive. All benign lesions observed, including fibroepithelial polyps, inverted papillomas, and hemangiomas located in the ureter or the ureteropelvic junction can be narrow, elongated, and worm-like.

In many instances, visual inspection alone may not be adequate for diagnosis. High-grade UTUC can be confused with inflammatory lesions or may be obscured by tumor growing submucosally or proximal to obstructive edema. There may be calculus material on the surface of a neoplasm with the resultant appearance of a solid calculus. Other tumors with a necrotic surface can appear the same as a soft, infection stone covered with inflammatory debris. In these and many other situations, visual inspection alone is not adequate for diagnosis.

Aids to visual diagnosis of neoplasms such as narrow-band imaging (NBI) and confocal laser endomicroscopy have been used in the bladder to detect carcinoma *in situ* or additional exophytic tumors. NBI is an optical image-enhancement system that makes use of blue and green wavelengths of light, which are readily absorbed by hemoglobin to enhance surface tumor detection by providing contrast between normal mucosa and microvasculature. Since malignant lesions tend to have a rich vascular component, they appear dark brown or green against white mucosa thus enhancing lesion detection. One report of NBI for use in cases of UTUC found a 23% improved detection rate among 27 patients in which additional tumors were seen or borders of tumors were enhanced and noted to extend beyond what was observed with white light alone [27]. NBI also has value in differentiating benign inflammation, as seen from indwelling stents, from subtle malignant luminal lesions [28]. Unlike photodynamic diagnosis modalities, NBI requires no extrinsic fluorochrome, an attractive aspect for use in the upper tracts.

## Endoscopic biopsy technique

Ureteroscopic biopsy is necessary to sample neoplasms in the upper urinary tract to determine the presence of malignancy, and to determine the grade. The rate-limiting step of ureteroscopic biopsy is the size of the working channel within the ureteroscope, which dictates the size of the biopsy instrument that can be used. For example, a piece of tissue obtained with a 3 Fr cup biopsy forceps is less than 1 mm in diameter and is usually too small to be prepared for histologic study using standard techniques. It is often lost in the process (see Video 50.1a). In contrast, it is a relatively large fragment of tissue for cytologic techniques. It can be prepared as a cell block and stained and examined as a histologic preparation to give a diagnosis and possibly grade.

Several different biopsy instruments and techniques are available. Abdel-Razzak and colleagues [29] evaluated samples from 55 procedures in 44 patients with a possible diagnosis of UTUC. They compared the diagnostic yield, considering only those samples that were specifically positive or negative for malignancy, excluding those that were “suggestive” or equivocal. The techniques compared aspiration of urine at the level of the lesion, wash and aspiration with saline solution at the area of the lesion, and direct tissue sampling with brush, basket, or biopsy forceps.

The tissue sampling techniques gave the best yield, particularly the flat wire basket for large friable tumors and the cup forceps for more sessile lesions. The brush was less effective, and under endoscopic vision was observed to move the more flexible tissue without removing fragments. It may be more useful with flat or sessile lesions. Aspiration and wash proved to be valuable in providing a diagnosis for some patients in whom the other sampling techniques were inconclusive.

A flat wire basket is quite effective for removing large fragments of papillary tissue with a small-diameter ureteroscope (see Videos 50.2a–c and 50.6). We highly recommend this instrument for biopsy of UTUC whenever applicable since it has been shown to be superior to the 3 Fr cup biopsy forceps in securing a diagnosis of UTUC in suspected lesions [30]. Under endoscopic vision, the basket is placed on the tumor and partially closed. The entire unit consisting of tumor sample, basket, and ureteroscope is then removed from the ureter and bladder. This can often remove a large sample even up to 1 cm in diameter, which is adequate for cytologic or histologic study. The ureteroscope is then replaced to repeat the inspection and biopsy or treat the neoplastic lesion.

The most important steps in handling the tissue for pathologic diagnosis is to work closely with the cytopathologist [31–34]. Samples are examined with both a smear and cytospin preparation. If there is any macroscopically visible tissue in the sample, a cell block is also prepared. This sample often demonstrates both the architecture of the neoplasm and the individual cells to allow grading of UTUC in many of the samples adequate for cell block. Multiple samples of the lesion are taken.

**Box 50.1 Specimens for cytology.**

- Bladder urine
- Aspirate at tumor
- Biopsy
- Aspirate after biopsy
- Aspirate after treatment

In addition, urine and saline wash samples of the lesion before and after biopsy and/or treatment are also obtained (Box 50.1).

## Grading with ureteroscopy

Grading of UTUC is important in determining prognosis and directing therapy. Grade obtained from ureteroscopic biopsy has been shown to reflect the grade of the overall tumor with reasonable accuracy. In 42 patients, Keeley and colleagues [35] found that the grade seen on a ureteroscopic biopsy prior to surgical treatment matched that in the final pathologic specimen in 38/42 (90%) of cases. Daneshmand and colleagues [36] showed an overall accuracy of 90% in patients who had surgery early after biopsy and in those who had surgery within 2 months of ureteroscopic diagnosis. In a larger, more recent series, Brown et al. demonstrated ureteroscopic grading accuracy in 112/119 (94%) of patients [37]. Other groups, however, have expressed concern over grade discordance between ureteroscopic and surgical specimens such that 23/24 (96%) of grade 1 lesions and 23/57 (40%) of grade 2 lesions were upgraded [38]. This exceptional finding is likely explained by the use of multiple grading systems for urothelial carcinoma used over the years, which are not simply interchangeable. In the surgical pathology literature, grade 2 UTUC lesions as defined by the 1973 World Health Organization (WHO) classification have demonstrated significant heterogeneity such that up to 50% of them would qualify as high-grade lesions according to the 1998 WHO system [39, 40]. This is very important to consider whenever interpreting studies involving the ureteroscopic treatment of UTUC over time since most studies are retrospective single institutional experiences taking place over many years in which the grading systems had changed. To consider all 1998 “low-grade” UTUCs as 1973 grade 1 cases would certainly explain the high rate of grade 1 upgrading to grade 2 in the 2012 Mayo series. Nevertheless, the possibility of UTUC tumors being heterogeneic in regard to grade must be considered, especially in view of the findings with urothelial carcinoma of the bladder in which up to 29% of primarily low-grade non-muscle invasive tumors had a high-grade component of at least 5% tumor volume [41]. The heterogeneity of grade 2 lesions also explains the benefit of combining site-specific cytology with ureteroscopic biopsy in patients with grade 2 UTUC to provide a more accurate diagnosis [42].

## Staging

Pathological stage has been shown to be the best predictor of prognosis in patients undergoing treatment for UTUC [43, 44]. Many factors are responsible for unreliable UTUC staging with ureteroscopic biopsy techniques including small specimen size due to limits of instrument size, relative thinness of the ureteral wall which could lead to extravasation with aggressive biopsy and the variable morphologies of the intrarenal collecting system resulting in “hard-to-reach” lesions. It is impossible to expect reliably complete excisional biopsies in the upper tract. Contemporary series report stage concordance rates of only 49–68% with the overwhelming trend demonstrating understaging of ureteroscopic biopsies [42, 45, 46]. Reliably determining the depth of invasion of the primary tumor or other simultaneous lesions remains difficult. One series advocated multiple deep biopsies with cup forceps in an attempt to determine the presence of tumor in the lamina propria [47]. Most series have not reported accuracy in determining the depth of invasion.

The grade of the primary tumor has often been associated with stage, but it cannot be considered truly accurate staging. In Keeley’s series [35], increasing stage was noted with increasing grade seen on ureteroscopic biopsy. Brown and colleagues also found that the grade on endoscopic biopsy correlated with the final pathologic stage in nephroureterectomy specimens [37]. Findings from these two studies demonstrated that low-grade UTUC on ureteroscopic biopsy correlated with noninvasive stage ($\leq$pT1) in 73–86% and that high-grade UTUC on biopsy results in more invasive cases ($\geq$pT2) in 66%. Other series of patients treated surgically have also demonstrated the relationship of increasing stage with increasing grade [48].

Cross-sectional imaging is essential for determining the presence of overtly metastatic disease but historically has not been very accurate in predicting subtly invasive disease (pT2–pT3). Favaretto et al. recently presented a model which combines ureteroscopic biopsy results with cross-sectional imaging and predicts $\geq$ pT2 disease with an accuracy of 71% [49]. Endoluminal ultrasound has been used in two series in an attempt to determine the depth of invasion [50, 51]. It has shown some value but is severely limited by the availability of the instruments.

Optical coherence tomography (OCT) is a new technological advancement that makes use of backscattered light to produce micrometer-level resolution cross-sectional images such that layered tissue anatomy can be appreciated. A 2.7 Fr probe can be placed through the lumen of a flexible or semirigid ureteroscope at the level of a urothelial lesion for cross-sectional imaging. Depth of imaging is reported at 2 mm and OCT staging is binary such that invasive disease is classified as $\geq$ pT1. An early validation study compared OCT stage to surgical stage after RNU and demonstrated 100% concordance in seven cases using the binary classification [52]. One case could not be staged due to tumor thickness going beyond OCT imaging depth. More experience is needed before the utility of this modality is fully appreciated.

## Complications of biopsy

There remains some concern that ureteroscopic biopsy of UTUC can disseminate tumor cells locally or systemically. The possibility of pyelovenous or pyelolymphatic backflow has been cited as a possible mechanism. In a single case report, tumor cells were found outside the kidney in a nephroureterectomy specimen after ureteroscopic biopsy [53]. However, in a review of 13 nephroureterectomy specimens following ureteroscopic biopsy, no unusual metastatic pattern was seen [54]. In a well-controlled study of 96 patients, Hendin and colleagues [55] found no difference in long term or disease specific survival in patients with UTUC who had surgical treatment preceded either with or without ureteroscopic biopsy (Table 50.1). Hara and colleagues [56] reported the usefulness of ureteroscopic biopsy and added 50 patients to those who have had ureteroscopic biopsy without development of metastatic disease. These series have concluded that ureteroscopic biopsy can be a safe and very valuable procedure without any documented evidence of tumor dissemination.

**Table 50.1** Effect of ureteroscopic biopsy.

| | Biopsy | None |
|---|---|---|
| No. of patients | 48 | 48 |
| Metastases | 12.6% | 18.8% (NS) |
| Died with recurrence | 10.4% | 10.4% (NS) |

Data from Hendin et al. [55]. NS, not significant.

## Selection of patients for ureteroscopic biopsy

Ureteroscopic biopsy is of value in any patient with an upper tract filling defect in whom the diagnosis is in question, such as those with a filling defect and voided urinary cytology without a definitive (positive) diagnosis for malignant cells. The presence of individually malignant-appearing cells (positive cytology) indicates either carcinoma *in situ* or a high-grade neoplasm. Biopsy may be avoided in patients with cytology that is definitively positive for malignant cells and who have a large irregular upper tract filling defects, which can be considered classic for UTUC. Even these patients should have endoscopy to rule out associated bladder tumor.

## Natural history and prognosis after extirpative surgery

The rationale for conservative endoscopic therapy of UTUC was based initially on the success of other conservative treatment modalities and the natural history of this neoplasm. The behavior and prognosis of UTUC, in both the ureter and the intrarenal collecting system, has repeatedly been shown to be related to the grade and stage of the lesion. In many early, published series of extirpative surgery for UTUC, the vast majority of cancer-related deaths were in those with high-grade disease, in whom muscle invasion was also frequently present. Survival of 49 patients with Grade I UTUC of the ureter or renal pelvis collected at the Mayo Clinic over a 22 year period was identical to that of an age-matched control group [57]. In contrast, the survival with higher-grade UTUC correlated with tumor stage and grade and was consistently lower than a control group [58]. Lymph node-positive disease also was dependent on tumor grade. In a series by Charbit and colleagues [48], lymphadenectomy was negative in all patients with low-grade tumors in whom it was performed while 39% of those in patients with higher-grade tumors were positive.

### Endoscopic therapy

Endoscopic therapy in the upper tracts for UTUC treatment is a natural extension of the well-accepted techniques for treating lesions in the bladder, only with smaller instruments imparting some unique limitations. The neoplasm itself, including its diagnosis, grade, location, and size, must be considered in any decision for endoscopic treatment in an individual patient (Table 50.2). There are several ureteroscopic techniques for the treatment of

**Table 50.2** Selection of patients for ureteroscopic treatment.

| Tumor factor | For | Against |
|---|---|---|
| Size | Small | Large |
| Configuration | Papillary | Sessile |
| Number | Solitary | Multiple |
| Distribution | Single | Circumferential or extensive |
| Grade | Low | High |
| Cytology | Negative | Positive |

UTUC and they include mechanical removal, electrosurgical resection, fulguration, and laser therapy.

The techniques used for the ureteroscopic biopsy of tumors result in the removal of tissue volume. A flat wire basket can remove several millimeters of papillary tumor with each application (see Video 50.6). Although the cup biopsy forceps removes a small volume with each bite, repetitive sampling can remove a small tumor (see Video 50.1a). The base of the tumor can then be coagulated with one of the other instruments (see Video 50.1b). Electrosurgical techniques similar to those used in the bladder have been applied for small distal ureteral neoplasms using longer, small-diameter endoscopes. Over time, this tedious procedure has been superseded by other more efficient techniques.

Ureteroscopic electrocoagulation of UTUC is possible using 2 or 3 Fr probes which can be passed through the channels of small-diameter rigid or flexible ureteroscopes. Care should be maintained to avoid fulgurating large areas of the ureter, which can result in stricture formation. This electrocautery technique is also useful for lesions within the intrarenal collecting system often in the lower pole medially where laser fibers may limit deflection of the ureteroscope. The 2 Fr electrode is slightly more flexible and can fulgurate with lateral contact rather than directly forward approach needed for a laser (see Video 50.5b).

Laser techniques have been applied safely and efficiently for UTUC treatment. Small fibers of 200–400 μm core diameter can be passed through the flexible ureteroscope. The two most commonly utilized lasers presently available can effectively treat UTUC with coagulation, ablation and resection. The neodymium:YAG laser was first used for treatment of bladder tumors and for renal pelvic and ureteral neoplasms in open surgical procedures achieving long-term cures [59]. It was subsequently used ureteroscopically to ablate urothelial carcinoma of the ureter [60]. In a comparative series, Schmeller and Hofstetter [61] demonstrated the success of laser ablation of upper tract tumors with the development of fewer ureteral strictures than after electrocoagulation.

The neodymium:YAG laser can penetrate up to 5 mm into tissue after several seconds of exposure. This can be controlled by positioning the fiber onto the tumor without directly aiming it toward the wall of the ureter and by moving the fiber across the surface of the tissue to avoid prolonged exposure. Ureteral damage may be limited by aiming the fiber and the beam parallel to the surface of the ureter. Within the kidney, especially the renal pelvis, where there is a greater surface area and less risk of scarring and stricturing, the neoplasm can be coagulated safely with the neodymium:YAG laser [62] (see Video 50.3). The laser is activated at 20–30 W on continuous mode and moved over the surface to coagulate the tissue. The effect can be seen as the color of the tissue changes to white. The laser fiber will char if it is activated in contact with tissue. For a relatively large lesion obstructing the ureter or an infundibulum, it may be necessary to remove some of the coagulated tissue with a basket or grasper to determine whether viable tumor remains. Since the laser can penetrate to a depth of approximately 5 mm, it may not affect the entire depth of the tumor. There have been no reports of significant renal or vascular injury or damage to associated organs from forward scatter of the neodymium:YAG laser that has been used in the renal pelvis.

The holmium:YAG laser has been widely applied for urologic indications. It is a solid-state pulsed laser that can fragment calculi and can coagulate and ablate tissue. This laser produces light at a wavelength of 2100 nm carried along a low-water-content fiber. The laser energy is absorbed within less than 0.5 mm of tissue or fluid and has essentially no risk of forward scatter. The effect observed is the only tissue effect achieved. It is particularly useful for ureteral lesions since it can ablate and remove a visually occlusive neoplasm to open the lumen for access [63–65] (see Video 50.4).

In use, the laser fiber must be placed in contact with or very close to the tissue to be treated. The laser is then activated at energies from 0.5 to 1 J at a frequency of 6–10 or even 15 Hz. Irrigation is maintained to clear the visual field of tissue debris. It is often necessary to discontinue treatment to allow the field to clear, since considerable debris is formed during treatment. Bleeding occurs occasionally and can be controlled better at lower energies or by moving the fiber slightly away from the tissue to diffuse the laser beam and improve coagulation. There is also clinical evidence that using longer pulse duration such as 700 microseconds, rather than the 350 microseconds often used for lithotripsy, will also improve coagulation (see Video 50.5a). The very limited penetration allows precise control and the laser, thus, can be used for ureteral lesions located at the level of the iliac vessels and the renal pelvis near the renal vessels. Great care is employed to avoid ablation and resection through the wall of the ureter or renal pelvis itself.

These lasers are best used in synergistic combination. The effects of the neodymium:YAG and holmium:YAG lasers are complimentary. The neodymium:YAG laser can be used to coagulate the major volume of tumor since it penetrates several millimeters and can achieve coagulation effect within the depth of the tissue. The coagulated tissue can then be removed mechanically or even more effectively with the holmium:YAG laser. The holmium:YAG is used to resect the tissue to the level of the wall of the ureter or renal pelvis. Thus, the benefits of each device can be used to the best advantage (Figure 50.1).

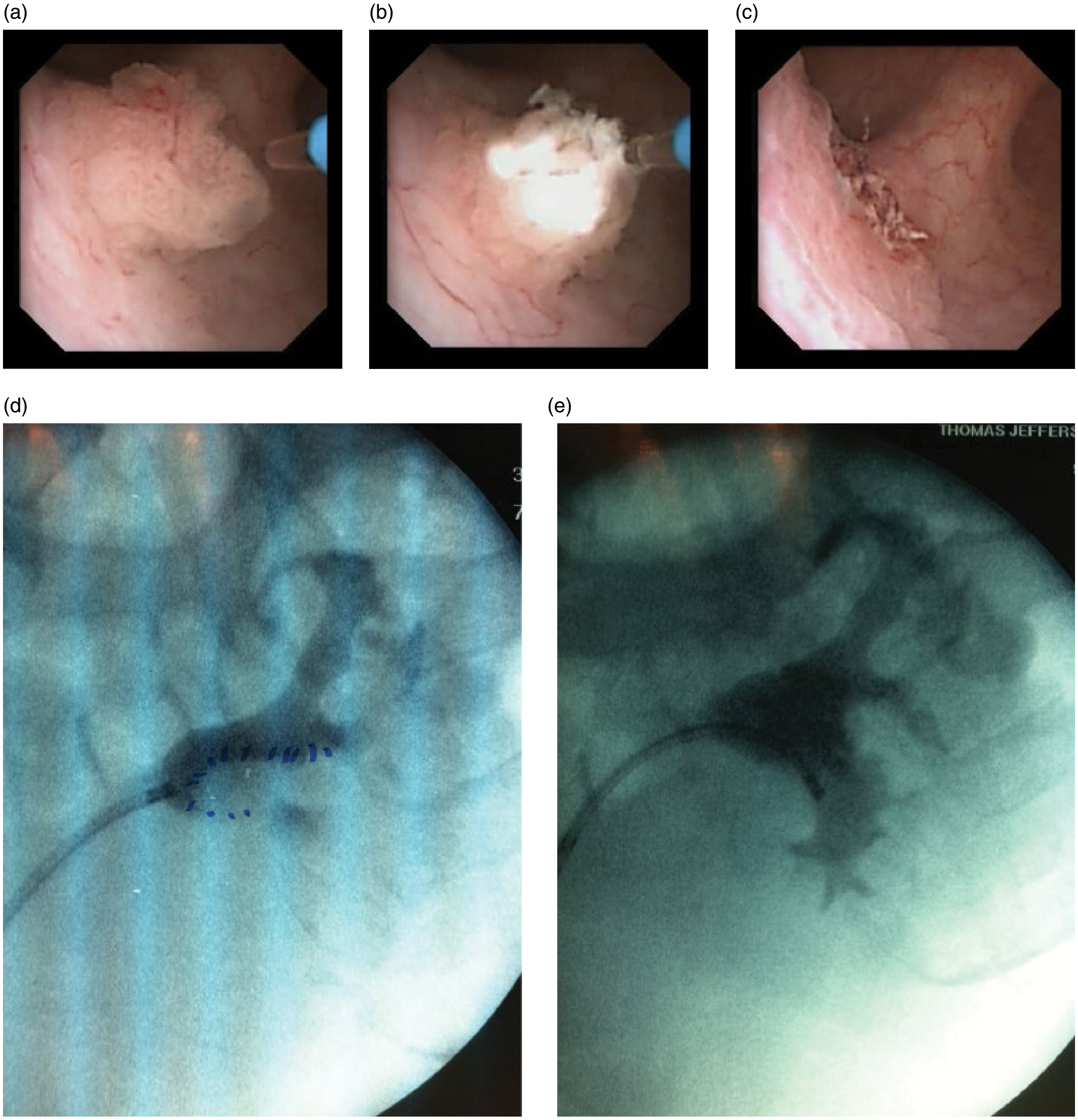

**Figure 50.1** (a) Digital flexible ureteroscopic image of a low-grade UTUC of the renal pelvis prior to laser resection. (b) Coagulation of the papillary tumor with the neodymium:YAG laser. (c) Complete ablation of the coagulated tumor which was resected with the holmium:YAG laser reveals the normal contour of the collecting system. (d) Fluoroscopic view of the left collecting system with contrast irrigation demonstrates a large papillary lesion in the renal pelvis with extension to a lower pole infundibulum. (e) Fluoroscopic view of the collecting system after ureteroscopic laser resection demonstrates the absence of masses and no evidence of extravasation. Moderately sized lesions can be effectively treated with the combination Nd and holmium:YAG laser which allows for less luminal bleeding and better visualization.

## Results of treatment

Ureteroscopic treatment of UTUC has been employed and studied for well over 30 years. There are many small retrospective series with variable tumor characteristics treated with non-uniform techniques and follow-up protocols. These are reported with various endpoints such as cancer-specific survival (CSS), local recurrence rates in the upper tract and bladder, renal preservation rate, and progression of disease defined in many different ways. Reports of metastatic disease are not uniformly presented, likely representing underreporting. Cohorts describing short- to intermediate-term results are plentiful while larger series with longer follow-up approaching 5 years have been published more recently. The indications for ureteroscopic treatment of UTUC have expanded from small low-grade lesions in patients with imperative indications to medium- and larger-sized lesions in patients with normal contralateral kidneys. Generally, recurrence rates become higher with longer follow-up, and treatment of larger, and high-grade, lesions. Non-malignant ureteral strictures are not uncommon as a result of repetitive manipulations over time.

## Recurrences

UTUC recurs at significant rates similar to locally treated bladder tumors. It is impossible to determine whether these new neoplasms are the result of implantation of cells from the original tumor or if it is related to a field change in the urothelium. Successful treatment depends on several factors A meta-analysis by Cutress et al. summarize the local recurrence rates and CSS of 20 contemporary ureteroscopic series in the treatment of UTUC [66]. Clearly, this is influenced by the grade of the original lesion with rates between 48 and 54% for low- to intermediate-grade lesions and as high as 60–76% for high-grade lesions. The grade of the original lesion also affects CSS with most series reporting rates of 86–100% with mean follow-up of 5 years or less (Table 50.3). Equally important are the length of follow-up and the size of lesions being treated. These factors vary widely from series to series but in general, local recurrence rates increase with longer follow-up and larger sized lesions. When considering the more recent series in Table 50.3, local recurrence rates of 77–90% are seen with series of more than 48 months follow-up [75, 77–79]. An exception to this trend was noted in the 2008 Mayo series with a 55% local recurrence rate with 59 month follow-up but the average lesion size treated in this series was only 8 mm [74]. In general, these recurrent lesions are small and can be treated endoscopically. A notable exception is when there is progression in grade from low- to a newly developed high-grade lesion. The rate of such grade progression has been defined by Grasso et al. as 15% at a mean of 38.5 months. This should be mentioned to patients considering ureteroscopic treatment for UTUC during initial consultation [78].

**Table 50.3** Recurrence after ureteroscopic treatment of upper urinary TCC.

| Series | No. of patients | Mean follow-up (months) | Recurrence (%) | DSS[a] |
|---|---|---|---|---|
| Martinez-Piniero et al. [68] | 28 | 31 | 29 | 93 |
| Tawfiek and Bagley [69] | 205 | NS | 31.7 | NS |
| Keeley et al. [70] | 41 | 35 | 28 | 100 |
| Elliot et al. [67] | 44 | 60 | 38 | 86.5 |
| Chen and Bagley [7] | 23 | 30 | 65 | 100 |
| Daneshmand et al. [36] | 26 | 31 | 88 | 100 |
| Suh et al. [71] | 18 | 21 | 37.5 | 100 |
| Johnson et al. [72] | 35 | 32 | 68 | 100 |
| Sowter et al. [73] | 35 | 42 | 74 | 100 |
| Thompson et al. [74] | 86 | 59 | 55 | 100 |
| Pak et al. [75] | 57 | 53 | 90 | 95 |
| Cornu et al. [76] | 35 | 24 | 60 | 100 |
| Gadzinski et al. [77] | 34 | 58 | 84 | 100/86[b] |
| Grasso et al. [78] | 66 | 52 | 77 | 87 |
| Cutress et al. [79] | 73 | 54 | 68 | 90 |

[a] Disease-specific survival.

[b] High-grade patients.

**Box 50.2 Factors related to increased risk of tumor recurrence.**

Multifocality
Tumor grade
Tumor size
Abnormal cytology
Previous bladder tumor
? Tumor location

Several characteristics of primary UTUC appear to be related to the risk of recurrence (Box 50.2), some of which are similar for those of bladder tumors. Recurrent disease is more likely for tumors over 1.5 cm in diameter than smaller lesions. There is also a higher risk of recurrence for high-grade tumors treated either ureteroscopically or by open surgery. There is evidence that positive urinary cytology at the time of treatment is a poor prognostic sign. The effect of the location of the primary tumor, whether in the intrarenal collecting system or ureter, has been inconsistent with some series reporting a higher rate for intrarenal neoplasms and others finding no difference or more frequent recurrence after ureteral primaries. However, multifocal lesions have consistently been seen to be associated with more frequent recurrences, both in the upper tract and in the bladder.

## Bladder tumors

There is significant risk of new bladder tumors developing in patients with upper tract neoplasms. The simultaneous initial presentation of urothelial carcinoma of the upper tract and bladder has been observed to be 17% in patients without prior history of bladder tumors [80]. The vast majority of bladder recurrences (80–90%) develops within the first 2–3 years of UTUC treatment [80] and tends to be nonmuscle-invasive in 88–95% of cases [81, 82].

In a recent meta-analysis including 8275 patients from 18 international centers undergoing RNU for UTUC between 2007 and 2014, Seisen et al. reported a pooled intravesical recurrence rate of 29% (range 21.5–46.9%) at median time 22.2 months with median follow-up of 43.8 months [83]. In contrast, Cutress et al. reported data on 22 ureteroscopically treated UTUC cohorts and noted a collective rate of intravesical tumor recurrence in 34% of patients with mean follow-up ranging between 14 and 73 months in another recent meta-analysis [66]. In two series specifically noting patients without previous bladder tumors, the rate was 34 and 33% [73, 76] (Table 50.4). In series with extended follow-up, the rate of bladder tumor occurrence is higher. Cutress et al. noted a 42% rate of bladder recurrences with mean follow-up of 52 months in 73 patients [79] while Grasso et al. noted 61% of 66 ureteroscopically treated patients developed bladder lesions with mean follow-up of 52 months [78].

**Table 50.4** New or recurrent bladder tumors: after ureteroscopic treatment of UTUC.

| Reference | Bladder tumor | Percentage |
|---|---|---|
| Sowter et al. [73][a] | 12/35 | 34.3 |
| Thompson et al. [74] | 37/83 | 44.6 |
| Daneshmand et al. [36] | 6/30 | 20.0 |
| Chen and Bagley [7][b] | 41/101 | 40.5 |
| Cornu et al. [76] | 14/35 | 40.0 |
| Cutress et al. [79] | 31/73 | 42 |
| Grasso et al. [78] | 40/66 | 61 |
| Combined | 181/423 | 42.8 |

[a] No history of bladder tumor.
[b] Reviewed series to 2001.

It is difficult to compare patients treated ureteroscopically or surgically because of selection bias in treating patients. The endoscopically treated patients have lower-risk tumor characteristics but bladder tumor occurrence is similar in both groups. This fact highlights the need for diligent cystoscopic surveillance for UTUC patients regardless of primary treatment modality. Furthermore, this also raises the question for the need of postoperative intravesical chemotherapy in ureteroscopically treated UTUC patients even without the immediate simultaneous presence of a bladder tumor. As seen in the ODMIT trial with bladder tumor-naïve UTUC patients undergoing RNU, the rate of new bladder tumor development within the first postoperative year was lower in those receiving a one-time dose of intravesical mitomycin (16%) versus those who did not (27%) [84].

## Large tumors

Large neoplasms of the upper tract can be treated successfully ureteroscopically in some patients. It may be necessary to stage treatment at intervals of approximately 6 weeks. A combination of neodymium:YAG laser, coagulation, or electrocoagulation with holmium laser resection is effective. If visibility deteriorates with bleeding or tumor debris, it may be impossible to distinguish the margin of the tumor. The second resection may allow more precise treatment. Some tumors that regrow too rapidly or are too large to be treated ureteroscopically may require a percutaneous nephroscopic procedure or even nephroureterectomy.

## High-grade tumors

Numerous reports have correlated the presence of high-grade UTUC with invasive disease on extirpative surgical specimens [35, 37]. Therefore, the presence of high-grade UTUC precludes the employment of ureteroscopy as primary treatment with the intent to cure. Endoscopic treatment for high-grade UTUC is reserved for those patients medically unfit for extirpative surgery, those with renal insufficiency or those with solitary renal units unfit for conservative extirpative surgery who would otherwise need dialysis but are unwilling to commit to it. In these situations, ureteroscopic management should be considered palliative with the goal of stopping gross hematuria and limiting the need for hospitalizations. The same ureteroscopic techniques would be employed with focus on coagulation of bleeding tumors and ablation of obstructing tumors whenever possible. In certain cases, stent dependence is accepted in order to maximize drainage especially if malignant obstructing tumors are present and require extensive coagulation, which may lead to ureteral stricture formation. Patients undergoing ureteroscopic treatment for high-grade UTUC should be counseled on the very high probability of eventual development of metastatic disease, end-stage renal disease, or both. Although there have been rare reported cases of successful long-term ureteroscopic treatment of high-grade cases [71], the median overall survival for such patients typically has been noted to be 29.2 months (range 6–52 months) [78].

## Surveillance

Surveillance after ureteroscopic treatment of upper tract neoplasms is essential because of the high local recurrence rate in the ipsilateral renal unit and the bladder. Almost every paper reviewing experience with this treatment has cautioned that endoscopic surveillance is necessary. Similar to surveillance for bladder cancer, cystoscopy in UTUC patients is performed every 3 months for the first year, every 6 months for the second year, and yearly thereafter. Evaluation of the upper tracts for new or recurrent tumors can be maintained radiographically or with diagnostic ureteroscopy. It is important to note that ureteroscopy is the most sensitive technique to evaluate the upper tract and should be used routinely in follow up surveillance. Keeley and colleagues [70] found that the sensitivity of retrograde ureteropyelography for detecting recurrent upper tract tumors was only 25% in patients with UTUC history undergoing strict ureteroscopic surveillance. In another series [85], urinalysis, voided cytology, and retrograde ureteropyelography were compared in patients with ureteroscopically visualized and treated tumors. None of those tests could accurately and routinely detect tumors as well as endoscopic findings, which were defined as the gold standard. There was a high specificity of bladder urine cytology and urinalysis, which do support their use. If they are abnormal, earlier endoscopy should be undertaken. At this time, the role of FISH in detecting recurrent UTUC appears to be minimal.

Various surveillance protocols have been proposed. Some authors recommend excretory urography or retrograde ureteropyelography at intervals of 3–6 months with ureteroscopy reserved only when specifically indicated. However, the greater sensitivity of direct endoscopic inspection must be recommended as the preferred technique for surveillance. Ureteroscopy is continued at intervals of 3 months until the upper tract is clear, at which time the patient is examined ureteroscopically at 6 month intervals. Cystoscopy and cytology with urinalysis are continued at intervals of 3 months during the first 2 years (Table 50.5). Evaluation of the contralateral collecting system with retrograde pyelography should be performed at least yearly and possibly at each 6 month interval. Cross-sectional imaging with contrast, as tolerated by the patient's renal function, should be performed yearly to rule out locally advanced, extra-luminal disease.

## Complications

Complications can occur with any ureteroscopic procedure but there are some that appear to be specific to ureteroscopic tumor treatment. Many of the problems related to dilation of the ureterovesical junction can be avoided by the use of small-diameter rigid and flexible ureteroscopes. Electroresection is rarely used, and therefore the complications inherent in that procedure are avoided. With any of the techniques commonly used, electrocoagulation, laser coagulation, or resection with a neodymium:YAG or holmium:YAG laser, there remains

**Table 50.5** Surveillance.

| Interval | Action |
|---|---|
| 3 month intervals | Cystoscopy<br>Cytology |
| 6 month intervals (after tumor-free) | Ureteroscopy |
| 6 or 12 month intervals | Imaging of contralateral kidney (IVP or retrograde) |
| 12 month intervals | Cross-sectional imaging (CT or MRI) |

**Table 50.6** Strictures after ureteroscopic treatment of UTUC.

| Reference | No. of patients | Stricture | % |
|---|---|---|---|
| Suh et al. [71] | 16 | 2 | 12.5 |
| Daneshmand et al. [36] | 30 | 5 | 16.7 |
| Johnson et al. [72] | 35 | 3 | 8.5 |
| Sowter et al. [73] | 40 | 4 | 10.0 |
| Chen et al. [86][a] | 139 | 19 | 13.7 |
| Overall | 260 | 33 | 12.7 |

[a] Combined series to 2001.

a risk of stricture from scarring of the ureter or an infundibulum. A review of complications from published series of ureteroscopic treatment of upper tract tumors indicates a ureteral stricture rate of 13% which is considerably higher than the less than 1% seen for stone treatment [86]. This may be an inherent risk of ureteroscopic tumor treatment, since the ureter itself is specifically traumatized with the treatment of the neoplasm. In comparison, damage to the ureteral wall during stone treatment is diligently avoided (Table 50.6).

Perforation remains a strong theoretical risk. However, reported series have not shown any strong propensity toward intraluminal tumor dissemination, implantation, extraluminal tumor, or tumor extension [55].

## Adjuvant therapy

Adjuvant chemotherapy or immunotherapy is an attractive option in the treatment of UTUC particularly because of the high recurrence rate. Due to the rarity of UTUC, no prospective, randomized trials have ever proven the efficacy of Bacille–Calmette–Guerin (BCG) or mitomycin C (MMC) as intraluminal adjuvant therapy following endoscopic management. Thus far, the literature offers mostly retrospective, single-institution, non-randomized case control studies containing relatively small numbers of patients with heterogeneous tumors with both ureteroscopic and percutaneous treatment approaches. Furthermore, no method of delivery to the upper tract has ever been standardized and these range from slow infusions via PCN tubes and ureteral catheters to passive application to the upper tract by bladder infusion with a stent. Two of the largest retrospective series published to date showed no benefit in terms of local recurrence rates in those given MMC with up to 63 months' mean follow-up [79] and those given BCG with up to 61 months' mean follow-up [87]. Thus, adjuvant therapy with either BCG or MMC has been seen to be feasible, with relatively low side effects, but efficacy has not been demonstrated. The safety and potential advantages of adjuvant therapy have been suggested in several short series but this treatment has no proven role.

## Cost of treatment

The application and the need for endoscopic resection and surveillance for upper tract tumors have raised concerns regarding the costs of this management. Pak and colleagues [75] examined the direct costs of renal-sparing conservative measures versus nephroureterectomy and subsequent chronic kidney disease or end-stage renal disease. In a cohort of 57 patients with a minimum follow-up of 2 years, renal preservation was 81% with CSS of 94.7%. On examination of Medicare payments, even the worst-case scenario of a solitary kidney with recurrences at each follow-up for 5 years versus nephroureterectomy and dialysis for the same period would save over US$250 000. This same savings could alleviate the expense of five cadaveric renal transplantations.

## Familial neoplasm of the upper urinary tract

Hereditary nonpolyposis colorectal cancer syndrome (HNPCC), also known as Lynch syndrome (LS), is an autosomal dominant genetic disorder which is characterized by germ-line mutations in DNA mismatch-repair genes, including *MSH-2*, *MLH-1*, *MSH-6*, and *PMS-2*. The syndrome is associated with predisposition to colorectal cancer and extracolonic tumors, especially the endometrium, but also including the breast, the ovary, and the upper urinary tract. An international retrospective cohort study performed by the world's largest LS research centers determined the lifetime risk of UTUC development in LS carriers was 8.4% but on further risk stratification was noted to be as high as 28% in men with *MSH-2* mutations with peak age of diagnosis between 50 and 70 years of age [88].

Observational studies suggest that the clinical behavior of UTUC in LS patients differs from sporadic cases of UTUC. Crockett et al. examined the Creighton University HNPCC database and found 39 patients with UTUC, the majority of who had confirmed mutational analysis [89]. When compared to sporadic UTUC cases, LS patients with UTUC present were on average 8 years younger, had a greater tendency towards ureteral tumor location versus intrarenal location, and had a slight female preponderance. A series of UTUC patients with *MSH-2* mutations treated with ureteroscopy and laser ablation has been reported [90]. Similar to Crockett's report, these patients were relatively young at presentation at a mean age of 56.5 years and demonstrated a greater tendency for ureteral lesions. This series had a notable rate of metachronous bilateral UTUC (6/13) with a mean time of 49 months between eventual bilateral UTUC development. Although selection bias in this small series must be taken into account, the risk for bilateral disease in this population must be seriously considered. Furthermore, given the relatively younger age at presentation, conservative management with endoscopic treatment should be entertained as first line therapy whenever clinically feasible [89–91]. Panel recommendations have been put forth suggesting annual urinary analysis in LS carriers with three or more red blood cells per high-powered field as an initiator for further work-up. Although routine imaging was not recommended in every case, strong consideration should be given to CT urogram, particularly in those patients already undergoing periodic cross-sectional imaging for other malignancies especially when *MSH-2* carrier status exists or family history of UTUC is present [92].

## Benign neoplasms

Benign urothelial neoplasms are rare in the renal pelvis and ureter. Many individual cases or short series have been reported and include fibroepithelial polyps, inverted papillomas, and hemangiomas as well as the more commonly noted ureteritis cystica.

Fibroepithelial polyps (FEPs) are mostly benign ureteral luminal lesions originating from the mesodermal components of the ureteral wall and are covered in otherwise normal urothelial epithelium. Very rarely they are associated with UTUC [93] and therefore routine pathologic analysis is required for a complete evaluation. FEPs typically appear in young patients as a smooth pedunculated mass in the upper urinary tract, often occurring at the ureteropelvic junction with polyp length ranging from 0.5 to 4 cm [94], although longer FEPs have been reported. Historically, these lesions have been treated by open surgical resection. However, the availability of small ureteroscopes and appropriate biopsy or resection devices, such as used for UTUCs have permitted ureteroscopic diagnosis and treatment. With increasing use of flexible digital ureteroscopes, the stalks of these FEPs are more clearly appreciated than ever, allowing for laser resection with holmium laser and complete removal with minimal trauma to the ureteral surface [95]. Follow-up after treatment is required only to confirm healing without significant stricture.

Inverted papillomas have also been considered a benign lesion, although there has been concern because of the association with UTUC and the difficult histopathologic diagnosis. The most common presentation has been with hematuria [96]. However, they can also cause obstruction with hydronephrosis. Endoscopically, they appear as a smooth mucosal based neoplasm. Often, there is a relatively narrow base encompassing less than one-quarter circumference of the ureter. The lesions lack the papillary configuration of low-grade UTUC, but can be confused with a higher-grade lesion. Endoscopic biopsy is a crucial diagnostic study. It is particularly helpful to excise the entire lesion [97]. Follow-up should be maintained both to confirm the patency of the urinary tract and because of the possible association with new UTUC. These neoplasms can be treated adequately ureteroscopically.

## Conclusion

Ureteroscopy plays a central role in the diagnosis and treatment of UTUC. Larger lesions may require a percutaneous approach. Lesions that are more extensive, high-grade, or unable to be controlled endoscopically require nephroureterectomy, which can usually be performed laparoscopically.

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# 51

# Retrograde Endopyelotomy

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## Introduction

Advances in technology, instrumentation, and techniques have changed the practice of urology, especially over the past two decades. One of the areas of major impact has been the treatment of ureteropelvic junction obstruction (UPJO), which is defined as an anatomic or functional impedance of urine flow from the renal pelvis into the ureter [1] (Figure 51.1). This condition can be congenital or acquired, the congenital form being the more common. UPJO, although relatively uncommon, warrants prompt attention to alleviate symptoms and prevent deterioration of renal function. Several factors can play roles in the development of UPJO, including intrinsic aperistalsis of the involved ureteral segment, crossing aberrant vessels causing direct compression of the ureter, renal stone disease, and previous surgical or endourologic manipulation.

The advent of smaller-caliber endoscopes [2], and development of laparoscopic reconstructive techniques, laser technology, and robotics has diversified the treatment options for this condition.

Although the efficacy, and decreased morbidity, hospital stay, and need for analgesia with endopyelotomy have been clearly demonstrated, several issues have still not been completely resolved. Should patients be managed initially by the ureteroscopic approach? What are the exclusion criteria for these endoscopic procedures? What are the relative merits of antegrade versus retrograde approaches? In the era of minimally invasive laparoscopy and robot-assisted surgery, is there still a role for retrograde ureteroscopic endopyelotomy?

In this chapter we discuss the technique and results at our institution for retrograde ureteroscopic endopyelotomy for the treatment of UPJO.

## History

Several reconstructive procedures have been described for the management of UPJO since Trendelenburg's first description of such a procedure in 1886. Open surgical correction was the only mode of treatment for this condition before the introduction of endoscopic and laparoscopic techniques, and has been considered the gold standard of treatment for this condition, with success rates of over 90% [3]. However, associated morbidity is not unusual with open surgery. Specifically, there is fistula formation in 2.6% of patients, stricture of the ureteropelvic junction (UPJ) in 2.4%, and the need for nephrectomy in 3.2% [4].

The present-day endourologic approach to the management of UPJO can be traced back to the original descriptions of Albarran, Keyes, and Davis. Albarran did the first endosurgical repair of the UPJO in 1903, which actually described a ureterotome externe [5]. Keyes performed a similar procedure successfully in 1915 [6]. Both the antegrade and retrograde endopyelotomy follow the concept of Davis's intubated ureterotomy, first described by Davis in 1943. In 1985, Bagley et al. reported a combined percutaneous and flexible ureteroscopic approach for the management of an obliterated UPJ [7]. Wickham and Kellet described the first ureteroscopic pyelolysis of the UPJ in 1983 [8], and this was repeated by Inglis and Tolley in 1986 [9]. Thomas et al. described their experience of ureteroscopic endopyelotomy in which pre-stenting was performed to facilitate ureteroscopy in 1996 [10]. A single-setting, one-stage procedure was subsequently described by Soroush and Bagley in 1998 [11].

There are now multiple different options for the treatment of UPJO, including antegrade nephroscopic

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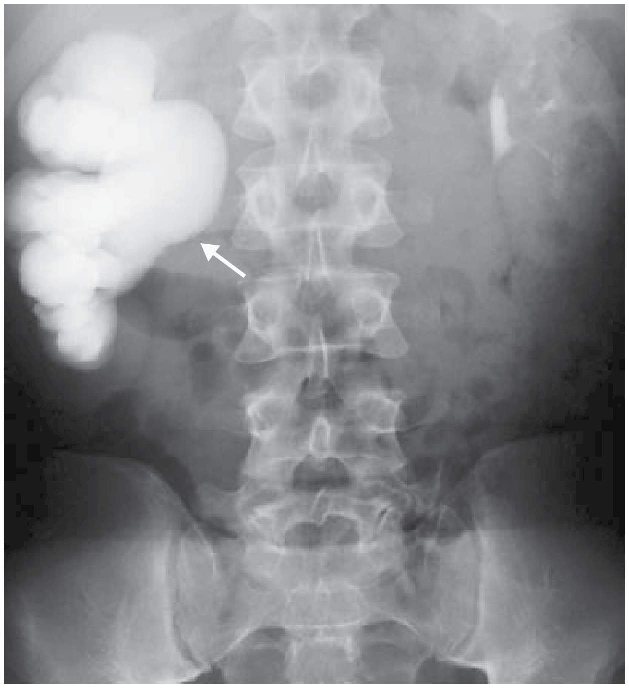

**Figure 51.1** Intravenous pyelogram of a right ureteropelvic junction obstruction (arrow).

endopyelotomy, retrograde ureteroscopic endopyelotomy, Acucise™ (Applied Medical, Rancho Santa Margarita, CA, USA), and laparoscopic and robot-assisted pyeloplasty, as well as the traditional open surgical pyeloplasty [12]. As mentioned above, open surgical dismembered pyeloplasty has been considered the gold standard for the treatment of UPJO, with success rates of over 90%. However, many institutions have considered endopyelotomy a possible first-line therapy option for the treatment of this condition [13–16].

Currently, a retrograde endopyelotomy can be performed in three ways: (i) using a rigid ureteroscope and a cold-knife, electrocautery, or holmium laser incision; (ii) using a flexible ureteroscope and electrocautery or laser incision; and (iii) in rare select cases, using a balloon with a cutting wire (Acucise) [15]. The technique of dilation and cold-cut incision with a peripheral cutting balloon, which was originally designed for angioplasty, had been reported mainly for ureteral strictures other than UPJO [17–19]. For UPJO, a recent retrospective case series was described in infants under 18 months of age [20]. This has not yet been reported in literature for adult patients with UPJO. It must be mentioned that the use of Acucise is not recommended for primary UPJO because of incidences of hemorrhage following use of this device.

Different series have reported success rates for retrograde ureteroscopic endopyelotomy to be in the range of 73–90% [10, 11, 21–24]. As compared with other treatment options, ureteroscopic retrograde endopyelotomy is less invasive, requires less operating room time, enables the procedure to be performed on an outpatient basis or with a very short hospital stay, and is associated with a shorter convalescence period [1, 13, 25–29]. Also, the initial report of ureteral stricture formation because of thermal injury from transmission of the electrocautery current has been eliminated with the use of insulated ureteroresectoscopes and electrocautery and rigid or flexible ureteroscopes with holmium laser fibers [30]. With the miniaturization of ureteroscopes, the use of the rigid resectoscope is no longer advised.

## Patient selection and preoperative preparation

The presumptive clinical diagnosis of UPJO can be evaluated and/or confirmed with a renal ultrasound, intravenous pyelogram (IVP), diuretic renal scan, retrograde pyelogram, computed tomography (CT) scan, Whitaker test, or with a combination of these, as is clinically indicated. The renal scan, besides aiding in the diagnosis of a UPJO, gives a quantitative differential renal function, which can be used to choose the best treatment option and, further, to allow for follow-up evaluation of the renal function.

A high-resolution spiral CT angiography is highly recommended to assess for the presence of an aberrant crossing vessel. For practitioners with experience and access to endoluminal ultrasound equipment, it can also be used to identify crossing vessels [31]. The UPJ area can also be evaluated ureteroscopically for the presence of pulsations before performing the endopyelotomy incision.

Although ureteroscopic retrograde endopyelotomy is applicable to most patients with UPJO, there are some absolute and relative exclusion criteria. Among the absolute contraindications are patients with active infection and bleeding diathesis.

Patients with concurrent renal calculi and UPJO, and patients with a nephrostomy tube in place, should be treated with an antegrade approach so that both the renal stone and the UPJO can be managed in a one-stage procedure. Patients with a relatively long length of obstruction, usually greater than 2 cm, are best managed either with open surgical, laparoscopic, or robot-assisted techniques. Patients with ipsilateral differential renal function of less than 20% and severely decreased parenchymal thickness can be given a trial of drainage and re-evaluation [15] or should be offered a laparoscopic simple nephrectomy for a poorly functioning or nonfunctioning kidney. Patients with massive hydronephrosis should be treated with dismembered pyeloplasty, either open surgical, laparoscopic, or robot-assisted, because of the need for trimming and reduction of the redundant renal pelvis. Controversy exists with regard to patients with high insertion of the UPJ and crossing vessels. Although once considered a contraindication because of poor results, published series report that the type of ureteral insertion has no significant impact on the outcome of endopyelotomy [32], and that patients with crossing vessels had long-term success with retrograde endopyelotomy [14]. We routinely perform laparoscopic robot-assisted pyeloplasty in both cases with a high insertion UPJO or a known crossing vessel [12]. In the case of recurrent UPJO after pyeloplasty in adult patients, a trial of retrograde endopyelotomy should be considered as it has been noted to have success rates greater than 80% in such cases [33]. Lastly, patients with known intractable stent intolerance should be considered candidates for either an antegrade endopyelotomy or an open pyeloplasty with a nephrostomy tube, and not for ureteroscopic endopyelotomy.

Once the surgeon and patient have decided on the retrograde approach for management of a UPJO, an indwelling ureteral stent is usually placed to drain the obstructed renal unit for 1–2 weeks. This procedure not only drains the obstructed renal unit, but also stabilizes its renal function, dilates and straightens the UPJ, and facilitates subsequent passage of the ureteroscope into the renal pelvis. Above all, preoperative placement of the stent allows evaluation of any degree of stent intolerance and may identify improvement of renal function after drainage.

### Informed consent

On the day of the scheduled endopyelotomy, any final questions are answered, and an informed consent is obtained after explaining and discussing with the patient the expected outcomes and benefits of the procedure (e.g. improved renal drainage, preservation of renal function, diminished risk of calculus and infection, minimally invasive procedure), its associated risks or complications (bleeding, infection, possibility of conversion to open surgery, recurrence, etc.), and the other minimally invasive treatment options available. Patients are informed that postoperative evaluations may show some residual pelvicaliectasis, especially in those with long-standing UPJO.

## Step-by-step operative technique

The required instrumentation is listed in Table 51.1. After either a general or a spinal anesthesia, the patient is placed in the lithotomy position. Caution is taken so that all pressure points are well cushioned, and antiembolic

**Table 51.1** Required instrumentation.

| | |
|---|---|
| Holmium laser ureteroscopic endopyelotomy | 7.5 Fr rigid and/or flexible ureteroscope |
| | 200 or 365 μm holmium laser fiber at the following settings:<br>• 1.5–2.5 J,<br>• 10–15 Hz. |
| | Super-stiff guidewire (0.038 inch) |
| | Single Action Pumping System (Boston Scientific, Marlborough, MA, USA) |
| | Endopyelotomy stent (Boston Scientific or Applied Medical, Rancho Santa Margarita, CA, USA) |
| | Routine cystoscopy and fluoroscopy setup |
| Ureteroscopic endopyelotomy with electrocautery | 11.5 Fr ureteroresectoscope (Karl Storz, Culver City, CA, USA; Richard Wolf, Rosemont, IL, USA) (Figure 51.2):<br>• insulated electrocautery knife,<br>• cold knife,<br>• electrocautery attachments. |
| | Single Action Pumping System (Boston Scientific) |
| | Super-stiff guidewire (0.038 inch) |
| | 5 Fr open-ended catheter |
| | Endopyelotomy stent (Boston Scientific or Applied Medical) |
| | Routine cystoscopy and fluoroscopy setup |

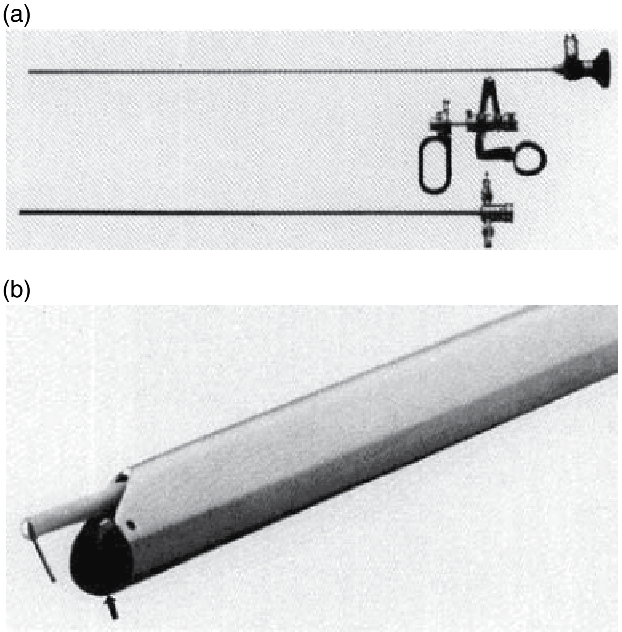

**Figure 51.2** (a) 11.5 Fr Ureteroresectoscope with insulated tip. (b) Close-up view of ureteroresectoscope shows insulated cutting electrode in place (arrow).

stockings are used in high-risk patients. With the use of a cystoscope, and under fluoroscopic guidance, a retrograde pyelogram is performed to confirm the length of the UPJO segment, and subsequently a super-stiff guidewire is passed and coiled into the renal pelvis. If the patient had a previously placed indwelling ureteral stent, it is removed and used to pass the guidewire prior to removing the stent. A retrograde pyelogram can assess for any resolution of hydronephrosis and can be used as a prognostic indicator.

The next step varies depending on whether the endopyelotomy is done with electrocautery through a ureteroresectoscope or whether a holmium laser is used through a modern rigid, semirigid, or flexible ureteroscope. In regions where the holmium laser is not available, an insulated electrocautery electrode can be used to incise using the cutting current.

## Holmium:YAG laser ureteroscopic endopyelotomy

A 7.5 Fr self-dilating rigid, semirigid, or flexible ureteroscope is passed alongside the super-stiff guidewire using generally accepted ureteroscopic techniques. A balloon dilator can be passed over the guidewire and the ureteral orifice dilated in the case of difficulty advancing the ureteroscope within the ureter. If necessary, another guidewire can be passed through the ureteroscope and the narrow area subsequently balloon dilated.

Once at the UPJ, this is first inspected for the presence of any transmitted pulsations. A 365 μm holmium laser fiber, when using a rigid or semirigid ureteroscope, or a 200 μm fiber in the case of a flexible ureteroscope, is passed through the working channel of the ureteroscope. At a setting of 1.5–2.5 J and a frequency of 10–15 Hz, the UPJ is incised under direct vision either laterally or posterolaterally to avoid the risk of injuring any unsuspected crossing vessel. The incision is carried on until periureteral fat is seen and the UPJ is wide enough to permit easy passage of the ureteroscope into the renal pelvis (Figure 51.3).

After hemostasis of any venous bleeding is performed, the laser fiber and ureteroscope are removed. The UPJ area is dilated up to 24 Fr using a balloon dilator under fluoroscopic guidance. The concept of balloon dilation of the UPJ is based on Davis' intubated ureterotomy, in which the incised and dilated ureteral fibers regenerate around the ureteral stent over a 6 week period [6] (Figure 51.4).

The balloon dilator is then removed. An endopyelotomy stent is placed under fluoroscopic control, leaving the 14 or 10 Fr end at the UPJ (depending on the stent

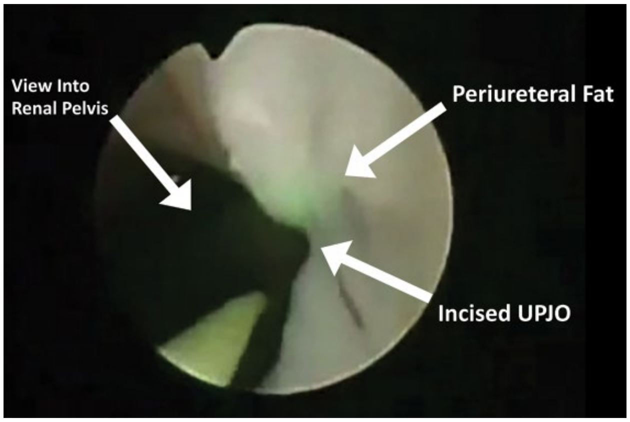

**Figure 51.3** Periureteral fat seen after the ureteropelvic junction was incised with a holmium laser.

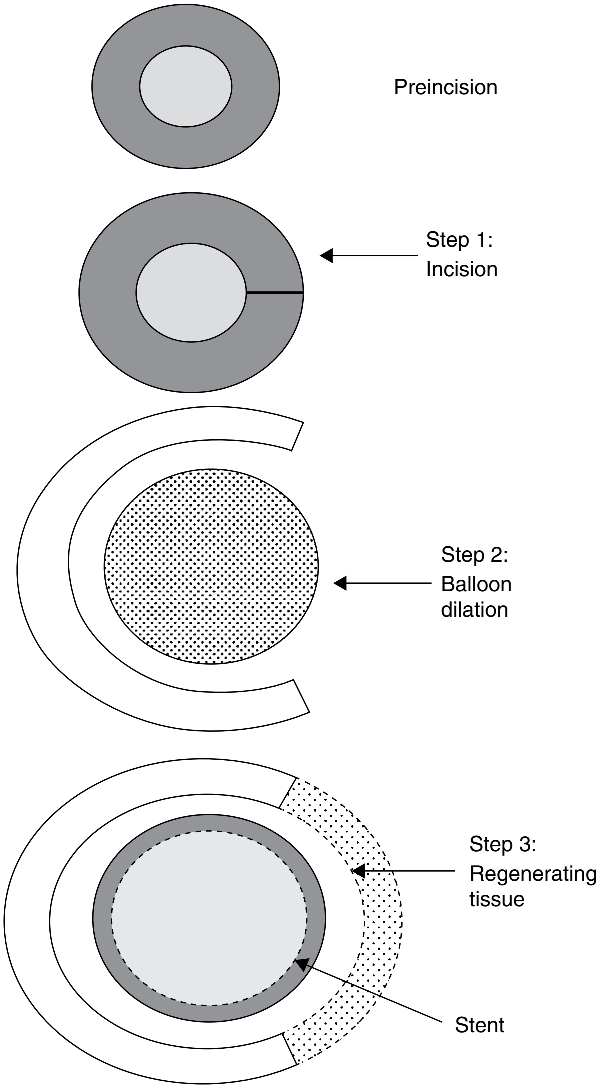

**Figure 51.4** Tissue regeneration after incision and balloon dilation.

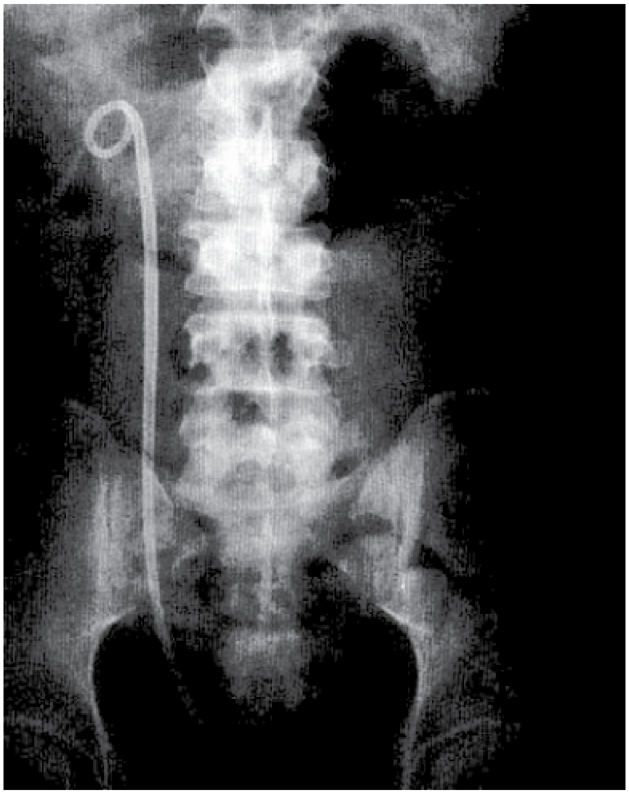

**Figure 51.5** Endopyelotomy indwelling stent in place after ureteropelvic junction obstruction incision.

used) and the 7 Fr end coiled in the bladder (Figure 51.5). Alternatively, a 7 or 8 Fr double-J ureteral stent can be left in place. The authors recommend using a ureteral stent one size longer than anticipated to prevent downward migration of the renal coil into the incised UPJ. If the stent is malpositioned, this can lead to leakage of urine into the retroperitoneal space with formation of a urinoma.

As the ureteral stent can reflux urine from the bladder to the incised UPJ, an indwelling Foley catheter is placed to drain the bladder for 48 hours. This helps to maintain a low-pressure system in the urinary uract and to prevent urinary reflux through the ureteral stent into the incised UPJ, which also may leak into the retroperitoneal space, possibly causing formation of a urinoma.

## Ureteroscopic endopyelotomy with electrocautery

A 5 Fr open-ended catheter is passed over the super-stiff wire. The open-ended catheter works as an insulator, preventing contact with the electrocautery element, and avoiding transmission of current along the length of the guidewire if contact is made. Also, once the wire is removed, the open-ended catheter may serve to continuously drain the renal pelvis of the irrigant used during the procedure.

The 11.5 Fr ureteroresectoscope is passed directly alongside the insulated guidewire with the cold knife in place. The electrocautery element is right-angled and would impede vision if placed during the insertion of the ureteroresectoscope [1]. If there is difficulty accessing the ureteral orifice or the intramural ureter, a balloon dilator can be passed over the guidewire to dilate the area. If there is resistance advancing the ureteroresectoscope along the ureter proximal to the UPJO, a smaller self-dilating ureteroscope can be passed to passively dilate the ureter and to inspect for the cause of the narrow area. If necessary, another guidewire can be passed through the self-dilating ureteroscope and the narrow area is balloon dilated.

Once at the UPJ, the cold-knife working element is exchanged for the electrocautery element. Either water or 1.5% glycine solution is used as the irrigant during monopolar electrocautery for incision.

The UPJ is first inspected for the presence of any transmitted pulsations, and then incised laterally, between 8 and 9 o'clock on the right and between 3 and 4 o'clock on the left. Short and shallow strokes should be performed, and aggressive and deep incisions should be avoided. Any bleeding site is controlled by means of spot electrocoagulation. The incision is carried down until periureteral fat is seen, and the ureteroresectoscope enters the renal pelvis with ease.

The ureteroresectoscope and the open-ended catheter are removed. The rest of the subsequent steps, balloon dilation, stenting, and Foley catheter drainage, are the same as described above for the holmium:YAG laser endopyelotomy. As mentioned above, if the holmium laser is not available, then a flexible insulated electrocautery electrode can be used instead.

### Postoperative care

The vast majority of patients are discharged either the same day or within the first 24 hours following the procedure. Oral antibiotics, usually fluoroquinolones, are given for 3–5 days. Oral antispasmodics and/or oral anticholinergics are given as needed in case of irritative bladder symptoms. The Foley catheter is removed, often by the patient, after 48 hours. The ureteral stent is removed cystoscopically in clinic in 6 weeks.

Diuretic MAG3 renal scans or IVP are performed 4 weeks after ureteral stent removal. Patients are followed-up with renal ultrasound or renal scan every 4–6 months during the first year and yearly thereafter or as needed.

Success following endopyelotomy is measured by evaluating improvement of the function and drainage of the involved kidney and alleviation of symptoms. After correction of the obstruction at the UPJ, postoperative radiographic images from an IVP or CT scan often show residual pelvicaliectasis resulting from long-standing obstruction and dilation that may not completely resolve.

## Results

We analysed the outcome of 139 consecutive patients who underwent retrograde ureteroscopic endopyelotomy at Tulane University Health Sciences Center between 1989 and 2002. These patients included seven pediatric patients, four solitary kidneys, two horseshoe kidneys, and one ptotic kidney.

The average postoperative hospital stay was less than 24 hours. Seventy-nine percent of the patients were discharged home on the same day, and 97% of them within 24 hours. Of the 139 patients, 32 (23%) required subsequent procedures to treat recurrence of obstruction, showing an overall long-term success rate for retrograde ureteroscopic endopyelotomy of 77%. Fourteen of these patients (10%) required major open or laparoscopic surgical intervention, including nephrectomies for severe hydronephrosis and nonimprovement in renal function in three (2%) cases, emergent nephrectomy for severe bleeding in one (0.7%), dismembered pyeloplasties in eight (5.7%), and spiral flap pyeloplasties in two (1.4%).

Eighteen (12.9%) patients required minor procedures, which included cystoscopy and balloon dilation of the UPJ in 13 (9.3%), repeated retrograde endopyelotomy in four (2.8%), and long-term indwelling stent exchange in one (0.7%). There were no ureteral strictures secondary to manipulation or the earlier use of the larger ureteroresectoscope in our series.

After analysing the failures of treatment in this series, two factors were obviously associated with poor results (no improvement of symptoms, drainage, and function after endopyelotomy): (i) a long-standing obstruction with a decrease in ipsilateral renal function of less than 20% of the total renal function and (ii) a severely dilated renal pelvis, which did not improve on drainage with an indwelling ureteral stent.

After evaluation of these results, we conclude that patients with patulous redundant renal pelvis and borderline salvageable renal function should be considered candidates for alternative treatment modalities, such as open or laparoscopic/robotic pyeloplasty or nephrectomy, rather than endopyelotomy.

## Complications

Since its initial description by Young in 1912, retrograde ureteroscopy has come a long way and has gained widespread acceptance as an option for the treatment of multiple pyeloureteric conditions. Further advances in technology have led to the introduction of smaller-caliber ureteroscopes with the capacity to accommodate accessory instruments necessary to perform diagnostic and therapeutic upper urinary tract procedures.

As with ureteroscopy, the complications and adverse events associated with retrograde ureteroscopic manipulation of the ureter have decreased dramatically in the past two decades. Smaller-caliber ureteroscopes, the advent of laser technology, improved paraphernalia, and, above all, experience in the procedures, should be given credit. Although these advances have decreased the need for open ureteral surgery, iatrogenic injury can still occur with the endoscopic technique. Possible iatrogenic complications of ureteroscopy include ureteral perforation, stricture, false passage, ureteral avulsion, bleeding from the ureteral mucosa or adjacent structures, infection, and sepsis. Multiple studies have reported the overall complication rate of ureteroscopy to fluctuate between 1 and 15% [34–36]. Complication rates have substantially decreased following introduction of smaller-caliber rigid and flexible ureteroscopes.

The reported incidences of pain, fever, false passage, and urinary tract infection were 5.5, 1.4, 0.4, and 1.6%, respectively, in one large ureteroscopy series [37].

Other complications associated with incision of the UPJ can include bleeding from adjacent aberrant vessels, stent migration through the UPJ incision, and UPJO recurrence. Significant bleeding requiring emergent nephrectomy or selective angioembolization is another possible complication that justifies the need for vascular or three-dimensional (3D) radiographic studies to identify aberrant vessels. The use of a complete lateral incision at the UPJ helps to prevent injuries to those vessels, based on detailed anatomical studies of renal vascular anatomy [38].

Minor complications of retrograde ureteroscopic endopyelotomy include proximal stent migration, stent intolerance, minor bleeding, and urinary tract infection after manipulation. Most of these complications are alleviated after removal of indwelling ureteral stents. The routine use of antispasmodic and anesthetic drugs after surgery improves tolerance to the stent and decreases complaints from the patient.

## Current role of retrograde endopyelotomy

With the proliferation of robotic technology, robotic pyeloplasty has replaced ureteroscopic endopyelotomy as the primary treatment option for UPJO. In these institutions, retrograde endopyelotomy is reserved for initial management of any UPJO recurrence following robotic pyeloplasty. However, the indications for retrograde endopyelotomy have not changed in institutions where laparoscopic and robotic pyeloplasty are unavailable.

## Comparison of treatment approaches and conclusions

Multiple endourologic and open surgical techniques are now available for the treatment of UPJO. The choice of technique relies primarily on the urologist's experience with each procedure, available equipment, and the need to perform another concomitant procedure.

Antegrade endopyelotomy requires expertise in percutaneous renal surgery, with detailed knowledge of the intrarenal anatomy and adequate experience in "real-time" two-dimensional fluoroscopic imaging. This is the preferred technique when treating concomitant intrarenal calculi, but it is also associated with a larger potential for complications and morbidity. The occurrence of pneumothorax, adjacent organ trauma (i.e. bowel, spleen, liver), and hydrothorax are possibilities that need to be explained to the patient prior to the surgery. Antegrade and retrograde endopyelotomy share the potential for hemorrhage from injury to aberrant crossing vessels; however, antegrade access may also be associated with hemorrhage from the percutaneous renal tract and with a higher risk of infection owing to external urinary drainage through the percutaneous nephrostomy tube.

Acucise retrograde endopyelotomy is no longer popular, but, if performed, relies on fluoroscopic imaging and not on direct visualization during cutting of the UPJ. High-quality fluoroscopic imaging is critical for optimal electrode placement. Short-term success rates of this procedure have been comparable to those obtained with retrograde ureteroscopic endopyelotomy and range from 66 to 84% [39]. Extreme caution should be exercised when using this technique in the presence of aberrant crossing vessels. Preoperative CT scan with angiographic phase and 3D reconstruction has been shown to be adequate to collect information regarding periureteral vasculature at the level of the obstruction [40]. Incision at the lateral position of the UPJ should minimize the risk of vascular injury while performing this procedure. Use of this technique has dramatically decreased because of lower success rates noted with long-term follow-up [41].

Multiple different indwelling stents can be used to maintain patency of the UPJ after an endopyelotomy. At our institution we use a 7 or 8 Fr double-J ureteral stent with postoperative results similar to those obtained with endopyelotomy stents. It is always important to use an indwelling stent one size longer than anticipated in order to avoid downward migration of the stent that could compromise endopyelotomy healing.In many high-volume centers, laparoscopic and robotic pyeloplasty has supplanted retrograde ureteroscopic endopyelotomy as the first-line treatment for UPJO because of good long-term outcomes (i.e. greater than 90%), comparable to those of open pyeloplasty. While robotic pyeloplasty has replaced retrograde ureteroscopic endopyelotomy as our first-line treatment for most symptomatic UPJO, it is our belief that retrograde ureteroscopic endopyelotomy continues to have a place in providing a safe and adequate treatment for patients suffering from a short-segment UPJO with good renal function and non-patulous renal pelvis. With the advent of smaller scopes and devices, this technique has evolved to include larger children as possible patients. Adherence to strict endourologic principles and direct visualization makes retrograde ureteroscopic endopyelotomy a safe and effective treatment modality. Furthermore, this procedure has a short learning curve and can be performed in almost all general hospitals where ureteroscopy is performed.

Lastly, this procedure should always be part of a urologist's treatment armamentarium, because adult patients who have failed laparoscopic, robotic, or open surgical pyeloplasty can be managed with ureteroscopic retrograde endopyelotomy as a secondary procedure.

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## 52

# Endoscopic Management of Mid-ureteral Obstruction

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## Introduction

Strictures of the ureter are challenging to diagnose, technically difficult to treat once diagnosed, and associated with significant psychological overlay due to their frequent iatrogenic etiology. Although sometimes successfully treated with a single endoscopic procedure, mid-ureteral strictures tend to recur, and may lead to renal loss if the obstruction is not expeditiously diagnosed and relieved. Mid-ureteral strictures are anatomically, physiologically, and surgically distinct from both proximal and distal ureteral strictures. Therefore, the endourologist must possess an intimate understanding of ureteral anatomy and physiology to avoid injury to the ureter, and to provide definitive management for these injuries when they do occur. This chapter will review strictures of the mid ureter, including the anatomy, prevention, diagnosis, and treatment.

## Anatomy

The adult ureter is 25–30 cm long and 1.5–6 mm wide in its unobstructed, physiologic state [1]. The course of the ureter in the retroperitoneum is relatively constant, and is generally found just lateral to the transverse processes of the lumbar vertebrae (Figure 52.1). Knowledge of the anatomical relationships of the ureter may prevent iatrogenic injury [1]. Posterior to the proximal ureter, the genitofemoral nerve runs along the psoas muscle [2, 3]. Anteriorly, at the level of the kidney lower pole, the ureter is crossed by the gonadal vessels. In close proximity to the abdominal ureter is the sigmoid mesocolon [4].

Just below the pelvic brim, the ureter crosses over the common iliac artery near its bifurcation. The iliac artery pulsations may serve as an important ureteroscopic landmark. The ureters then course inferoposteriorly, along the pelvic sidewall, anterior to the internal iliac artery and outside of the parietal peritoneum. The ureters then run anteromedially into the bladder [5]. The ureter is divided into three anatomic portions, with the middle portion overlying the bony pelvis. The ureter also has three anatomic narrowings including the ureteropelvic junction, the level where the ureter crosses the common iliac artery, and the intramural ureter [6].

Familiarity with the ureteral blood supply may prevent inadvertent devitalization during ureteral dissection. The ureter has a segmental blood supply from the aorta and renal, gonadal, common iliac, and internal iliac arteries. Above the pelvic brim, the arterial supply originates medially while it originates laterally below the brim [6].

Histologically, from inner to outer, the ureteral layers are the urothelium, mucosal vascular plexus, muscular layer, and adventitia. In the upper ureter, the inner muscular layer parallels the long axis of the ureter. The outer muscular layer has a circular or oblique orientation. The mid and distal ureter have an additional outer longitudinal layer. The adventitia contains vertically arranged arteries supplying the ureteric wall [6]. Dissection of the ureter should proceed outside these vessels to avoid compromising its blood supply. Preservation of these vessels will allow collateralization from other levels even if some blood supply must be sacrificed [7].

The venous drainage parallels the arterial supply. The lymphatic drainage of the ureter consists of the lateral aortic (lumbar), common iliac, external iliac, and internal iliac lymph nodes. The nervous supply of the ureter arises from adjacent renal, aortic, and hypogastric autonomic plexuses. Pain fibers enter the spinal ganglia and the spinal cord at segments T11 through L1 or L2, taking the same course as the sympathetic fibers [5].

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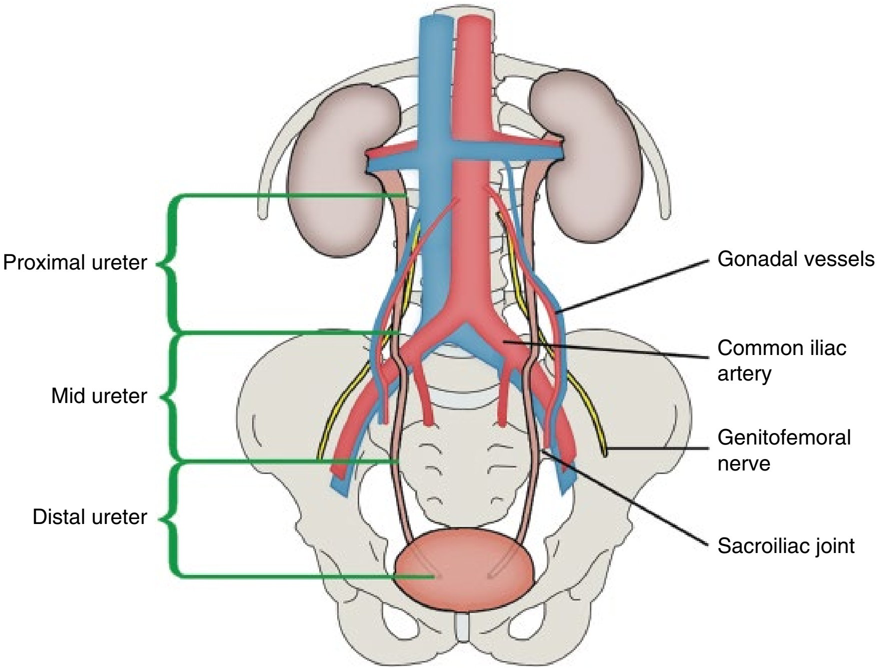

**Figure 52.1** Anatomical relationships of the ureter.

## Classification and etiology of strictures

A ureteral stricture is a pathologic narrowing of the ureter, resulting in dilation of the urinary system proximal to that point with resultant delayed urine transit. Strictures may be extrinsic, intrinsic, or intraluminal. This classification system is valuable since the different types of obstruction may be treated differently. For example, intraluminal obstruction may be successfully treated by endoscopic ablation or removal of the obstructing agent, while extrinsic obstruction is difficult to treat endoscopically and requires drainage and treatment of the extrinsic etiology of the obstruction.

Strictures can also be classified as ischemic or non-ischemic. This definition is also clinically relevant because ischemic strictures may not respond as well to endoscopic procedures [8]. Strictures have also been classified as inflammatory versus non-inflammatory [9], but it is unclear if there is any clinical relevance to this classification system [10]. Table 52.1 lists the etiologies and classifications of ureteral obstruction.

Strictures often arise iatrogenically due to surgery, by clipping, suture ligation, thermal injury, or devascularization. Gynecological surgery is the most common cause of iatrogenic ureteral injury and hysterectomy is the leading procedural cause, occurring at a rate of 0.5–1.5% [10, 11]. Abdominal hysterectomy is more likely to lead to ureteral injury (2.2%) compared to vaginal hysterectomy (0.03%) [10]. Unfortunately only 13–66% of injuries are detected intraoperatively, with the remainder diagnosed postoperatively [10].

**Table 52.1** Etiologies of mid-ureteral strictures according different classifications.

| Ischemic | Non-ischemic | Extrinsic | Intrinsic | Intraluminal | Inflammatory |
|---|---|---|---|---|---|
| Radiation | Impacted stone | Iatrogenic ligation | Bilharziasis | Fungus ball | Tuberculosis |
| Surgery | Idiopathic | Retroperitoneal malignancy | Endometriosis | Sloughed papilla | Retroperitoneal fibrosis |
| | Primary ureterovesical junction obstruction | Aneurysm | Fibrosis | Stone | Schistosomiasis |
| | Postendoscopy | | Submucosal stone | Transitional cell carcinoma | Neoplasm |
| | | | | | Iatrogenic injury |

The incidence of ureteral injury from colon and rectum surgery is on the rise [4, 12]. The types of colorectal surgery most likely to injure the ureter are transverse colectomy (0.05%), right hemicolectomy (0.08%), proctocolectomy (0.26%), left hemicolectomy (0.28%), sigmoidectomy (0.33%), subtotal/total colectomy (0.35%), anterior resection (0.58%), and abdominoperineal resection (0.76%) [12]. Rectal cancer is the most common underlying disease associated with ureter injury at the time of colorectal surgery [12].

Urological surgery is another well-recognized cause of ureteral stricture. In the initial experience of endoscopic stone treatment, large-caliber ureteroscopes [13] and lithotrites like the electrohydraulic probe led to a major complication rate (defined as perforation, avulsion, or stricture) of 6.6% [14]. In the modern era, with the advancement of technology to include smaller, tapered, and more flexible ureteroscopes and instruments the stricture rate for uncomplicated ureteroscopy is 0.3–0.6% while the perforation rate for intact extraction of stones is 4% [15, 16]. The danger arises when these injuries are not recognized intraoperatively, and are associated with silent obstruction, risking renal loss. This concern has led the American Urological Association to recommend routine ultrasound of upper tracts following ureteroscopic manipulation for stone removal [17].

A long-standing, impacted, ureteral stone can also lead to ureteral wall damage and stricture formation (Figure 52.2). Roberts et al. reviewed 21 patients with long-standing ureteral stones (mean 8 months) [18]. After treatment, 24% developed strictures. The authors identified longer duration of impaction and iatrogenic ureteral perforation during ureteroscopy as risk factors for future stricture formation [18].

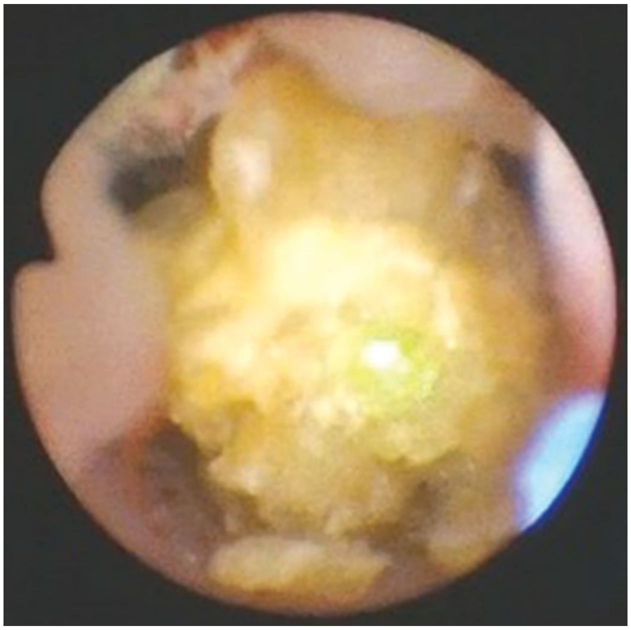

Figure 52.2 Impacted ureteral stone. Note mucosal edema and ingrowth around stone.

An entity called congenital mid-ureteral stricture represents a rare cause of mid-ureteral obstruction and may be confused with either ureteropelvic junction or ureterovesical junction obstruction. This highlights the importance of retrograde pyelography prior to treatment of ureteral strictures [19, 20]. Segmental excision is curative and the etiology may be chronic *in utero* ischemia at the level of the mid ureter because of the vascular watershed between the aorta and iliac vessels.

## Presentation

An injury to the mid ureter may present clinically in a variety of ways. In the case of acute iatrogenic ureteral transection the patient may be acutely septic while in the case of a ligated but intact ureter, the patient may present with ipsilateral flank pain, recurrent pyelonephritis, and/or an unexplained rise in serum creatinine. Urine extravasating into the peritoneal cavity may cause peritoneal irritation and findings of an acute abdomen. In contrast an incomplete stricture may be asymptomatic, and identified incidentally only upon abdominal imaging. In an international review of almost 2000 ureteroscopy patients, the majority of strictures were symptomatic but three (0.15%) were asymptomatic. The presence of pain after stent removal had a 64.3% positive predictive value and a 99.8% negative predictive value for stricture.

## Diagnosis

There are several methods available to assist the urologist in the evaluation of strictures (Table 52.2). One of the simplest and least invasive initial studies is ultrasonography. B-mode ultrasound will detect dilation of the renal pelvis and/or calyces although ureteral dilation is sometimes obscured by overlying structures or bowel gas. Using Doppler sonography the resistive index (RI), defined as [peak systolic velocity – end diastolic velocity]/peak systolic velocity, is generally less than 0.7 in an unobstructed system [21]. Although a RI above 0.75 is correlated with obstruction, compared to normal kidneys (RI 0.6) and healthy controls (0.58; $P < 0.05$) [22], a threshold RI of 0.7 has only a 44% sensitivity and 82% specificity for diagnosis of ureteral obstruction [23].

Historically intravenous pyelography was employed in the diagnosis of suspected ureteral injuries (Figure 52.3). This modality is still available in many centers, although

**Table 52.2** Diagnostic modalities used to evaluate mid-ureteral strictures. Costs are listed in US dollars.

| Modality | Advantages | Disadvantages | Sensitivity | Specificity | Cost |
|---|---|---|---|---|---|
| Computed tomographic (CT) urography | Superior spatial resolution<br>Non-invasive | Significant radiation source<br>Contrast reactions | High | High | $1565 |
| Magnetic resonance (MR) urography | No radiation<br>Ideal for diagnosing extrinsic causes | Poor ability to diagnose stones<br>Nephrogenic systemic fibrosis<br>Expensive, time-consuming | High | High | $2048 |
| Diuretic renography | Provides split function<br>Provides functional information regarding obstruction | Subjective interpretation<br>Inconsistent results | High | Medium to high | $1138 |
| Ultrasonography | No ionizing radiation<br>No need for intravenous contrast medium | Operator dependent<br>Image quality dependent on body habitus and overlying structures | Med to High | High | $410 |
| Whitaker test | Provides objective information regarding obstruction<br>Can identify bladder pressure abnormalities | Invasive<br>Unfamiliar to many radiologists | Medium | Low to medium | Variable |

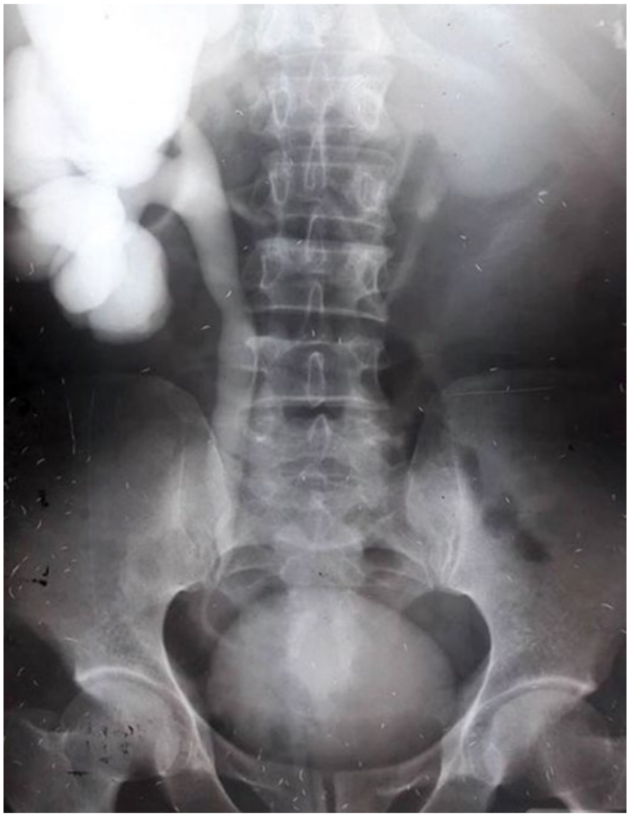

**Figure 52.3** Intravenous pyelogram showing abrupt narrowing of contrast at the level of the mid ureter. Courtesy Dr Mohamed Keheila and Dr Waleed Elsayed.

the results are not as sensitive or as specific as computed tomographic (CT) urography [24].

CT imaging represents the most common modality employed to evaluate ureteral obstruction. Unenhanced CT scanning is the gold standard for the initial evaluation of suspected nephrolithiasis [17], but does not reliably determine non-stone-related causes of ureteral obstruction. In such instances, CT urography provides superior spatial and contrast resolution by opacification of the collecting system [25] enabling it to detect stones, urothelial masses, and congenital anomalies. Disadvantages of CT urography include the need for intravenous contrast, which can lead to nephropathy (defined as a rise in serum creatinine of 0.5 mg/dl or 25%) and contrast allergy [26]. Risk factors for contrast nephropathy include renal impairment, diabetes, age, congestive heart failure, dehydration, multiple myeloma, and high-osmolality agents [26], and these risk may be mitigated by hydration, discontinuation of nephrotoxic agents, reduced contrast dose, *N*-acetylcysteine, and use of iso-osmolar or low-osmolality contrast medium. When precise anatomical details are required and intravenous contrast is contraindicated, CT pyelography can be performed by injecting contrast through a nephrostomy, or by direct needle puncture of the collecting system. In a study by Ghersin et al., CT pyelography successfully detected the cause of ureteral obstruction in 20/20 patients who failed first-line imaging [25].

Diuretic renography provides objective evidence regarding ureteral obstruction. In this procedure the patient is hydrated and challenged with furosemide (usually 40 mg intravenously), administered when the tracer peaks in the affected system. Obstruction is defined as the time required to clear half of the radionuclide (T½) greater than 20 minutes, while a T½ of <10 minutes is considered unobstructed. T½ times between 10 and 20 minutes are indeterminate [27]. However, if furosemide is given too early during the filling phase it may lead to a flat drainage curve and a false impression of poor drainage [28].

In addition, severe hydronephrosis and chronic renal insufficiency may lead to false positive results [28, 29]. It is also important to remember to place a bladder catheter in patients with vesicoureteral reflux, high bladder storage pressures, or those with indwelling ureteral catheters [28].

Magnetic resonance (MR) urography is also useful for identifying ureteral obstruction. Semins et al. compared MR urography in a 3-T scanner with HASTE sequences to noncontrast CT in colic patients [30]. MR had an 84% sensitivity for obstruction but identified a stone in only 50% of patients with stones on CT [30]. Specific situations where MR urography may be useful are in radiation-sensitive populations such as children, pregnant women (done without gadolinium), and patients with extensive prior radiation exposure. In an iatrogenically created ureter obstruction animal model the sensitivity and specificity of diuretic renal scintigraphy, MR urography, and ultrasound RI were 93.3 and 88.8%, 86.6 and 77.5%, and 86.6 and 77.5% respectively. However, no one modality was able to correctly predict all cases of obstruction-related apoptosis [31].

Antegrade and retrograde pyelography are familiar to most urologists, simple to perform, and the results are usually easy to interpret (see Figure 52.4). However, these techniques require radiation exposure and are invasive, usually requiring an anesthetic. These modalities provide the stricture severity, length, and potential etiology.

The invasive Whitaker test assesses whether hydronephrosis is obstructive by antegrade perfusion of the kidney with saline or dilute contrast at 10 ml/min. The pressure is measured simultaneously within the renal pelvis and bladder. Obstruction is diagnosed when the renal pelvis minus the bladder pressure is $>22\,\text{cmH}_2\text{O}$ [32]. This test may underdiagnose obstruction in the face of massive hydronephrosis [33]. Usually, the Whitaker test is performed when there is disagreement between other imaging modalities leading to ambiguity in the diagnosis [32].

Intraluminal ultrasound using a 12.5–30.0 MHz probe deployed in the ureter may provide information regarding the nature of the ureteral wall and periureteral tissues, and information regarding any associated foreign body (stone) within the ureter or periureteral tissues [34]. Also, a mixture of indocyanine green injected in a retrograde manner into the collecting system may help identify the location of a stricture and help to identify the diseased ureter (remains dark) from the healthy fluorescing ureter during robotic ureteroureterostomy [35].

## Stricture prevention

The best way to prevent mid-ureteral stricture disease is to use immaculate surgical technique and to preserve a robust ureteral blood supply. During ureteroscopy, the mid ureter is the most susceptible region for major ureteral complications including the highest rates of ureteral avulsion (0.3%) and perforation (1.6%) [36]. Small-caliber ureters occurring in small patients, children, young males, duplicated systems, and following radiation or inflammatory processes are at the highest risk for injury [37, 38]. In these situations prestenting may allow passive ureteral dilation for 1–2 weeks and reduce this risk [39]. Prestenting may also be beneficial prior to complicated abdominal or pelvic surgery where extrinsic pathology and inflammation may make ureteral identification difficult [40, 41].

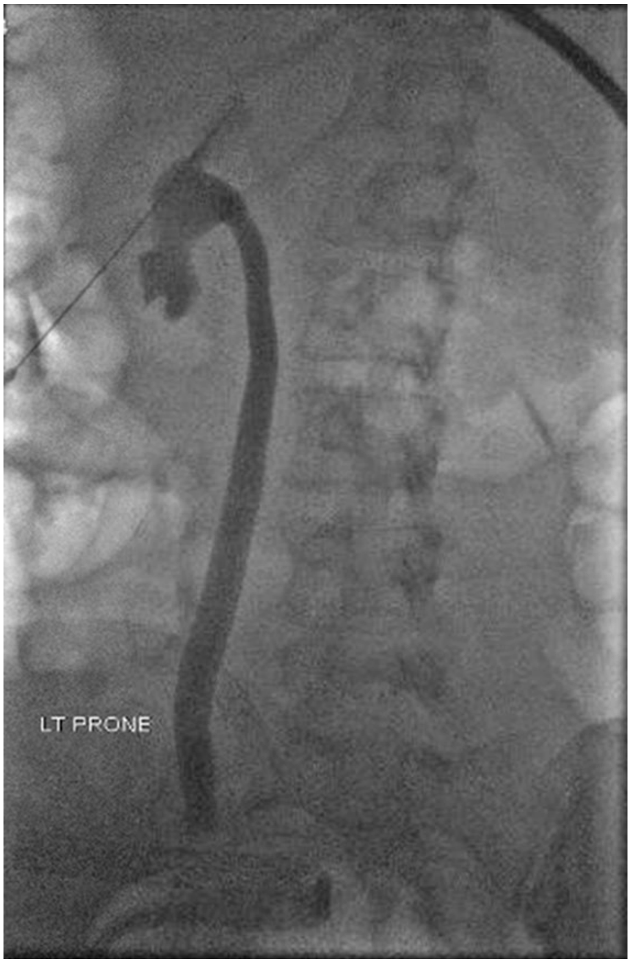

**Figure 52.4** Antegrade nephrostogram showing complete ureteral obliteration at the mid ureter.

Fluoroscopic stone identification over the dense bony pelvis is more difficult. Also, in men the deep pelvis and the angulation as the ureter crosses the iliac artery make semirigid ureteroscopy more challenging and potentially dangerous. Attempting to force the semirigid ureteroscope past the iliac vessels may result in flap creation or ureteral perforation. In addition, pulsations from the iliac artery can cause inadvertent injuries during lithotripsy. Use of flexible ureteroscopy will decrease the risk of perforation in this region. Cases of “scabbard”-type ureteral avulsion have been reported when semirigid ureteroscopes have been used in tight ureters [42]. This type of avulsion occurs when the ureter is completely transected between two points, and is removed intact with the ureteroscope. Blind basket extraction in the ureter should be avoided, as it has been linked with cases of ureteral entrapment and avulsion [43].

When performing laser lithotripsy, one should avoid firing directly adjacent to the mucosa, utilize the lowest possible power settings that will achieve efficient fragmentation, and use caution when advancing the ureteroscope and fiber. If a significant perforation occurs, it is prudent to terminate the procedure immediately and leave a double-J stent to prevent submucosal stone fragment migration or enlargement of the injury. It is uncertain whether routine stenting reduces the ureteral stricture rate following uncomplicated ureteroscopy [14, 44, 45]. However, stent placement following ureteroscopy complicated by residual fragments, a urothelial flap, use of a ureteral access sheath, or a long-term stone may minimize the risk of subsequent stricture [46].

Any patients undergoing intact stone extraction who have residual pain or dilation on renal ultrasound should be evaluated with a CT urogram to evaluate for stricture [17].

## Management of mid-ureteral stricture disease

There are many options for the treatment of a mid-ureteral stricture including observation, endoscopic approaches (stenting, balloon dilation, and endoscopic incisional procedures), and more complicated open and minimally invasive reconstructive approaches (uretero-ureterostomy, ureteroneocystostomy with psoas hitch, Boari flap, transureteroureterostomy, and ileal ureter).

The least invasive option for the management of a mid-ureteral stricture is serial observation. Ureteral strictures that are not accompanied by pain and are not resulting in urinary tract infections, stone formation from urinary stasis, or renal deterioration on nuclear renography may be closely monitored to ensure progression of the disease does not occur [47]. However, poor follow-up may jeopardize renal function and the decision for observation must consider many subtle factors. For example, if diuretic renography shows obstruction in an asymptomatic patient but the function is preserved, the surgeon may choose observation. In contrast the surgeon may intervene in a symptomatic patient with a borderline T½ on diuretic renography, and decreasing function. All treatments should be embarked upon with restraint, after extensive counseling including all the options and following a carefully documented and detailed informed consent in order to avoid medicolegal complications.

Once the surgeon decides to intervene, the next decision is the optimal timing for the operation. In the 13–66% of patients presenting with intraoperative ureteral injury the treatment should be embarked upon immediately. In patients who are medically unstable or with complications following their ureteral injury, a period of 6–12 weeks with a nephrostomy tube or stent to allow inflammation to resolve is reasonable [48].

## Retrograde and antegrade stenting

Immediate temporary renal decompression can be accomplished in either an antegrade or retrograde fashion and the approach of choice may vary depending upon the clinical presentation. In patients presenting with acute hydronephrosis, refractory pain, or infection the initial evaluation and management is cystoscopy, retrograde pyelography, and ureteral stent placement. Stent placement bypasses the obstruction while preserving renal function and is also sometimes therapeutic. Antegrade or retrograde stenting has been shown to durably resolve ureteral strictures occurring in the transplant setting in up to 75% of cases [49]. Similarly, stenting of short-segment strictures due to irritation, edema, or inflammation (i.e. tuberculosis) while the underlying cause is corrected may resolve strictures in 49% of patients [50]. The limitations of retrograde stenting include discomfort, migration, infection, decreased effectiveness with extrinsic compression, and encrustation [51, 52]. Although changing stents every 3 months avoids encrustation, it is a less desirable long-term management strategy. Newer metallic and coiled wire stent designs have attempted to improve drainage with extrinsic compression with a 65% success rate at a 5 month mean follow-up [53, 54].

Retrograde stenting (double-J) has the advantage of being completely intracorporeal, while a nephrostomy tube has both an intracorporeal and an external component, making the nephrostomy more prone to inadvertent dislodgement. Another advantage of a retrograde ureteral stent is that the strictured lumen is stented open to prevent a dry ureter. In contrast the nephrostomy has the advantage of bypassing virtually any downstream obstruction and can allow for antegrade studies or therapies. The nephrostomy tube, however, by diverting the urine, may convert a partial to a complete ureteral obstruction due to a dry ureter.

Song et al. reviewed retrograde stenting in a series of patients with gynecologic malignancy and found an initial 81% success rate. However, 37% eventually received nephrostomy drainage at a mean 9.1 month follow-up [55]. Factors associated with stent failure on multivariate analysis were preoperative serum cystatin C levels >2.5 mg/l and stricture length longer than 3 cm [55]. Unlike previous studies [56], bladder invasion did not predict stent failure. Due to the high failure risk of an indwelling double-J stent, many authors advocate for nephrostomy drainage in cases with extrinsic compression. Park et al. [57] reviewed a small patient series with metastatic nongenitourinary cancer and determined that ureteral stenting failed in each case, but nephrostomy successfully relieved each obstruction. In a larger study by Ku et al. [58], patients with advanced malignancy and ureteral obstruction were approximately ten times more likely to fail indwelling ureteral compared with nephrostomy drainage.

One longer-term stent option to relieve ureteral obstruction is the thermoexpandable metallic stents that have been employed for the treatment of benign and malignant obstruction. In one of the largest series to date, Agrawal et al. described their long-term experience [59]. At a mean follow-up of 16 months, 14 of 55 patients (25%) required stent replacement, mostly due to stent migration, but only three patients had stricture progression that required a stent change.

When decompression is needed for a benign etiology (most commonly a stone), a randomized German study found superior outcomes across all variables in the nephrostomy group compared with the double-J stent group [60]. In another study, Pearle et al. randomized patients with septic obstructing stones to stent versus nephrostomy. In contrast to the prior study, there was no difference in efficacy or duration of analgesia, but retrograde stent placement was twice as costly [51]. Ultimately, the decision for nephrostomy or double-J stent depends upon a number of factors including the etiology, the likelihood of success with each procedure, the need for future therapies, the availability of the facilities and staff, and – perhaps most importantly – the patient's wishes.

## Balloon dilation

Initially developed for coronary arteries, balloon catheters have been shown to cause linear tears in the ureter, in a manner similar to an endoureterotomy [61, 62]. Both retrograde and antegrade balloon dilation are possible, but a retrograde approach is favored when the urethra, bladder, and ureter are in continuity. In this procedure a 5 or 6 Fr open-ended catheter is employed to perform a high-quality retrograde pyelography. Next, a flexible-tipped lubricious wire is passed via an open-ended catheter past the stricture and into the renal pelvis. The endhole catheter is then pushed above the stricture and the lubricious wire is converted to a standard or stiff guidewire. Alternatively, a single hybrid wire could be utilized. Next, the appropriate diameter (12–24 Fr) and length (4–10 cm) balloon catheter is inserted using fluoroscopic localization ensuring that the two radiopaque markers are straddling the stricture (Figures 52.5 and 52.6). Using half-strength contrast the balloon is inflated and held for 1–2 minutes. Optionally ureteroscopy can be performed to ensure complete dilation. A 6 Fr ureteral stent is routinely left in place for 4–6 weeks following the dilation (See Video 52.1). Reported short-term success rates of ureteral balloon dilation for short-length strictures are usually 48–55% [61, 63].

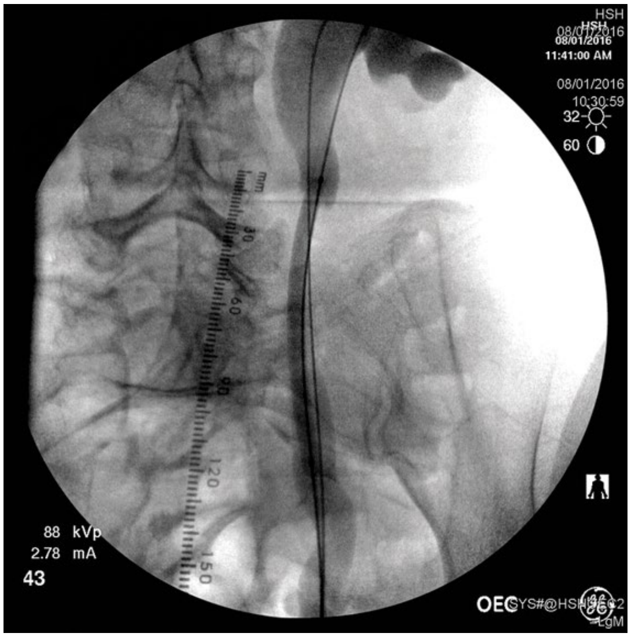

**Figure 52.5** An 18 Fr, 10 cm balloon is shown here dilating a proximal to mid-ureteral stricture.

## Endoureterotomy

Endoureterotomy is a relatively simple procedure where a full-thickness incision is made in the ureter to open a stricture [8]. It may be accomplished using different methods including a variety of electrified or nonelectrified cutting instruments and is frequently employed with balloon dilation. Since the earliest descriptions, the principles of endoureterotomy have changed little, except for the method of making the incision. The heterogeneity of studies (size and type of laser fiber, combination with balloon dilation, renal function, presence of crossing vessels, degree of hydronephrosis, and size and duration of stent) makes it difficult to compare studies

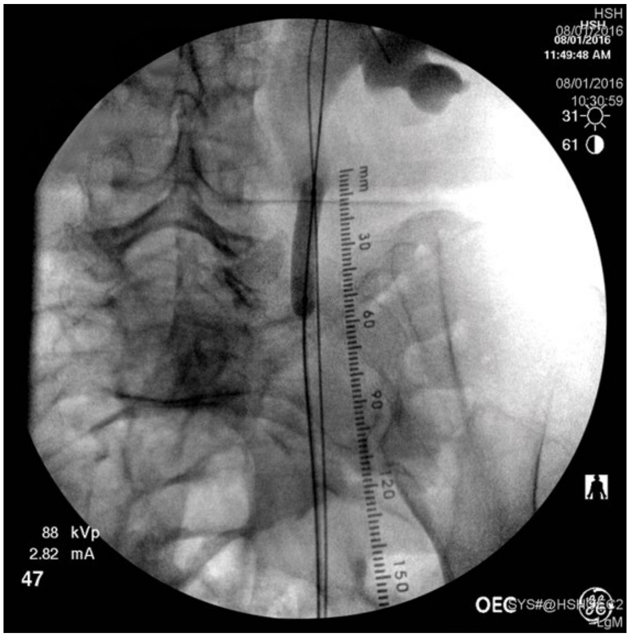

**Figure 52.6** A 24 Fr, 4 cm balloon is shown here dilating a proximal to mid-ureteral stricture.

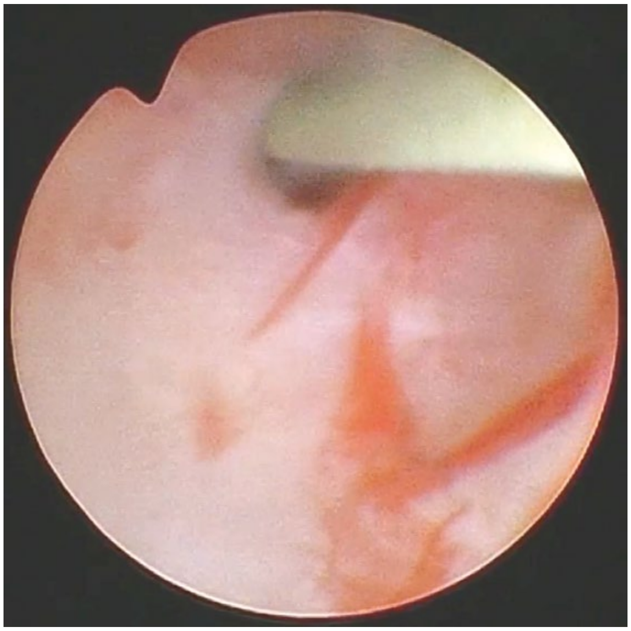

**Figure 52.7** Endoscopic view of a very narrow mid-ureteral stricture, with a safety wire passing through the stricture.

or identify a gold-standard technique for the performance of endoureterotomy.

The first step of endoureterotomy is to perform a retrograde pyelogram to delineate the stricture. Next a safety wire is placed across the stricture and a ureteroscope is used to evaluate the stricture site to exclude neoplasm or submucosal stone (Figure 52.7). If electrical energy is to be used an insulated wire should be employed. Next, a balloon catheter is used to dilate the stricture. Following this, a full-thickness incision of the ureteral stricture is created, directed away from the blood supply and extending 5–10 mm above and below the stricture. Currently, the most widely used and best-described instrument for incision is the holmium laser due to its shallow tissue penetration (<0.5 mm), excellent tissue vaporization, and coagulation properties [64]. Symptomatic patients have improved outcomes presumably because the stricture was not as long-standing, as well as those with a history of stone passage managed conservatively or with shock-wave lithotripsy [7]. Poor prognostic factors include poor renal function, presence of associated or crossing vessels, severe hydronephrosis, ischemic strictures, strictures >2 cm, and stricture due to endometriosis [65, 66]. Despite these limitations, the European Association of Urology state in the Laser guidelines that “Retrograde endoureterotomy is considered a first-line treatment option for ureteral strictures,” with a Grade C recommendation [67]. Most endoureterotomy failures occur 3–9 months after the procedure [68, 69], although some failures occur as late as 18 months after endoureterotomy [70]. This underscores the need for extended surveillance in all patients undergoing endoscopic treatment of ureteral strictures.

A special subtype of endoureterotomy is the hot-wire balloon (Acucise™) endopyelotomy [71]. This device was not frequently used for mid-ureteral strictures due to the risk of iliac artery injury if the balloon was not positioned correctly [72]. Although initially very popular, this technique has fallen out of favor due to difficulty controlling the cutting action, the risk of hemorrhage, and the much higher success rates seen with techniques employing direct vision and laparoscopic and robotic procedures [73].

## Rendezvous procedures

One dreaded potential iatrogenic complication is complete ureteral transection. This type of injury, when not detected intraoperatively, can lead to sepsis and the potential for renal loss. Diagnostic imaging will demonstrate no ureteral continuity (Figure 52.8 and Video 52.2). These injuries, when occurring in the mid ureter, are best treated by a reconstructive procedure like a Boari flap or psoas hitch since a blind puncture or cut outside the mid ureter may result in iliac injury. If there are contraindications to such techniques and the length of the stricture is less than 3 cm, one endoscopic approach that may be attempted is the “rendezvous” technique or endoscopic realignment. This technique involves feeding a wire antegrade into the retroperitoneum, then

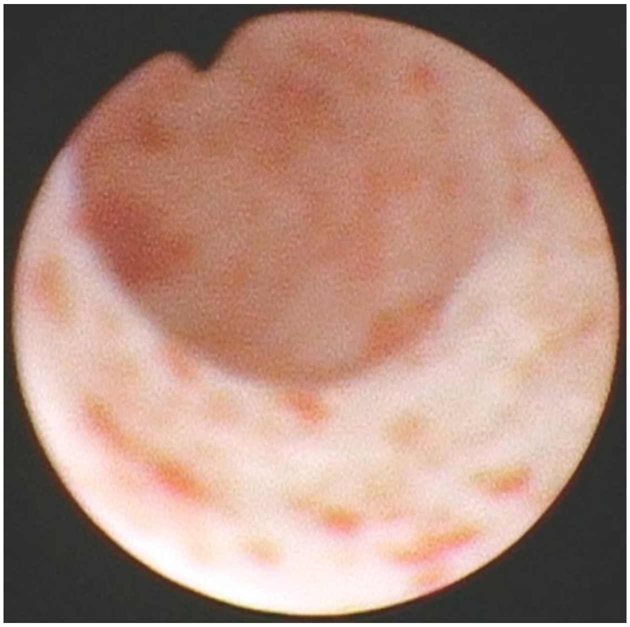

**Figure 52.8** Endoscopic view of a completely obliterated ureter.

grasping this wire with a semirigid ureteroscope from below to establish through-and-through access [74]. Alternatively use of a flexible ureteroscope from above and a semirigid ureteroscope from below provides the surgeon with greater control [75]. Using the latter technique Liu et al. achieved a 75% success rate at a mean of 21.5 months of follow-up. Tsai et al. achieved 100% success in 10 patients treated using this technique at a mean of 16 months of follow-up [76].

## Laparoscopic and robotic approaches

While more invasive than endoscopy, laparoscopic and robotic approaches have the advantage of removing the diseased ischemic tissue and creating a widely spatulated, tension-free mucosa-to-mucosa seal of the urothelium. In the mid ureter a laparoscopic or robotic ureteroureterostomy may be performed. The patient is positioned in a dorsal lithotomy position with moderate to steep Trendelenburg. Next, the ureter is mobilized above and below the stricture, and the pathologic segment is excised and sent for pathologic analysis. The ureter is then spatulated at both ends for a distance of at least 5–15 mm. The posterior anastomosis is performed using a 4-0 Vicryl suture, in either a running or interrupted fashion. Once the posterior portion is complete, a double pigtail stent is inserted across the repair, and the anastomosis is then completed. A drain is left postoperatively and the stent is left indwelling for 6 weeks [77].

Buffi et al. reported their experience with five lumbar and iliac ureteral strictures ranging from 5 to 30 mm long that were treated with a robot-assisted laparoscopic approach [78]. In all cases intraoperative flexible ureteroscopy was used to identify the stricture margins and there were no recurrences. Complete mobilization of the kidney can be performed if necessary to obtain additional length for the anastomosis. Overall, outcomes for laparoscopic and robotic ureteroureterostomy are good, although sample sizes in the majority of studies are small.

Mid-ureteral strictures longer than 3 cm may be treated with a high psoas hitch or Boari flap or more traditional approaches including an ileal ureter, autotransplantation, and transureteroureterostomy. The steps of a robotic ureteral reimplant for a stricture at the junction of the mid and distal ureter are demonstrated in Video 52.3.

When faced with longer-length strictures, excisional techniques are insufficient. Traditionally, long ureteral strictures have been treated by Boari flap, ileal ureter substitution, or autotransplantation. Each of these techniques have been reported using a robotic approach and for more details of these surgeries we refer the reader to Chapter 103. One group has looked at reducing the invasiveness of repairing long-length ureteral strictures by applying the buccal mucosal graft used in urethral reconstruction [79]. The authors noted a 100% success rate in three patients at a median 15-month follow-up. Other groups have experimented with different types of grafts, including lingual mucosa grafts and tubularized peritoneal flaps with varying success [80, 81]. Duty et al. reported on the use of appendix as an onlay flap for laparoscopic reconstruction of proximal and mid-ureteral strictures [82]. This approach has some drawbacks compared to the buccal mucosal graft as it enters the digestive tract, and two out of six patients required reoperation, including one nephroureterectomy. Laparoscopic ileal ureter has been described but should not be required for most mid-ureteral strictures [83].

In this chapter we have discussed the presentation, diagnosis, prevention, endoscopic incisional and laparoscopic and robotic excisional techniques for management of mid-ureteral strictures. Endoscopic management offers a minimally invasive solution to about half of patients presenting with mid-ureteral strictures. Following appropriate patient counseling it is reasonable to offer one or two trials of endoscopic management in short-length strictures (<2 cm), as long as split function is above 25% and other factors are favorable. However, patients with long-length strictures, ischemic strictures, or stricture due to extrinsic compression should probably proceed directly to excisional laparoscopic or robotic excisional techniques due to their higher success rates.

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# 53

# Endoscopic Management of Distal Ureteral Strictures

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## Definition

A stricture is a short or long narrowing of the ureteral lumen which leads to functional changes causing decreased or complete interruption of urinary flow distally into the bladder or urinary reservoir. Obstruction can be mechanical, with altered anatomy, or functional, with impaired peristalsis without a true narrowing. A narrow lumen at the vesical or pelvic junction is sometimes called stenosis. Strictures of the ureter can be acute, such as postsurgical cases and ischemia, or chronic, as in postradiation therapy. Some varieties of stricture are congenital, with altered histology. The treatment options are influenced by a variety of factors but are often dependent on cause and the patient's comorbidities and preferences.

## Regional, histological, vascular, and endoscopic anatomy

Knowledge and understanding of ureteral anatomy is an absolute necessity for management of all ureteral diseases and prevention of iatrogenic injuries.

### Regional anatomy

The adult ureter ranges from 22 to 30 cm in length and is 6.5–7 cm in neonates [1]. On radiographs, the ureter may be divided into thirds: the upper third is from the ureteropelvic junction (UPJ) coinciding with L2 vertebrae to the brim of the sacrum; the middle third is from the upper to the lower border of the sacrum; and the segment from the lower border of the sacrum to the ureterovesical junction(UVJ) is called lower or distal ureter. The upper ureter is called the lumbar or abdominal ureter and the distal segment is referred to as the pelvic ureter. The intramural ureter is about 1.2–2.5 cm in adults and 0.5–0.8 cm in neonates. The UPJ and UVJ or ureteral orifice have their own characteristics and configurations from normal to abnormal shapes and locations and their own specific procedures. In a contracted bladder the ureteral orifices are 2.5 cm apart, which can increase to 5 cm when distended.

The renal pelvis typically lies posterior to the duodenum on the right and the jejunum on the left. The ureter begins posterior to the renal artery and vein then descends in the retroperitoneum, moving anteriorly over the psoas muscle and passing under the gonadal vein at the level of the inferior pole of the kidney. It travels on the pelvic wall and at the ischial spine enters the pelvis, turns anteromedially, medially crossing the iliac vessels. The two ureters are 5 cm apart with physiologic narrowing at this point. The ureters then diverge laterally at the same course in both sexes with gender-specific differences. In men the ureter travels down medially and lies in the sacrogenital fold; it is dorsal to the vas deferens that crosses it medially. In women, the ureter is initially posterior to the ovary, passes posterior to the round (ureterosacral) ligament with the uterine artery travelling medially. It is about 2 cm lateral to the uterine cervix and courses anterior to the vagina's lateral border. In both men and women the ureters travel past the dorsal aspect of the medial umbilical ligament and superior vesical artery. The transition of ureter into the bladder causes the lower physiologic narrowing. The three narrow points of the ureter are the UPJ, the crossing point over the iliac vessels, and the UVJ, which is the narrowest. The typical S-shaped curvatures of the ureter can be appreciated on anteroposterior and cross-table views of the ureter [2]. See Figure 53.1.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

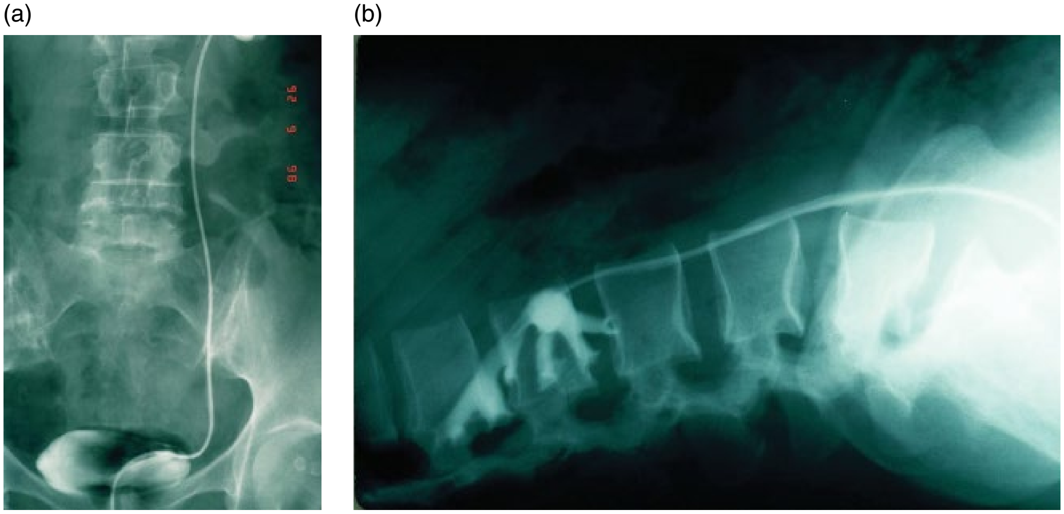

**Figure 53.1** (a) Anteroposterior view of the abdomen with a catheter in the left ureter showing the S-shaped (right–left, up–down) curvatures of the ureter. In older women the ureter dips down before turning up cephalad due to bladder or pelvic prolapse whereas in older men the so called J-hooking is due to elevation of the intramural ureter secondary to prostatic growth. (b) A cross-table view of the ureter with the patient in supine position shows the anteroposterior curvatures of the ureter.

## Vascular anatomy

The ureters are have multiple arterial sources as they travel caudally. The proximal ureter is essentially supplied by the lower pole renal arterial branches anteriorly. This section, referred to as the golden triangle, has significant value during donor nephrectomies, to preserve the only arterial supply to the ureter. The gonadal artery and the aorta also contribute to the upper ureter. The gonadal artery and common iliac artery provide the blood supply to the middle third of the ureter. The spermatic artery supplies up to 10% of ureteral blood supply. The distal ureter is supplied by branches of the common iliac and internal iliac arteries, superior vesical artery, and the uterine and vaginal arteries in women and inferior vesical artery in men.

Ureteral arterial vessels travel longitudinally within its adventitia and create a branched network, allowing for mobilization without risking its blood supply. The venous drainage is paired with the arteries and drains to the renal, gonadal, and internal iliac veins and vesical venous plexus. Knowledge of this vascular supply is crucial in ureteral surgery, because a devascularized ureter is subject to complications of stricture and leakage.

Lymphatic drainage of the upper ureter is into the lumbar and para-aortic nodes on the left, and the paracaval and interaortocaval nodes on the right. Lymphatics of the middle ureter drain to the common and internal iliac nodes, while those of the pelvic ureter drain to the internal iliac and vesical nodes. See Figure 53.2. Ureters have a richly innervated plexus arising from T12–L2 segments of the spinal cord with corresponding dermatome referral [3]. The kidney's sympathetic innervation is from T8 to L1 and travels along arterial branches, causing vasoconstriction, and the parasympathetic fibers arise from the vagus nerve, causing vasodilation. The loss of renal and especially ureteral innervation has significant implication in ureteral strictures. This is seen in transplanted kidneys, patients who have undergone extensive manipulation of the ureter, and procedures such as Boari flap or reimplantation. The lack of ureteral innervation can mask the clinical presentation.

## Histologic anatomy

In an adult the thickness of a nondilated normal ureter and peri-ureteral adventitia is about 3 mm. In a review of 212 unobstructed ureters on computed tomography (CT) scan 96% of the ureters had a diameter of 3 mm or less [4]. The ureter is lined with transitional cell epithelium, which consists of a short basal layer, one or more layers of columnar cells, and, most apically, umbrella cells. The umbrella cells are specialized to survive bathing in hypertonic urine and to stretch with distention of the lumen. Folds of mucosa help to protect against reflux of urine when the bladder is full [5].

Underneath the epithelial layer is a thick, fibroelastic matrix, known as the lamina propria. It is a packed layer of cells that allows for stretching of the ureteral wall when obstructed. The ureter has no mucosal or submucosal glands, and no submucosa. The thickest layer of the ureter is the muscularis, which is a layer of smooth muscle outside the lamina propria: the upper two-thirds have two layers of muscle: the inner arranged longitudinally and outer arranged circularly. The muscular layers contribute to peristalsis. The lower third has a thicker

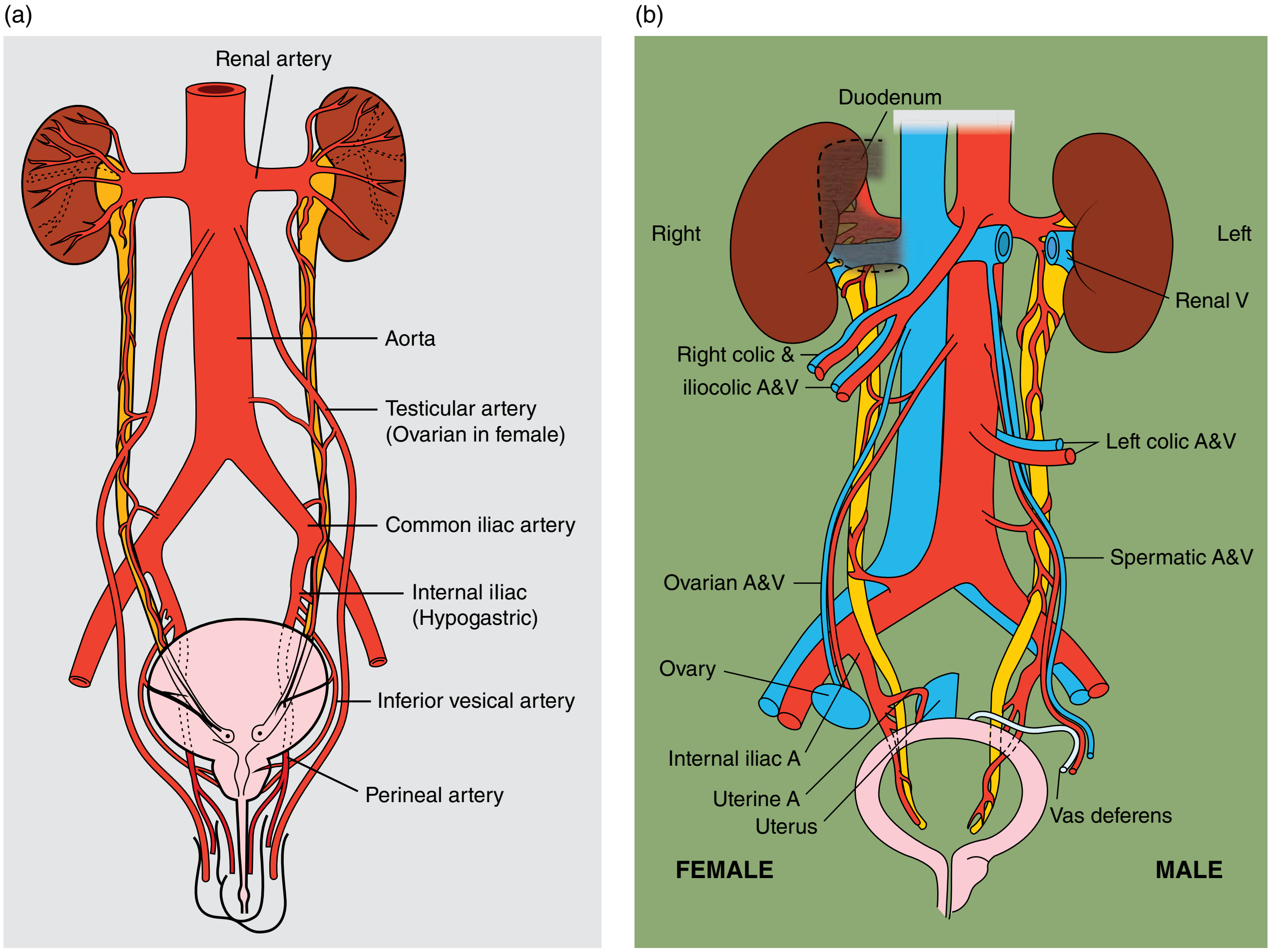
(a)
Renal artery
Aorta
Testicular artery
(Ovarian in female)
Common iliac artery
Internal iliac
(Hypogastric)
Inferior vesical artery
Perineal artery
(b)
Duodenum
Right
Left
Renal V
Right colic &
iliocolic A&V
Left colic A&V
Spermatic A&V
Ovarian A&V
Ovary
Internal iliac A
Uterine A
Uterus
Vas deferens
FEMALE
MALE

**Figure 53.2** (a) Vascular supply of the ureter. Note the longitudinal descending pattern of the upper ureteral blood supply, and the medial and lateral vascular supply of the mid and distal ureter [7]. (b) Paraureteral structures. This diagram illustrates the ureteral anatomy, vascular supply, and adjacent organs to help create a virtual anatomy in the operator's mind. A & V, artery and vein.

urothelium and three layers of muscle: the inner longitudinal, middle circular, and outer longitudinal. See Figure 53.3. The distal end of the ureteral musculature flattens and rolls under to allow the lumen to migrate to the vesical mucosal surface. In the intramural section the muscle layering is lost and all fascicles become oriented longitudinally and fan out to form the trigone. Within the bladder wall the ureter is loose (Waldeyer's separation) [6]. This anatomic description explains why, during endoscopic meatatomy in the 12 o'clock position, muscular layers are rarely noted [7]. The outer adventitial layer has fibroelastic connective tissue. This layer harbors the blood vessels, lymphatics, and nerves. This histological structure along with the richer vascular supply explain why the distal ureter is more resilient and forgiving as compared to the upper ureter during endoscopy and after iatrogenic injuries. The ureteral lumen is not actually a circle but folded epithelium that is stellate in form, mostly with five or six points. The points of the stars are the last to disappear with ureteral dilation and with further dilation the ureteral lumen takes a square shape and eventually a circle, allowing it to distend up to 17 times when obstructed [8].

The proximal part of the ureter is prone to higher shear stress during peristalsis compared to the middle and distal parts [9]. Disruption of the ureteral muscle layers during mechanical dilation of the ureter in conjunction with ureteroscopy is one of the main causes of subsequent strictures [10]. Pelvic surgery, skeletonization, and radiation can result in significant vascular compromise of the distal ureter, resulting in secondary strictures. The pattern of ureteral stricture and degree of dilation partly depend on this histological structure. The upper ureter, with fewer muscle layers and loose surroundings, allows for significant dilation which functions as a reservoir in cases of severe obstruction and allows for tortuosity to accommodate urine volume and keep the renal pelvic pressure low. The loose structure, on the other hand, makes this part

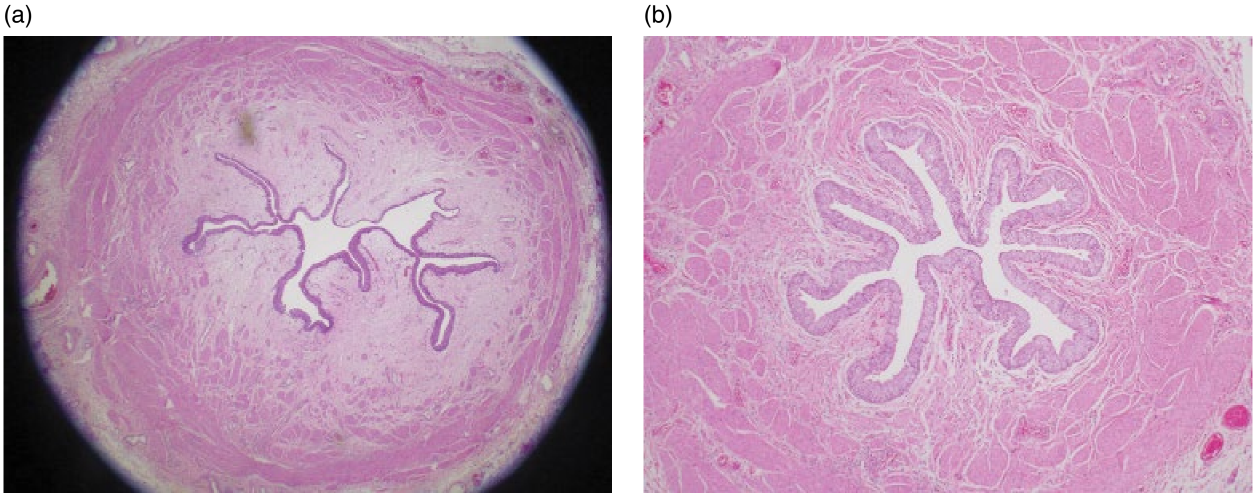

**Figure 53.3** Histology of the ureter. (a) Upper ureter: note the stellate appearance of the lumen. There are only two muscular layers in this segment; from the inside out: urothelial mucosal folds, lamina propria, longitudinal muscle, outer circular muscle, and adventia. (b) Cross section of the lower ureter showing increased thickness of the urothelium and additional muscular layer.

weaker and more prone to injuries. The majority of ureteral avulsions occur in this segment due to the lesser musculature and no paraureteral support. In the lower ureter the degree of dilation is less due to thicker muscle layers and also rather tighter space. In this segment, strictures from iatrogenic injuries and impacted stones are usually short in length with normal ureter below and above, except for cases of hydronephrosis. In cases of pelvic surgery, radiation, malignancies, and fibrosis the ureter is restricted externally and the obstructed segment is long with the appearance of an irregular piece of string. The ureter additionally loses its mobility and appears fixed, even with placement of a catheter; this is in contrast to a normal ureter that takes the shape of an open-ended catheter or balloon and looks straight [10–12].

## Virtual anatomy

Virtual endoscopic anatomy can be defined as a three-dimensional reconstruction of the ureter in the mind of the operator. This reconstruction includes what is visualized endoscopically to the regional/vascular/histological information described earlier. The key additional information relates to paraureteral structures. The surgeon can make the best judgment in selecting the procedure and the extent of the intervention, regardless of the nature of the procedure, to achieve the best and safest outcome. There are three layers of information: (i) visible intraluminal findings, (ii) visible and invisible ureteral wall histovascular anatomy, and (iii) invisible regional and paraureteral structures. The combination of these factors creates a three-dimensional virtual anatomy in the operator's mind. Figure 53.4 elaborates some of the details and recommendations for safe incisional sites.

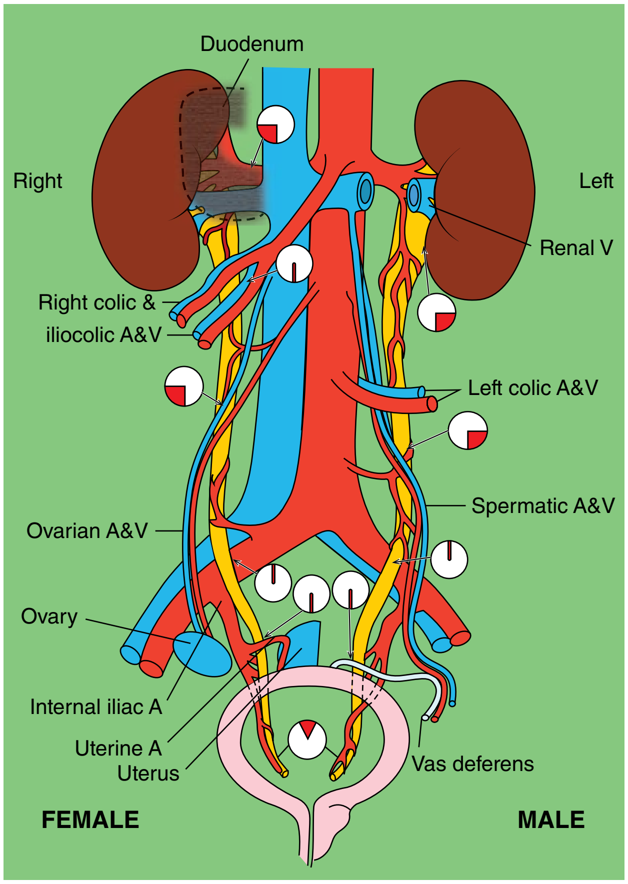

**Figure 53.4** Ureteral and paraureteral structures with the recommended sites of incision.

### Altered anatomy

Normal anatomy of the distal ureter can be altered by past surgical procedures, which renders the management of strictures more challenging for the surgeon. Recommendations to overcome them are described here.

## Ureteral reimplantation

Ureteral reimplantation is performed using a variety of techniques and in the event of subsequent obstruction it can potentially be difficult to access the relocated neo-orifice.

- **Cohen cross trigonal reimplantation**: this is carried out by advancing the intramural ureter by creating a new submucosal tunnel cross-trigonally. These ureters can be quite difficult. If rigid and flexible endoscopy in combination with angled catheters fails to negotiate the neo-orifice, antegrade insertion of a guidewire followed by either antegrade or retrograde dilation, preferably with a low-profile balloon, is the next step [13, 14].
- **Gil-Vernet trigonoplasty**: in this technique the area in front of the ureteral meatus is plicated, thus increasing the additional length to overcome the reflux. Access to this ureter may be slightly difficult; an angle-tipped catheter or a flexible cystoscope can overcome this problem [15].
- **Politano-Leadbetter**: this was the originally described technique of reimplantation for refluxing ureters. The ureter is detached and reimplanted posterolaterally into the bladder in an up–down fashion. Obstructions are usually due to poor location of the implant site causing kinking rather than luminal blockage. Access for true strictures is usually easy in an underdistended bladder [16].
- **Paquin technique**: this reimplantation technique is rarely used by pediatric urologists. This requires lengthening the intramural and inverted meatoplasty. Direct visualization of the lumen with a small scope or ureteroscope helps initial placement of the wire [17].
- **Lich-Gregoire technique**: in this technique an extended tunnel is created extravesically and the meatal anatomy is unchanged, so the ensuing stricture is mostly due to a very tight distal ureter and access to the ureter is usually easy [18, 19].
- **Modified Lich-Gregoire technique**: this technique is commonly used in transplantation where the tunnel is created extravesically with two variations for ureterovesical anastomosis. First is the fish-eye technique and is typically located anterolaterally in the bladder. Access to this neo-orifice is usually not very difficult. The cause of the stricture is either poor blood supply of a compromised ureter or a tight closure of the meatus and distal tunnel. Second, some transplant surgeons use the spatulated inverted distal ureter technique anchored to the bladder, creating a nipple. This technique has a low reflux incidence. In cases of true stricture the retrograde access can be very difficult. The patient may need a nephrostomy tube and antegrade guidewire placement. After dilation, an endoureterotomy can be done in a retrograde fashion. Double pediatric reimplants with a single tunnel create additional difficulties due to side-by-side ureters in a narrow tunnel and stenting of one ureter may cause mechanical obstruction of the second ureter. It may be necessary to stent both ureters with a smaller stent: 4.8–5 Fr. Another cause of ureteral obstruction of a short transplant ureter is rotation of a transplant kidney and angulation of the ureter at the UPJ or lower. Some of these patients require long-term stenting to stabilize the shape and curves of the ureter. Natives to transplant ureteroureterostomy has similar problems at times. See Figure 53.5.
- **Glenn-Anderson-O'Donnell-Puri technique**: this advances the orifice towards the bladder neck and is usually easy to access and dilate. Caution needs to be exercised if the opening is very close to the bladder neck in women. The O'Donnell technique is a submucosal injection of bulking agents without changing the anatomy. It is usually used for vesicoureteral reflux [20, 21].
- **Psoas hitch**: this is an additional maneuver to compensate for a shortened ureter. The implanted neo-orifice may be slightly higher or lateral depending on the technique and if it strictures it can usually be accessed in a retrograde fashion.

## Boari flap

Since the ureteral anastomosis is at the end of a tubularized flap it is rather far from the bladder neck, especially in male patients with an enlarged prostate. A flexible cystoscope or a semirigid ureteroscope is useful for reaching the obstructed anastomotic site for initial wire placement.

## Neobladder

Urinary reservoirs present special problems in cases of stricture and obstruction of the implanted ureter. Some of the implants form a chimney structure and some have a short tunnel with direct anastomosis to the bowel mucosa or are inverted with nipple formation.

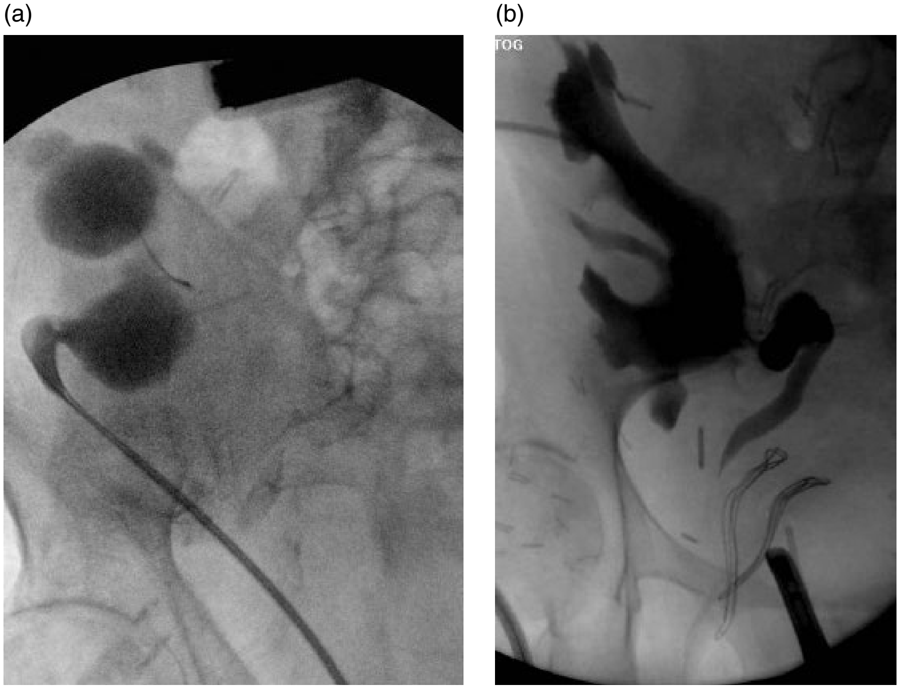

**Figure 53.5** (a) A rotated right lower quadrant transplant kidney (the renal pelvis faces laterally) with ureteral obstruction. (b) A right ureteroureterostomy with stricture and angulation.

The disadvantage is a lack of normal bladder boundaries to help identify the implant site.

## Extirpative and reconstructive pelvic surgery

Radical prostatectomy, abdominoperineal resection, hystero-oophorectomy, bladder neck reconstruction, pelvic floor reconstruction, and a variety of bladder neck suspension procedures can, at times, contribute to the development of ureteral strictures. This can be due to anatomic or histological causes such as dissection and cauterization.

Some pelvic reconstructive procedures can cause angulation and distortion of the natural course of the intramural ureter as well. The best approach is careful inspection of the area and placement of a guidewire to be followed with either mechanical dilation or incision in long and dense strictures. Posthysterectomy distal ureteral obstructions are mostly above the intramural section and are mechanical or ischemic due to thermal injury to the vasculature and the tissue directly. In such cases the lumen is not actually compromised. An initially valuable instrument is a semirigid ureteroscope, allowing direct access to the orifice. This allows the wire to be inserted, with the scope keeping the wire from curling (bellying) outward. The use of hydrophilic guidewires such as Sensor, Roadrunner, or Glidewire are additionally advantageous. After negotiating and stabilizing the access we generally change the Glidewire into a more stable wire such as the Amplatz superstiff wire or a Sensor wire. In cases of obstruction above the orifice a mini semirigid ureteroscope (6 Fr) is advanced to the area of narrowing to allow for direct and atraumatic insertion of the wire through the compromised lumen without creating any false passages. This can later be incised using a cold-knife endoureterotome without any thermal injury. See Figure 53.6 and Video 53.1.

## Pelvic malignancies

Bulky pelvic malignancies create a different type of challenge. A common example is a female patient with bulky uterine mass, postradiation. In these cases obstruction of the distal ureter is a combination of mechanical changes due to anteromedial dislocation and secondary postsurgical/postradiation histological changes. The stenotic ureteral orifice is located centrally on a mound facing the lateral aspect of the bladder: the mirror image of the natural orientation. The ureter then takes a medial and a sharp lateral curve towards the renal pelvis depending on the degree of the ureteral tortuosity. The use of Kumpe, Cobra, and other types of angiographic catheter

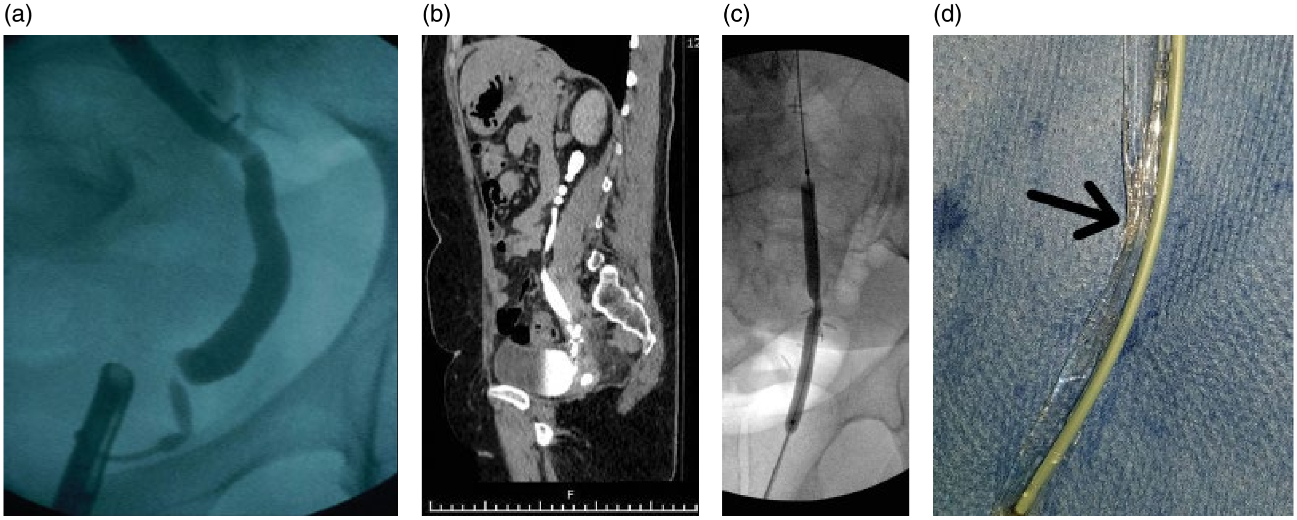

**Figure 53.6** (a) Retrograde pyelogram of a female in the immediate postoperative period after hysterectomy showing leftdistal stricture/obstruction secondary to suturing. The cold-knife incision intraluminally released the suture with no recurrence on follow-up. (b) CT urogram image of a female patient 5 weeks postradical hysterectomy and pelvic lymph node dissection with complaint of flank pain and urine leak from the vagina. (c) Radiographic appearance of resistance to balloon dilation with a ring effect (persistent waist). (d) Appearance of the balloon after removal showing persistence of waist: a sign that the stricture is not adequately dilated.

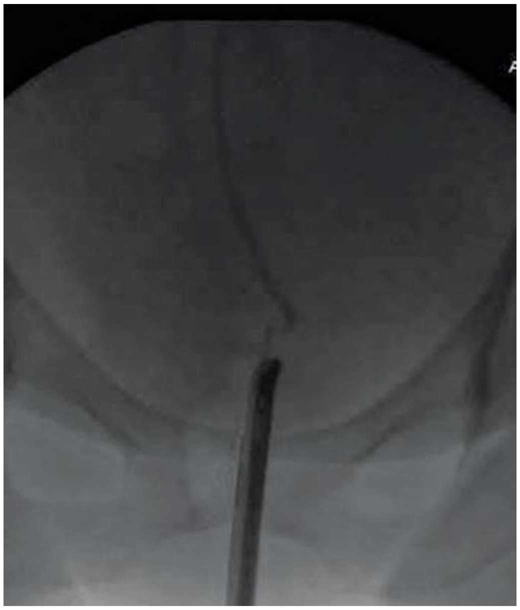

**Figure 53.7** Obstructed distal ureter due to bulky pelvic tumor. The orifice is medially and anteriorly displaced.

is very helpful to overcome these angulations and types of tortuosity [22]. See Figure 53.7.

## Instruments

A variety of instruments are used to manage ureteral strictures endoscopically or under fluoroscopy. Some are used by interventional radiologists in an antegrade fashion when urologists do not have enough expertise or, at times, desire to do the procedures. The majority of these can easily be used by urologists who have had adequate endourological training or exposure. The instruments used are from the urology and radiology armamentaria.

### Angled angiographic catheters

These catheters are used in parts of the ureter that are kinked or angulated. Intubate with a guidewire or Glidewire, rotated clockwise or counterclockwise while simultaneously advancing it. See Figure 53.8.

### Guidewires

There are multiple types of guidewire which are used in these procedures, with each specific guidewire designed for a certain purpose. The common types are stainless steel, PTF coated, stainless steel-coated with a hydrophilic tip (Sensor, Boston Scientific, Marlborough, MA, USA), all hydrophilic (Glidewire, Terumo, Somerset, NJ, USA; Roadrunner, Cook Medical, Bloomington, IN, USA), and coated rigid shaft with a floppy tip (Amplatz superstiff). They range in diameter (0.014–0.038 inches), length (140–150 cm), tip shape, and level of stiffness. The most common wires used in urology are 0.035 and 0.038 inches. The floppy soft tip varies from 3 to 5 cm depending on the product. Tip shape may be angled, straight, floppy, or J-shaped.

In general, the ideal endourologic guidewire should be sufficiently flexible and lubricated to negotiate a

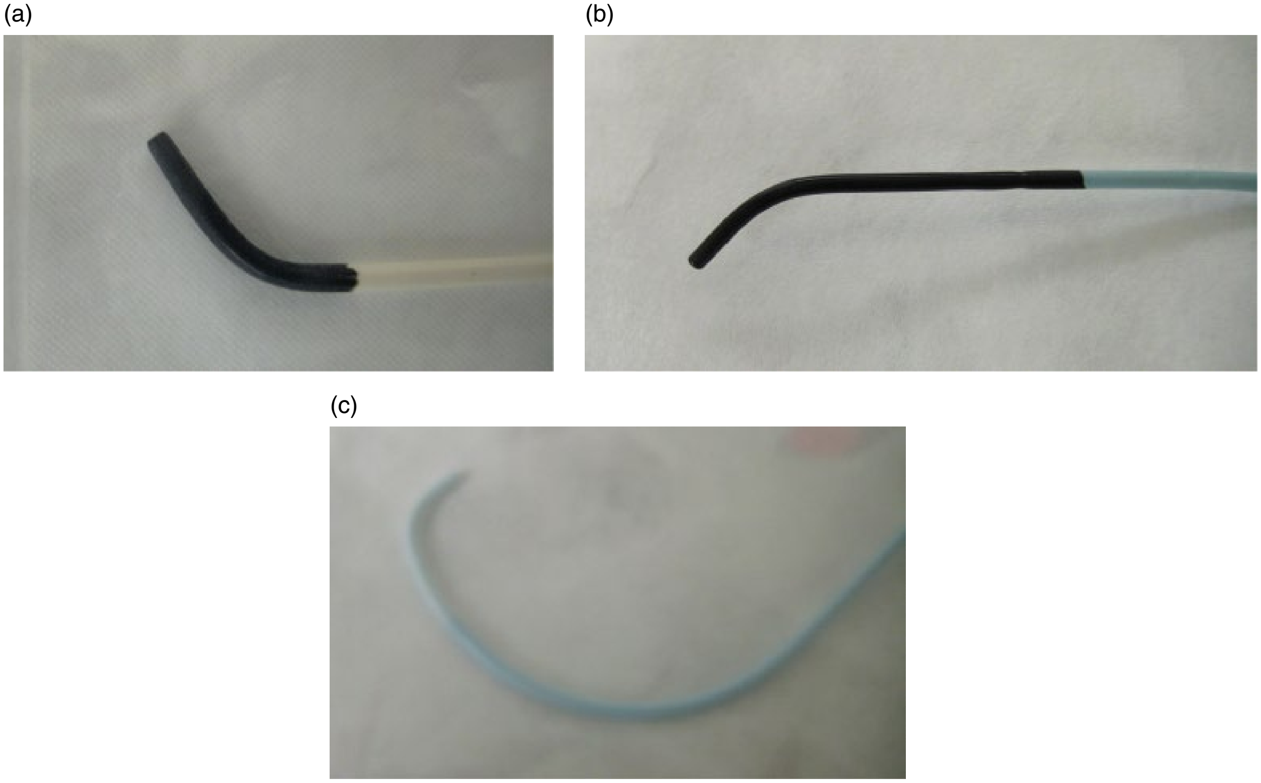

**Figure 53.8** Angle-tipped angiographic catheters for negotiating a stenotic orifice and tortuous ureter.

tortuous ureter and pass possible obstructions with adequate strength against bending for stability to pass the stent over.

If guidewires cannot pass the stricture, a hydrophilic guidewire (Glidewire) can be used bypass a strictured area. A disadvantage is that hydrophilic guidewires are very slippery and easily dislodge out of the ureter. An external device clipped to the end of the Glidewire makes it easier to handle and control [23].

## Meatotomy scissors

Meatotomy scissors, one of the oldest pieces of equipment in the urological armamentarium, is ideal for incising a stenotic ureteral orifice. The very first indication for meatotomy was for facilitating the passage of a stone through a small ureteral orifice. Endoscopic scissors are used to incise the orifice along its intramural course medially, This approach is taken because the distal ureter's blood supply enters it laterally, from the inferior vesical artery: 12 and 2 o'clock on the right and 10 and 12 o'clock on the left.

## Endoureterotomy scissors (Storz)

This is a type of single-action rigid or flexible scissors with the cutting edge facing outward when passed through a rigid ureteroscope. When the scissors are opened in the stenotic intraluminal portion and withdrawn, with proper orientation the dorsal aspect of the upper blade incises the ureteral stricture. This is called reverse cutting [24]. See Figure 53.9.

## Stricture knife (Cook Medical)

The stricture knife was also designed for semirigid ureteroscopes and is not commonly used. It includes a narrow-profile catheter with an inner scalpel which is advanced through the area of stricture and slowly withdrawn under direct vision to incise the stenotic area.

## Greenwald needle

This 3 Fr needle is inserted into the bed of a stricture to instill triamcinolone to decrease the rate of collagen production and thus decrease recurrence rate. Some studies have reported a 50% response rate at 5 year follow-up.

## Collin's knife-electrode

This 45° angled electrode is used to incise the intramural ureter and obstructed ureterocele using the standard transurethral resection set. If the opening of a ureterocele is accessible then a wide meatotomy can be performed.

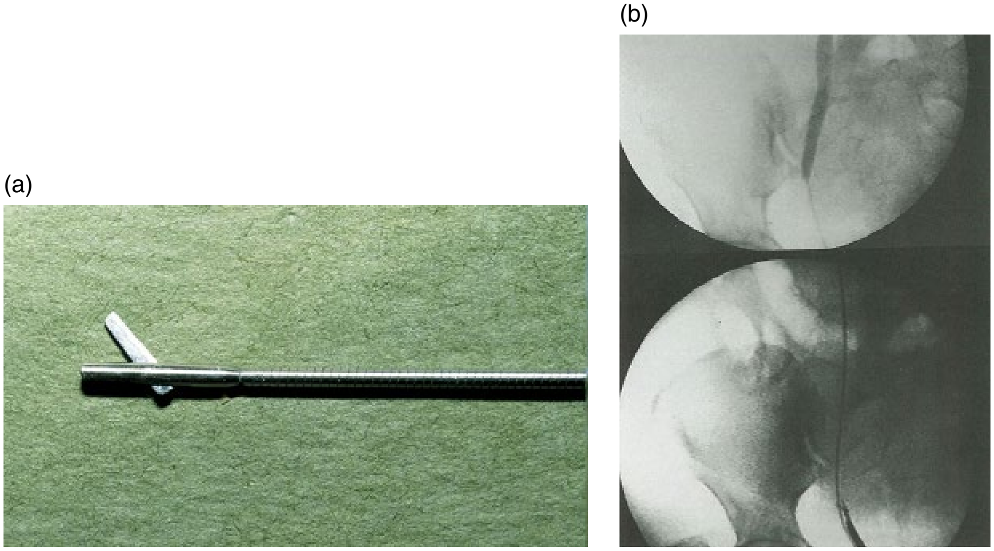

**Figure 53.9** (a) Close up of endoureterotomy scissors. The sharp dorsal aspect of this instrument is ideal for reverse cutting. (b) Radiographic appearance of endoureterotomy.

Most urologists recommend incising the base of the ureterocele horizontally at the medial aspect as this gives the best chance of avoiding reflux afterwards [25].

## Laser fiber

Neodymium (Nd):YAG and Ho:holmium lasers may be used with semirigid and flexible ureteroscopes to incise stenotic areas under vision. Both 200 and 365 μm fibers may be used depending what size ureteroscope is used. The 365 μm fiber fits the lumen of most semirigid ureteroscopes. The lowest possible energy must be used to minimize thermal injury. YAG should not be used primarily as it may cause necrosis.

## Angled Bugbee electrode (Greenwald)

This 3 Fr angled or straight electrode is used to incise a stricture using an electrical current. The downside is that the added electrical energy can damage an already compromised vascular supply.

## AQ Taper and Nottingham one-step dilators (Cook Medical/Boston Scientific)

These sequential or graduated fascial dilators (6–12 and 12–18 Fr) or a variation of Teflon dilators are advanced over a guidewire under fluoroscopic control to dilate a narrow segment of the distal ureter prior to ureteroscopy. This longitudinal force can result in tears and splitting of muscle layers that can potentially cause stricture formation (see Figure 53.10) [26].

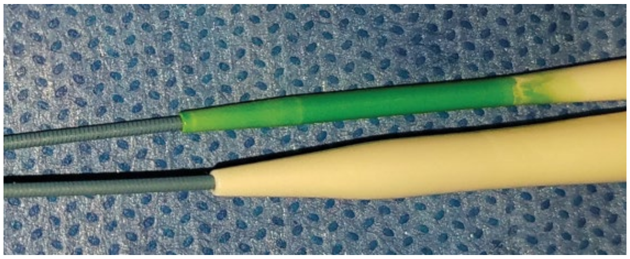

**Figure 53.10** Tapered 6–12 and 12–18 Fr fascial dilators. The tapered tip matches a 0.038 inch guidewire without any gap, avoiding tissue dragging and decreasing mucosal damage. The larger diameter of the dilator as compared to the smaller ureteral lumen still causes mucosal and muscular injuries.

## Bugbie dilators (Storz)

These stainless steel devices are available in single size or graduated size on a single shaft. Their purpose is for dilating stenotic distal ureters.

## Balloon dilators

Since the introduction of balloon dilators by Grüntzig in 1978, they have been used to dilate the ureter prior to ureteroscopy. Balloons are the most common form of stricture dilator. Dilated balloon outer diameters (OD) range from 15 to 24 Fr with marked lengths of 4–10 cm and tapered shoulders. The balloons have a set range of pressure tolerance and can rupture if overinflated. Use of a pressure gauge can avoid this problem. If a balloon is placed too close to a dense stricture it has a tendency to slide out of position. In narrow ureters it is often difficult to advance a balloon once it is inflated and deflated;

therefore, in long segments, it is best to advance the balloon to the proximal end and withdraw it segmentally. The balloon must be deflated completely, the syringe removed, and the valve open during withdrawal. This maneuver prevents the ureter from being dragged during withdrawal.

A balloon's maximum pressure tolerance is described in atmospheres (atm) or pounds per square inch (psi) and rarely in kilopascals (kPa), where 1 atm = 14.7 psi = 101.3 kPa. A simplified rounded formula is 1 atm = 15 psi = 100 kPa.

Uncontrolled overinflation of the ballon can result in rupture and possible disruption of the ureteral wall continuity. If a pressure gauge and Leveen (spiral cylinder)-type syringes are not available then smaller (2–5 ml) syringes can be used, but produce high pressures. A zero-tip balloon, which has no shoulder, can be used to dilate the point of obstruction before endoscopy.

Balloon dilation causes circumferential histological injury but is less traumatic than fascial dilators. In a study by Schwalb and Eshghi [10], mechanical dilation was found to cause more sites of immediate mucosal trauma. Six weeks later, mechanically dilated ureters showed extensive scarring and muscle loss. There was significantly less damage with balloon dilation and hydraulic dilation for ureteroscopy was atraumatic [10].

### Acucise endopyelotomy

The Acucise kit is used for fluoroscopic incision without endoscopy. A 10 Fr balloon, which helps define the area of stenosis, places the cutting wire against the tissue for direct incision. The inflated balloon (which may reach 24 Fr in OD) is left for 10 minutes after incision is made for tamponade. Placing the orientation of the cutting wire away from vessels and paraureteral vital structures is the key factor to avoid incising vital structures. The dilated balloon can create tense pressure and place the ureter directly against adjacent structures such as uterine, iliac gonadal, and lower pole vessels and once the electrical wire is activated it can potentially incise through the ureter and adjacent vessels. This instrument has been used in the treatment of UPJ obstruction as well as ureteral strictures [27–33].

### Endoureterotome (Wolf, Storz, Olympus)

A dedicated endoureterotome is most useful and yet is one of the most underused instruments in the ureteroscopic aramamentorium. There are three models of this rigid instrument with variations in their shape, length, and tip configuration – cutting cold knife, either straight (Storz) or half-moon-shaped (Wolf, Olympus) – which are described as follows.

#### Wolf endoureterotome

This is the most user-friendly of the three. It is a three-piece instrument and is part of the ureteroresectoscope set. The working element has a locking mechanism to hold the half-moon cutting knife in place. The rod lens is inserted through the element and into the sheath which is 41 cm long with an OD of 11 Fr. The rounded beak is at the top of the instrument. The cutting knife also has a hollow channel allowing a 0.025 inch wire which ensures that the blade follows the wire and remains intraluminal at all times. This instrument is also used for endopyelotomy.

#### Olympus endoureterotome

This device has similar elements to the Wolf but the length is 38 cm and the OD is 13 Fr. The beak is at the bottom. The advantage is that it has a larger half-moon cutting element that can slide over a 0.038 inch wire and is perfect for very distal strictures. The major disadvantage is the larger OD and so it is not ideal for higher lesions.

#### Storz endoureterotome

This instrument is actually a 36.6 cm long ureteroresectoscope with a similar type of working element. It has an OD of 11.5 Fr and an oval insulated tip. A straight or serrated knife is used for cutting. It is hard to advance this instrument to upper nondilated or tight ureters. It may be beneficial to initially stent the ureter to allow for passive dilation and decompression of the upper tract. See Figure 53.11.

## Stents

Stents vary in shape, size, design profile, and material and are almost always needed after any procedure associated with endoscopic or radiological treatment of ureteral stricture. Most stents are for general use while some are designed for stricture disease.

### Coating (antibiotic-eluting stents)

Antibiotic-coated stents have been tested on animals; rifampin-coated stents showed efficacy against *Enterococcus* infection. An *in vitro* study assessed the efficacy of a sustained-release varnish containing chlorhexidine against three common bacteria in the urinary tract (*Enterococcus*, *Escherichia*, *Pseudomonas*) and was shown to be effective against all three species. Triclosan-eluting ureteral stents changed every 3 months did not result in reduced infection rates in this chronically colonized group; however, the rate of symptoms and requirement for antibiotics were significantly lower [34–36].

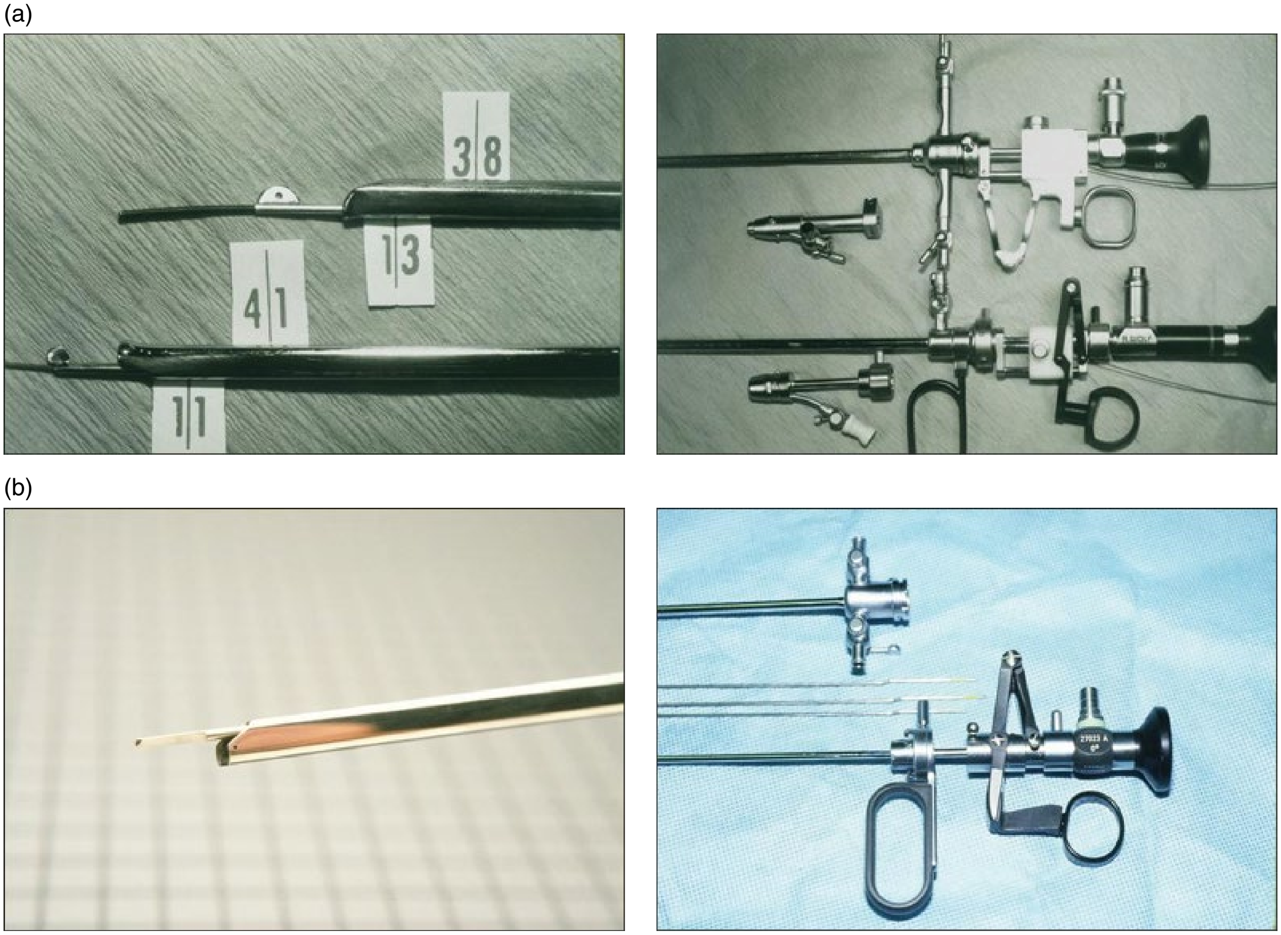

**Figure 53.11** (a) The Wolf and Olympus endoureterotome for cold knife incision with a half-moon guided knife. (b) The Storz endoureterotome with a straight knife.

In an animal study stents initially increased peristalsis but later reduced or stopped it. Stent material did not affect peristalsis but smaller stents caused less of an immediate effect on peristalsis than larger stents [37]. In another numeric analysis, a computational fluid dynamics simulation showed that curved stents with side holes provided better drainage compared to straight models [30].

- Regular double-pigtail stents: this type of stent, originally known and marketed as the J or double-J stent, had lesser proximal and distal curvatures compared to the double-pigtail stent with 360°. A large variety of polymers are used with an OD of 4.8–14 Fr at different lengths.
- Silicone stent (Cook Medical): this stent is made of pure silicone and is quite soft, resistant to encrustation, well tolerated, and recommended for long dwelling periods. This stent is ideal for cases of recurrent soft strictures or drainage problems.
- Endopyelotomy-endoureterotomy stents are used after the thus-named procedures, and are available in lengths of 22–30 cm and two different diameters of 10/7 Fr (Applied by Applied Medical Resources) and 14/7 Fr (Retromax™, Boston Scientific, Cook Medical) The larger OD is placed across the UPJ area ordinarily and reversed in lower ureteral strictures. We mostly use the smooth, tapered-profile 10/7 Fr stent. See Figure 53.12.
- Peripheral Stent (Cook Medical) is rarely used now. It was designed without a lumen but with vertical spiral grooves along the stent to expedite drainage. The concept was to keep the ureteral walls apart and allow urine to flow along the grooves.
- Metallic stents are primarily used in the treatment of recurrent ureteral strictures. They are considered an alternative to pigtail stents for their resistance to the compressive force of the stricture, and longer life span. They are made from biocompatiable nitinol (nickel titanium) Since the introduction of the Wallstent, the currently available stents are Memokath 051, Resonance, Allium, and Uventa. Ureteral strictures and obstructions caused by extrinsic pressure do not

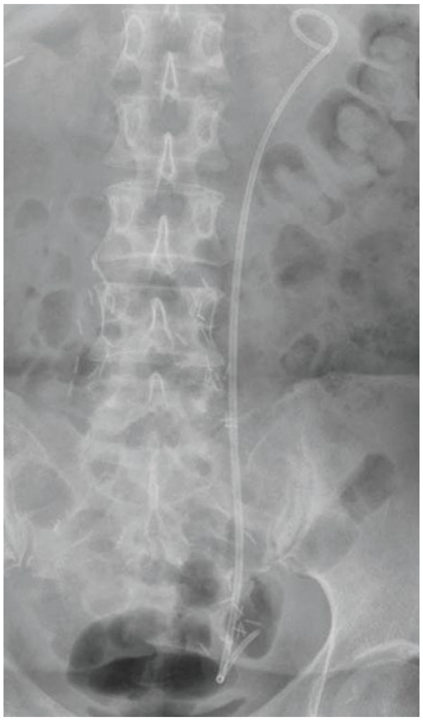

**Figure 53.12** 10/7 Fr endopyelotomy stent placed in reverse after endoscopic treatment of distal ureteral stricture.

drain well with stenting alone despite a short initial improvement. This is because a significant amount of flow is around the stent rather through the stent's lumen, which becomes encrusted.

- Nephrostent 8 & 10 Fr (Boston Scientific): this is a combination of a pigtail and nephrostomy tube. A pigtail stent is ideal after antegrade access and distal ureteral dilation or incision. Once the nephrostomy is cappedit functions as a indwelling stent. This stent can be interchanged over a guidewire and replaced by a single pigtail nephrostomy to allow the urologist to assess the patency of the distal ureter. It is an excellent choice for neobladders, pouches, and inaccessible reimplanted ureters.
- Transplant and pediatric stents (10–18 cm long) are classic double-pigtail stents that are custom-produced for shorter and smaller ureters with material specified for softness or rigidity as required.

## Etiologies of ureteral stricture

Ureteral obstructions and strictures are either intrinsic or extrinsic or a combination of both. They are further categorized as congenital and acquired, with subclassifications of benign or malignant.

### Congenital strictures

Congenital strictures are the most common type of intrinsic stricture (except for UPJ strictures which can be a combination of intrinsic and extrinsic). Categories include UPJ obstruction, ureteral strictures in conjunction with UPJ obstruction, primary obstructive megaureter, ureteral meatal stricture (stenosis), and obstructed ureterocele.

UPJ obstruction will be discussed elsewhere in this chapter but the basic principles of endoscopic incision discussed here apply to that as well. Megaureter is usually diagnosed in children and is defined as dilation of the ureter >7 mm. It can be divided into subsets of obstructive megaureter and refluxing megaureter. Obstructive megaureter is thought to arise from a malformation of the distal ureter at the ureterovesical junction (UVJ), with an aperistaltic segment leading to a small distal portion of stenotic or normal-caliber ureter with proximal hydroureter [38, 39]. See Figure 53.13.

Ureteral meatal stenosis is a congenital pinpoint orifice without previous instrumentation or stone impaction. The ureteral orifice is naturally the narrowest ureteral point of the ureter with an estimated 6 Fr lumen size. If this stenosis is functionally affecting drainage a simple meatatomy or dilation is adequate treatment.

A ureterocele is a cystic outpouching of the terminal ureter occuring in 1 in 4000 children, predominantly females. Some 80% are in ectopic locations, ranging from the bladder to the urethra; 80% are associated with a dysplastic or poorly functioning duplicated upper pole system. Obstructive symptoms in ureteroceles varies in patients and can range from being asymptomatic to having recurrent urinary tract infections (UTIs), hydronephrosis, and renal failure. Ureteroceles cause obstruction due to a stenotic ureteral orifice; however, in severely dysplastic ureteroceles they can also prolapse and cause bladder neck obstruction [40, 41].

### Acquired strictures

Acquired strictures fall into several broad categories: benign, malignant, iatrogenic, and idiopathic. In a review by Tyritzis and Wiklund, 35% of strictures were iatrogenic in nature, 35% had benign causes, 20% idiopathic, and 10% malignant [42].

Open or endoscopic procedures can result in iatrogenic mechanical and vascular damage to the ureter with an estimated occurrence of 0.3–2.5% in pelvic and endoscopic surgery [43]. With the increased volume of minimally invasive laparoscopic and robotic procedures, the overall incidence has increased 30% since 2000, attributed to increased difficulty in visualization and the inability to palpate the ureter compared to open surgery [44].

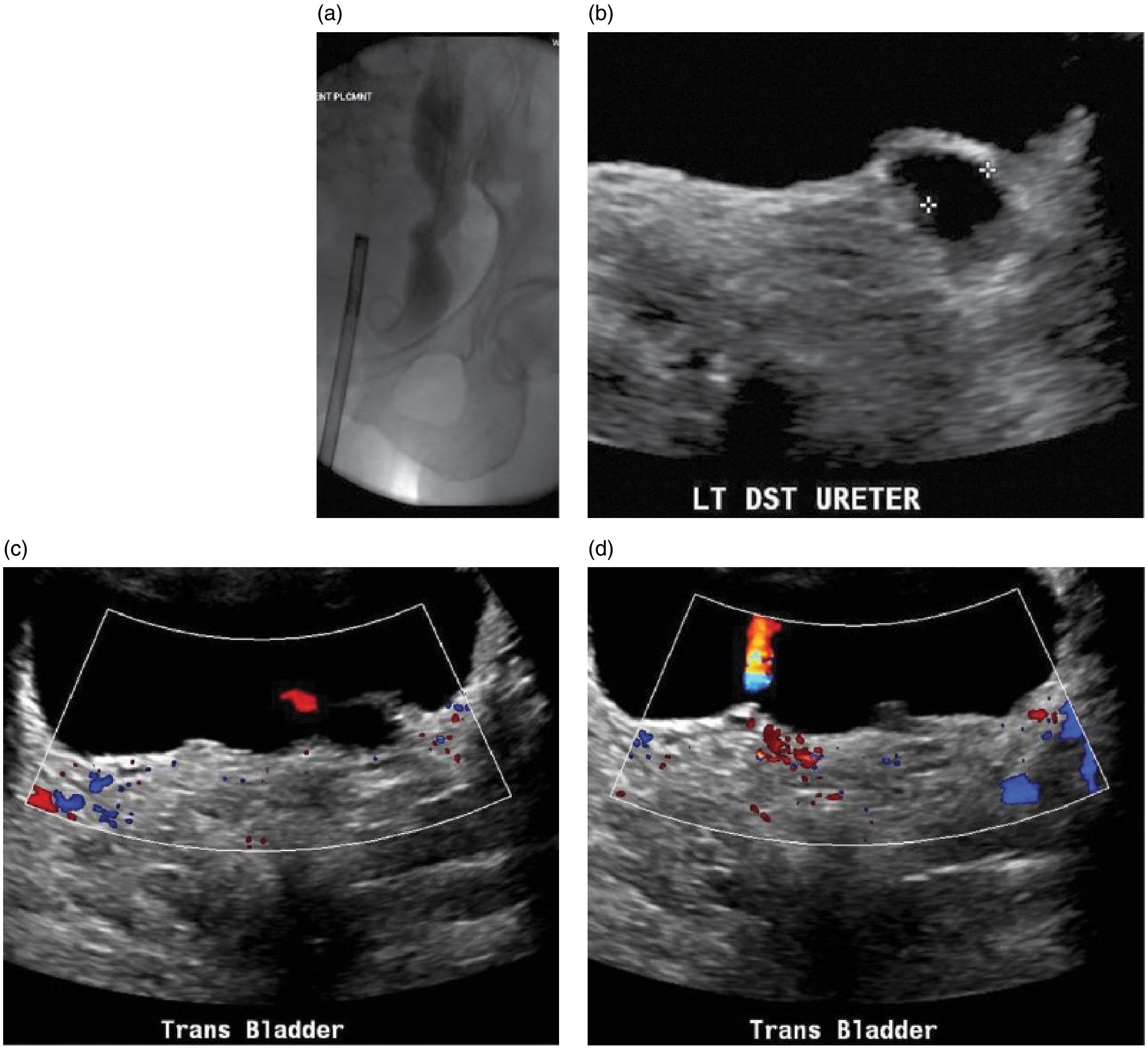

**Figure 53.13** (a) The appearance of a congenital obstructive megaureter. The distal obstructed lumen was incised with a cold-knife endoureterotome. (b) Obstructive megaureter after treatment, note the dilation of the left distal ureter, (c) Sluggish ureteral jet on the left due to poor peristalsis rather than obstruction. (d) Strong ureteral jet on the contralateral side.

Injury can range from thermal mucosal damage to perforation to partial or complete transection. In each case, the ureter or its end vasculture is intrisically damaged, leading to fibrosis and stricture.

The type of surgery responsible for ureteral injuries varies considerably by study. Gynecologic procedures account for 45–74% of ureteral injuries. The injury most commonly seen during hysterectomies occurs in the ureter distal to the crossing of the uterine artery. General surgical injuries account for 4–17%, mostly during colectomies; this is estimated at a rate of 0.3–10% of distal colectomies with the remaining occuring in vascular cases [45].

Urologic surgery accounts for the remaining iatrogenic injuries, estimated at 8–44% of all ureteral injuries during both endoscopic and open surgery. Ureteroscopic injuries are relatively rare, at a rate of 1–3% postinstrumentation. Passage of flexible or semirigid ureteroscopes can cause intraluminal trauma through shear forces, especially if the ureter is insufficiently dilated. A study by Karakan et al. [46] reported higher rates of injury with balloon dilation of the ureter and preoperative UTI.

Insertion of a ureteral access sheath can be associated with iatrogenic ureteral wall injury, especially in unstented narrow lumens. This is due to inserting a larger-diameter device, causing intraluminal shear forces. Holmium laser lithotriposy can cause iatrogenic damage but with penetration of only a few millimeters the damage is less than with Nd:YAG lasers. Nevertheless, accidental energy application, mechanical pressure, and stone fragments can cause localized ischemia and scar tissue. Use of a basket during treatment of stones can result in complete avulsion of the ureter [47]. Fam et al. reported on 77 patients treated endoscopically for impacted ureteral stones, and following the operation found a stricture rate of 7.8% [48].

Iatrogenic ureteral strictures occurring after open urologic procedures such as cystectomy and kidney transplantation are almost always the result of ureteral reimplantation or urinary diversion. Cystectomy has a ureteral anastomosis stricture rate of 2.7–8.8% [49]. In a review by Mano et al. of 1004 renal transplant recipients between 2000 and 2010, 2.6% developed ureterovesical anastomotic strictures [50]. The pathogenesis of ureterointestinal strictures is multifactorial and likely due to ischemia and postsurgical fibrosis [51].

### Benign strictures

Impacted calculi are responsible for up to 65% of benign strictures. The causes of stricture in these patients are multifactorial and intrinsic in nature. Persistent pressure of the stone against the ureteral mucosa and the resulting immune reaction to the stone itself can cause localized ischemia, leading to fibrosis and stricture [52]. Longer stone impaction leads to increased risk: Roberts et al. reported that ureteral stone impaction for longer than 2 months harboured a 24% chance of ureteral stricture, ureteral edema, and epithelial hypertrophy [53]. The edematous mucosa is more fragile and limits endoscopic work space, increasing the chance of mucosal damage [48].

Retroperitoneal fibrosis is a rare, commonly bilateral idiopathic and autoimmune disorder characterized by inflammation and fibrosis around an abdominal aortic aneurysm and surrounding retroperitoneal structures, and it can often cause external ureteral compression [54]. Retroperitoneal fibrosis typically develops as a plaque between the renal arteries and the pelvic brim with rare sacral involvement. As such, the distal ureter is usually unaffected. Retroperitoneal fibrosis accounts for roughly 15% of benign strictures [55] with the majority in the mid and upper ureter with medial deviation. The extrinsic compression leads to a narrow lumen, giving a classicstring-like appearance. The immediate segment above and the pelvicalyceal system are significantly dilated. This process is commonly bilateral.

Endometriosis is the presence of endometrial tissue outside of the uterine cavity and is a chronic inflammatory process stimulating surrounding angiogenesis. Chronic inflammation results in extensive adhesions, distortion, or compression of the ureter in less than 1% of cases [56].

Pelvic lipomatosis can cause compression of the bladder and is associated with possible displacement and narrowing of the distal ureters.

## Infection, trama, and malignancy

Infectious causes of ureteral strictures are rare (<9%), but when present are most often caused by tuberculosis and schistosomiasis [1]. Tuberculosis causes an asymptomatic infection causing destruction along the urinary system with fibrosis and stricture replacing normal tissue during the healing process. Wagaskar et al. reported on 31 patients presenting with urinary tuberculosis, of whom 29% had ureteral strictures [57]. Schistosomiasis is a disease caused by immune reaction to *Schistosoma* eggs, a parasitic flatworm mainly endemic in Africa and the Middle East. The worms migrate to the veins around the bladder and ureters which are extensive, and can affect the bladder and all layers of the ureter, leading to ureteral stricture, bladder neck contracture, and bladder cancer [58]. Al-Shukri et al. reported that ureteral stricture was the most common complication of genitourinary schistosomiasis with 91% of strictures occuring at the distal ureter [59].

Trauma accounts for a very small portion (1–4%) of ureteral strictures. Patients with extensive pelvic fractures and gunshot wounds are prone to these injuries that are usually diagnosed and treated early after the injury occurs. If distal ureteral stricture is a late sequela it can be approached endoscopically.

Malignant ureteral obstruction is caused by direct extrinsic compression of the ureter by local tumor, direct tumor infiltration, or encasement through retroperitoneal lymphadenopathy [60]. Malignant obstruction is often associated with intra-abdominal cancers, but can also be related to metastasis from other sources.

Radiation therapy is commonly used for pelvic malignancies such as prostate, bladder, cervical, uterine, and rectal cancers and the distal ureters, due to their close proximity to these structures, receive scatter radiation. Radiation causes microvascular injury by inducing inflammation in the intima of arteries, and occlusion of smaller arterioles known as obliterating endarteritis, leading to relative ischemia of the ureter [61–63]. Ureteral stenosis from radiation injury develops slowly, between 6 months and 20 years. See Figure 53.14.

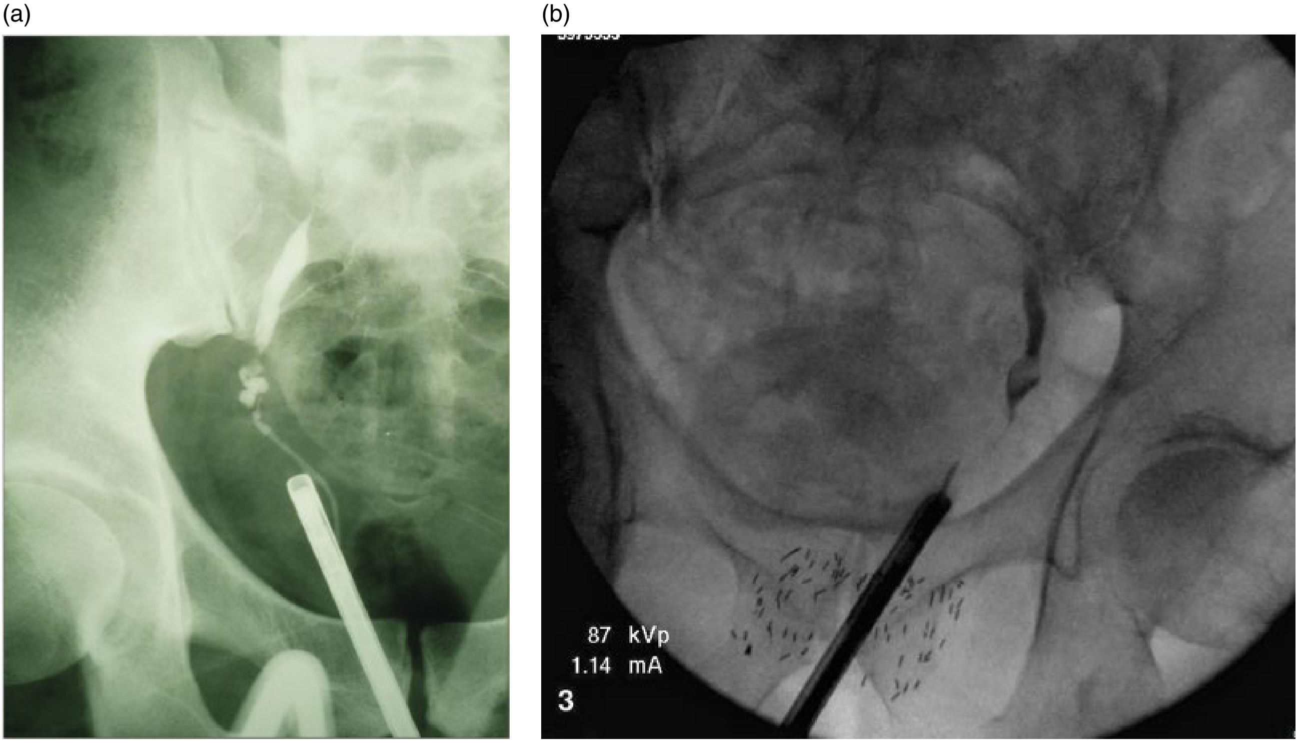

**Figure 53.14** (a) The appearance of a distal ureteral stricture secondary to tuberculosis. (b) Distal stricture secondary to radiation after placement of radioactive seeds causing ischemia of the trigone and intramural ureter.

## Clinical presentation and imaging

The diagnosis of a ureteral stricture depends on the level of suspicion and presentation of the patient. Patients with unknown stricture and few risk factors may present with renal damage and hydroureteronephrosis. They may be completely asymptomatic or have flank pain or recurrent UTIs. In patients with higher suspicion for stricture, strictures may be picked up on imaging before any deleterious effects occur.

### Subjective diagnosis

The most common subjective clinical symptom is dull versus sharp and acute or chronic flank or lower quadrant pain. It can be throbbing in an intermittent or constant pattern with possible radiation towards the groin, decreased urine output, or anuria in solitary and transplant kidneys. Significant abdominal pain, nausea, vomiting, fever, chills, and UTI symptoms similar to an obstructing UVJ stone are not uncommon. One major difference is in transplant patients whose renal arterial and ureteral innervation have been disrupted. Transplant patients do not experience any somatic pain and even in the face of severe hydronephrosis caused by ureterovesical or intramural obstruction due to disruption of renal ureteral nerves. They notice a decrease in urine output, general malaise, or a bloating sensation in lower abdomen. There may be signs of sepsis in advanced cases. Objective findings include elevated creatinine and white blood cell count, tenderness over the graft area, and hydronephrosis on the ultrasound.

### Objective diagnosis

Strictures are typically diagnosed on imaging. Standard CT scan will detect hydroureteronephrosis or raise the suspicion of stricture. Other techniques such as CT urogram, retrograde pyelography, or ureteroscopy are necessary to characterize the exact length and location of stricture. In patients with longstanding stricture, a nuclear MAG3 scan may help determine the extent of renal damage [64]. The most convenient initial evaluation is Doppler renal/bladder ultrasound which can detect hydronephrosis and assess ureteral jets for significant obstruction. Magnetic resonance imaging with hydration clearly outlines the ureter when contrast is contraindicated such as in transplant kidneys (see Figure 53.17, below).

### Treatment strategies

As a principle, except for short strictures or meatotomies in dense strictures that carry infection risk, it is advisable to initially place a stent and allow hydronephrosis to resolve prior to optimal definitive treatment. This passive dilation makes subsequent instrumentation easier and safer.

Meatotomy is a useful technique in treating ureteral meatal stricture. This category includes simple meatal stenosis, ureterocele, obstructive megaureter, and acquired UVJ scarring. Classically, some of these conditions have been treated with open or laparoscopic reimplantation of the ureter, but endoscopic approaches are effective as well [7, 65].

Meatotomy is preformed with meatotomy scissors, laser, or electrocautery. Scissors are preferred because they allow greater control and cause less scarring. The technique involves cannulating the ureteral orifice with a guidewire, followed by insertion of the meatotomy scissors. The right ureteral orifice is accessed with scissors angled posteromedially at the 5 o'clock position and the left at 7 o'clock and an incision is made. This is to preserve the submucosal tunnel and the muscular sheath and conserve the valvular function of the submucosal ureter or medial valve, thus preventing vesicoureteral reflux [66]. Next electrocautery is used if needed. The ureter's blood supply is lateral at this location and one must avoid damage in this direction. Arrabal-Martin et al. found a 94.5% patency rate at 36 months in their 18-patient series [66].

In cases where the stricture extends more proximally, such as in radiation induced cases after radioactive seed implants, the meatotomy can be extended in short bites until a lumen is identified. Balloon dilation and cold-knife endoureterotomy are other options. We do not recommend use of fascial dilators because of the shear effect that can occur after failure of a balloon, which indicates a dense stricture.

## Resection/incision of orifice: post-TURP and TURBT

In some cases of transurethral resection of bladder tumor (TURBT) and transurethral resection of prostate (TURP), a large median lobe or poor visibility can lead to thermal injury to the ureteral orifice, resulting in subsequent stricture. The initial treatment should be meatotomy and stenting, and failure to identify the orifice will require antegrade placement of a guidewire and subsequent dilation or incision with 3–4 weeks of stenting. In some cases, if the surgeon is certain about the location of the orifice, thin-layer resection with a cutting element or a Collin's angled electrode can unroof the obstructed ureter. This should be exercised with extreme caution and prior injection of contrast with columnization to the site of the orifice under fluoroscopic controlcan be helpful.

Balloon dilation is currently used as part of ureteroscopy for initial treatment of stricture or stenotic ureteral orifice. The dwelling time of an inflated balloon should be short in order to limit ischemia. If at maximum inflation pressure the stricture fails to dilate an alternative approach such as endoureterotomy should be used. In such cases the segment of the balloon corresponding to the area of stricture shows a "memory" (or "ring effect") of the failure to dilate the stricture (see Figure 53.6d). This is clearly an additional sign that the stricture is not adequately dilated.

Mechanical dilation with sequential fascial dilators in the early years of ureteroscopy were cumbersome and traumatic. For limited dilation and stretching of the distal ureter prior to ureteroscopy the one-step Nottingham dilator (6–12 Fr) is a reasonable solution if the tight distal ureter does not allow entry of the ureteroscope. The large (12–18 Fr) version should be used cautiously and for the right indications. Forcing a dilator through a stenotic area can result in splitting ("banana peel") of the ureter. Bougie dilators are not commonly used now due to the availability of smaller-caliber ureteroscopes and wider use of balloon dilators.

## Endoureterotomy: cold- and hot-knife incisional treatments

If a distal ureteral stricture does not respond to an initial balloon dilation our preference is perform cold-knife incision of the stricture under direct vision. The orientation of the cutting knife and incision is critical to avoid injury to surrounding structures (Figure 53.4). The half-moon knife sliding over a guidewire provides most control by maintaining an intramural position of the knife. The incision should be performed in *thin layers* for the required length and advanced segmentally, allowing the ureteral wall to expand. The end point is when the tip of endoureterotome reaches a dilated portion of the ureter. Digging or scooping into the wall should be avoided since it causes perforation without adequately incising the length of the stricture. If a straight knife is used, extreme caution must be exercised, extending the blade into the lumen to avoid through-and-through penetration of the tip. For very dense strictures we prefer the Wolf endoureterotome which has a narrower beak profile with a half-moon knife that will travel up and down the ureteral lumen with better control (Figure 53.16).

In the distal ureter a small semirigid ureteroscope can be used since most institutions do not have access to an endoureterotome; thus the urologist can use laser for incision under direct vision. If a straight knife is available it can be used for cold incision. For upper strictures that may be difficult to reach a similar procedure has been performed using laser or a 3 Fr electrode with a flexible

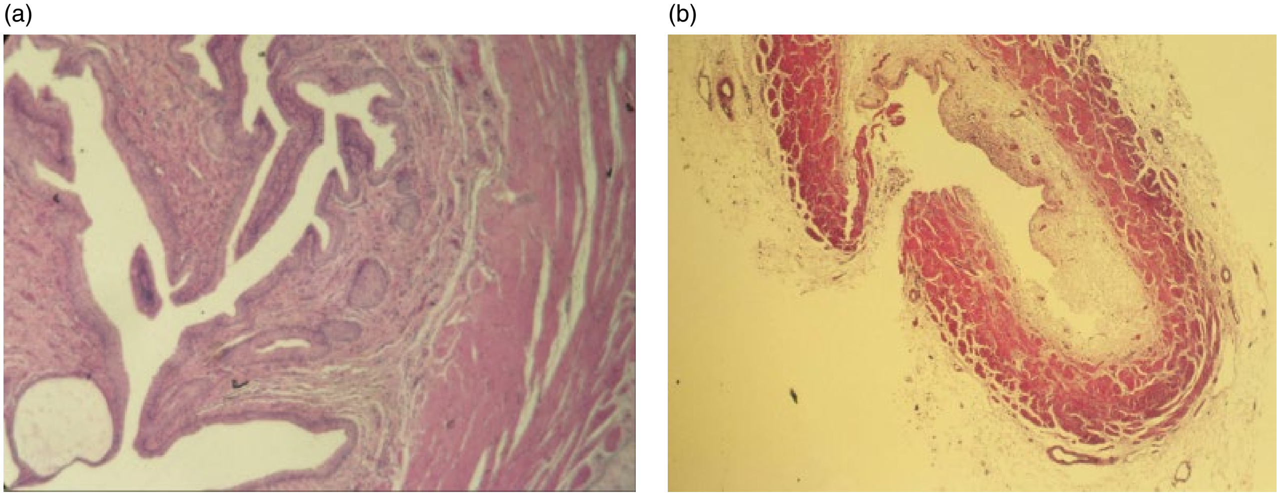

**Figure 53.15** (a) Scarring and disruption of muscle layers after facial dilation. (b) Appearance of ureter after balloon dilation, which shows significantly less damage.

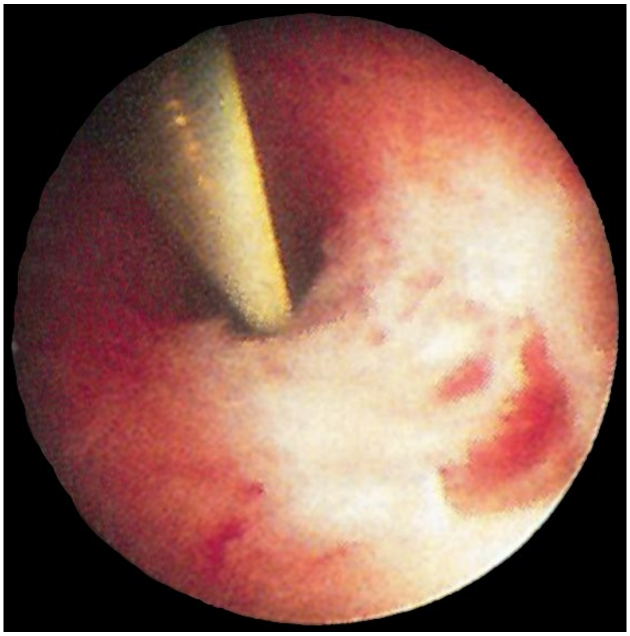

**Figure 53.16** Endoscopic view of endoureterotomy: the incision must be carried out in *thin layers*.

ureteroscope. An angled hot knife can also be used in a ureteroresectoscope with either Storz or Wolf instruments. This is not our preferred choice. Minimal laser and electrical energy should be used to minimize thermal injury to the tissue that already has compromised vasculature.

We generally make an effort to inject the base of the stricture with triamcinolone which may have some benefits in decreasing recurrence, although this may not be supported by level 1 evidence. The dose is 5–10 ml and if injection is not possible, then with irrigation off we flush the base of the stricture with the solution and let it soak for several minutes. In summary, we recommend application of the principles used in the urethra: cold-knife incision and injection of steroids in the stricture area.

## Combined antegrade/retograde management

Synchronous and metachronous antegrade/retrograde approaches are used in cases when retrograde maneuvers have all failed. There are generally two major categories – native and transplant kidneys – as covered here.

### Native kidneys

In this scenario, once the surgeon decides to abort the cystoscopic approach there are two options.

**Synchronous**

In this case the patient is placed in prone position in the split-leg position or on a regular endoscopy table with access to the urethra for flexible cystoscopy. After the urologist performs a percutaneous access a guidewire is inserted into the bladder in an antegrade fashion and retrieved with the flexible cystoscope and the dilation is done over the through-and-through wire followed by stenting. Neobladders and continent pouches can be managed in the same fashion. Similar to urethral stricture, an antegrade/retograde "cutting-to-the-light" technique has been used in managing ureteral strictures. We have found this to be useful only in short and fresh strictures. Long ureteral segments with poor vasculature have a high recurrence rate.

**Metachronous**

If the urologist decides not to proceed any further after the failed retrograde approach, percutaneous nephrostomy and antegrade manipulation can be done by interventional radiology. Management of a distal stricture is usually dependent on institutional policy or the urologist's preference to complete the procedure in a retrograde manner.

### Transplant kidneys

We usually prepare the patient for a simultaneous retrograde/antegrade approach with the patient in lithotomy position, since the kidneys are transplanted in the lower quadrant. C-arm and ultrasound monitors are placed on the opposite side of the kidney. In this arrangement both surgeons at the foot and side of the patient can monitor the procedure. The video monitor is best located over the patient's chest. A percutaneous nephrostomy is performed with ultrasound guidance or fluoroscopy; after access is secured a guidewire is directed into the bladder. It is not unusual for the wire to curl up above the stenotic ureter. A Kumpe or Cobra catheter is usually helpful to negotiate the tip of the wire into the bladder and the rest of the procedure is usually completed cystoscopically. One important difference between native and transplant distal ureter is that in the latter it is actually upper ureter and sometimes a short part of mid ureter that is anastomosed to the bladder; this has fewer muscle layers and is less resistant to shear forces and incision.

In rare situations when the orifice is occluded and cannot be cannulated we have approached it antegrade with a flexible ureteroscope and lasered across the obstructive membrane or trapped mucosa. An alternative approach is the placement of a ureteral catheter flush with the very terminal end of the ureter and to use a sharp metallic guidewire to penetrate into the bladder. This must be monitored cystoscopically to ensure the correct direction and orientation. If the wire is completely secure within the ureteral catheter, attachment of Bovie to the terminal end of a metal wire creates a cutting Bovie effect. This maneuver must be reserved for very rare cases and performed with caution and careful antegrade/retrograde control to stay intraluminal. With the use of modern endoscopic equipment and small-caliber lasers it is rare to need such an approach. We have used this maneuver in three transplant kidneys in the last 27 years.

## Stenting

Different stents are almost always needed as an adjunct after other therapy for ureteral strictures. Based on the length, severity, and etiology of the stricture, our practice is to use a 22–24 cm-long 4.8–5 Fr stent in the majority of our routine ureteroscopies which is quite comfortable for patients. In rare cases of long, tortuous ureters, and in the upper moiety of a duplicated system we use a 26 cm stent. Using the shorter stent prevents excessive contact and irritation of the trigon and bladder neck which is the main cause of a patient's irritative symptoms. Most strictures are managed with a 6 Fr stent. In long and dense strictures we use a tapered endopyelotomy stent in a reverse fashion, so the distal ureter is stented with the 10 Fr segment. Routine postoperative antibiotics are used in all patients and modified based on pre-existing or newly diagnosed infections, with anticholinergics or alpha-blockers as needed to ease irritative symptoms. Antibiotic-coated stents are not yet widely used.

### Follow-up protocols

The follow-up protocol directly depends on etiology, degree, length of the stricture, nature of the operation, surgeon's preference, and a host of other factors and comorbidities. Stent use is beneficial during the healing process, prevents extravasation of urine, and keeps luminal patency. On the flip side, stents can be a source of inflammation, and muscular and epithelial hyperplasia. Kerbl et al. compared different lengths of stent placement (1, 3, or 6 weeks) following endoscopic incision in a pig model and found no significant overall differences among the mean values [67]. Without a consensus on the needed duration of stenting, a period of 3–4 weeks would be reasonable for short and non-dense strictures. The majority of the literature data are based on 4–6 weeks of stenting; that is, the original Davis–Oppenheimer data [68] and endopyelotomy data described in 1986 [69], with some later data suggesting that a shorter period is adequate [70]. Patients with chronic or recurrent strictures may benefit from a silicone stent (Cook Medical) with an indwelling time of over 6 months with minimal encrustation. The size of stent is also a field of controversy. *In vivo* studies on pig models have shown no difference in patency, with larger stents being associated with higher rates of UTI, while a retrospective study by Wolf et al. showed an improved patency rate with stents larger than 12 Fr.

### Follow-up studies

The patient's clinical performance is the initial subjective postoperative assessment. Flank pain, fever, nausea, or vomiting can be some of the early warning signs of immediate recurrence or failed treatment. The interval also depends on the degree of pretreatment dilation and reservoir of the upper tract. As such, it may take a week or longer for patients with a previously dilated upper urinary tract to become symptomatic after recurrence of obstruction. In some cases of very chronic obstruction and poor renal function, patients with low urine production ("dry well") due to low renal pelvic pressure may never manifest classic symptoms of obstruction; therefore, objective assessment is required.

Our initial recommendation is renal ultrasound 2–3 weeks poststent removal. If this study is satisfactory, follow-up renal and bladder ultrasound with assessment of ureteral jet is recommended at 3 months in asymptomatic patients. A diuretic renal scan is recommended to quantfy function and drainage of the renal moiety if there is concern. A CT, MR urogram, and hydration diuretic MR urogram without contrast can all be very valuable for follow-up. See Figure 53.17. After the initial evaluations we usually rely on periodic ultrasound or occasional diuretic nuclear scan or CT/MR urogram. Unresolved situations in a symptomatic patient will need retrograde pyelogram and endoscopy. In patients with good renal function a virtual ureteroscopy can be valuable for assessing intraluminal space [64, 65, 69, 71–73].

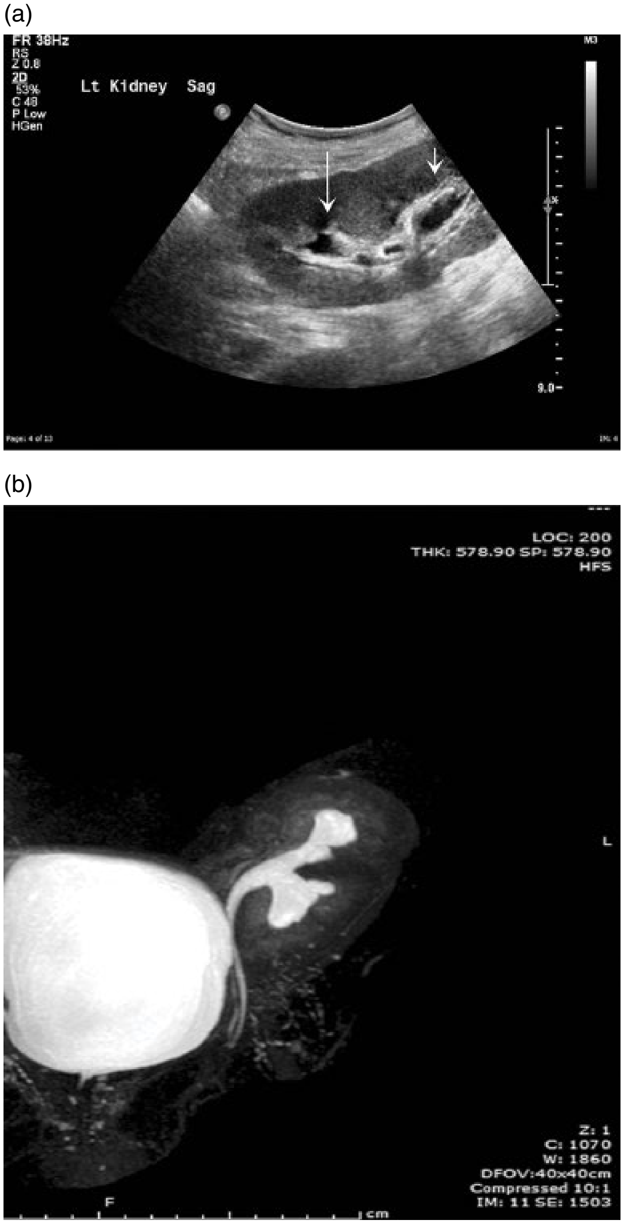

**Figure 53.17** MR urogram with hydration and without contrast in a left lower quadrant transplant kidney ruling out distal stricture.

See Video 53.2.

## Clinical outcome and analysis

Clinical studies have shown that endourological management of ureteral strictures varies due to the use of different modalities and lack of a uniform approach and stenting protocol, thus making a scientific analysis and comparison to open or laparoscopic techniques quite unrealistic. The decreased morbidity and sometimes ease of operation often make this approach a preferable first step.

### Stenting

Often the first step in treating a ureteral stricture is a stent or a percutaneous nephrostomy. Success rates for retrograde stenting have been reported at 75–88% for both extrinsic and intrinsic obstruction [74, 75]. However, the use of double-J stents for extrinsic ureteral obstruction has been associated with a high failure rate in long-term follow-up. Double-J stents rely on flow around the stent for drainage rather than intraluminal flow [75]. The type of pelvic malignancy likely plays a role in the differing success rates. In a study by Ganatra and Loughlin of 157 patients, obstruction by bladder, prostatic, or cervical cancer had a success rate of 15–21%. Invasion seen on cystoscopy was associated with a threefold failure rate [76]. Chitale et al. evaluated a staged approach to malignant ureteral obstruction with nephrostomy under local anesthesia and 1–2 weeks later antegrade ureteral stent. In the series, 24 out of 65 patients had an attempt at retrograde stent placement with a 21% success rate, while the staged approach had a 98% success rate [77].

The use of metal stenting to overcome malignant ureteral obstruction is controversial. Liatsikos et al. used metallic stents in 50 patients with a technical success rate of 100% for stenting of the stricture [60]. The immediate stricture patency rates in patients with extrinsic malignant ureteral obstruction and in patients with benign ureteral obstruction were 100 and 44%. Kim et al. [78] demonstrated poor long-term efficacy of self-expandable segmental metallic stents (Uventa) in chronic strictures with a success rate of 34%. Notably, 28% experienced major complications (≥Clavien-Dindo class IIIb), such as

**Table 53.1** Ureteral patency after treatment.

| Study | No. of patients | Etiology | Type of stent | Patency rate (%) | Mean follow-up (months) |
|---|---|---|---|---|---|
| Rosevear et al. [79] | 8 | Extrinsic, benign | Double J | 100 | 16 |
| Chung et al. [80] | 8 | Extrinsic, benign | Double J | 88 | 11 |
| Richter et al. [81] | 31 | Extrinsic, malignant | Wallstent (metallic self-expanding) | 58 | 42 |
| Yossepowitch et al. [82] | 92 | Extrinsic, malignant | Double J | 56 | 3 |
| Chung et al. [80] | 100 | Extrinsic, malignant | Double J | 60 | 11 |
| Ku et al. [83] | 68 | Extrinsic, malignant | Double J | 89 | 9 |
| Ganatra et al. [76] | 157 | Extrinsic, malignant | Double J | 64 | 14 |
| Rosevear et al. [79] | 29 | Extrinsic, malignant | Double J | 81 | 16 |
| Wenzler et al. [84] | 38 | Intrinsic, benign | Double J | 88 | 25 |
| Tal et al. [85] | 28 | Intrinsic, benign | Double J | 45 | 62 |
| Slavis et al. [86] | 3 | Intrinsic, benign | Wallstent | 100 | 51 |
| Reinberg et al. [87] | 3 | Intrinsic, benign | Wallstent | 100 | 12 |

**Table 53.2** Balloon dilation for ureteral strictures.

| Study | No. of strictures total (distal) | Etiology | Success rate total (distal), % | Follow-up (months) |
|---|---|---|---|---|
| Chang et al. [91] | 11 (7) | Benign | 71 (82) | 10 |
| Johnson et al. [92] | 24 (11) | Benign | 63 (50) | 21 |
| O'Brien et al. [93] | 24 (9) | Benign | 60 (56) | 17 |
| Kramolowsky et al. [94] | 14 (9) | Benign | 64 (78) | 22 |
| Netto et al. [95] | 19 (14) | Benign | 58 (57) | 24 |
| Ravery et al. [89] | 11 | Inflammatory | 40 | 16 |
| Eshghi and Schwalb [99] | 25 | Benign, infectious | 74 | 36 |

uretero-arterial, ureteroenteric, or ureterovaginal fistula, ureteral perforation, uncontrollable bleeding, and complete obstruction [78]. See Table 53.1.

## Balloon dilation

Balloon dilation of the distal ureter was first reported to be safe in a study by Clayman et al. in 1987 [88]. They showed that slow dilation produced less residual inflammation at 6 weeks. One week after dilation, trauma in the form of circumferential edema and thinning of the muscularis propria was present, but resolved by 6 weeks. See Table 53.2.

Ravery and colleagues presented their results of 11 ureteric strictures in patients with inflammatory strictures (tuberculosis, iatrogenic injury, radiation therapy, and parasitosis). Balloon dilation was performed at 10–20 atm for 5–15 minutes. With a mean follow-up of 16 months, the long-term success rate was 40% [89]. Richter et al. studied 127 patients with malignant ureteral strictures, 46 via balloon dilation (antegrade), wall stents in 31, endoureterotomy in 37, percutaneous ureteroneocystotomy in 34, and bougie and stents in 13 [81]. They found that balloon dilation was only successful in short benign ureteral strictures with intact vascular supply. Byun et al. evaluated 43 ureteral strictures: 22 malignant and 21 benign. The success rates at 36 months were much higher for benign then for malignant strictures (57 vs. 14%, $P < 0.001$). No patients with strictures greater than 2 cm were successfully dilated, supporting the use of balloon dilation for short benign ureteral strictures [90].

Overall success rates ranged from 50 to 82% in published studies [91–95]. The large discordance is success rates likely reflects the differing inclusion criteria and etiology. There still remains no consensus of the optimal balloon size and technique for the procedure. In the studies cited here, the number of cycles (1–10), balloon size of 4–10 mm, duration of inflation (up to 10 minutes), and stent size (6–16 Fr) were not uniform [96, 97].

A study by McIntyre et al. examined 1784 patients who underwent radiation for cervical cancer from 1960 to 1989 and found a 0.15% risk of developing distal ureteral stricture per year, culminating at 2.5% incidence at 20 years [98].

With improvement in endoscopic techniques and equipment, it is now the preferred initial treatment for benign ureteral strictures. Treatment success rates have been reported to range from 53 to 82% and appear to have increased success with shorter strictures and non-ischemic strictures [42].

Eshghi and Schwalb reported on 25 distal ureteral strictures, mostly postsurgical, with various lengths, dilated to 18 Fr. The 36 month success rate was 74% [99]. Liatsikos et al. examined the use of self-expanding metallic ureteral stents in 90 patients over a median of 15 months with a patency rate of 51% [100]. The Memokath 051 ureteral stent (a nickel-titanium stent) showed a success of 92% [97]. Due to its lower success rate compared with endoscopic incision modalities, balloon dilation is best reserved for short areas of stricture [89, 96, 101–103]. Overall, balloon dilation has a lower success rate then endoureterotomy and should likely be reserved for use only in short, non-ischemic strictures, if endoureterotomy is not feasible or significant comorbidities limit treatment options.

### Endoureterotomy

Endoureterotomy has multiple approaches with similar success rates. The different techniques – cold knife, the Acucise device, lasers, and electrocautery – are all summarized in this chapter. Success rates vary secondary to technique, etiology, and location. Overall success rates were 70–100% in reviewed studies, better than for balloon dilation.

Lopatkin et al., reported on 21 patients treated with retrograde cold-knife incision for their ureteral or UPJ strictures including seven strictures in the mid to distal ureter over a 22 month period, with a success rate of 86% in the ureter [104]. Schneider et al. also reported on using cold knife for 13 primary and 43 patients with secondary obstruction of the UPJ or ureter with a success rate of 83% at 15 months for distal stricture [110]. Wolf et al. reported on 38 endoureterotomies with a success of 78% at 28 months [64]. Factors associated with failure of endoureterotomy was renal function less than 25% an ischemic etiology and complete obstruction. In strictures >1 cm, the use of a stent >12 Fr and injection of triamcilinone improved outcomes.

Chandhoke et al. reported on the Acucise cutting balloon catheter on 28 patients with UPJ or ureteral obstruction, including five in the distal ureter. The symptomatic success rate was 80% in the distal ureter at 3 month follow-up [105]. Cohen et al. reported 29 month follow-up success, defined as radiographic resolution or symptom relief, in 80% of the distal strictures [106]. Preminger et al. reported on a multicenter trial on 40 ureteral strictures with a patency rate of 58% in the distal ureter [32].

Singal et al. reported use of holmium laser followed by balloon dilation on 12 ureteral strictures with a success rate of 78% at 9 months [107]. In a study by Ibrahim et al., 55 patients with a mean stricture length of 1.92 cm underwent retrograde laser endoureterotomy. Patients were randomized into single ureteral stent or double ureteral stent for 8 weeks after therapy. They found an overall successful treatment rate of 67%, and for strictures >1.5 cm the double ureteral stent had a success rate of 82% compared to 39% for a single ureteral stent [97, 108].

Eshghi and Schwalb reported on 61 strictures treated with a cold-knife endoureterotome and endoureterotomy scissors with no immediate side effect and 96% success at 24 months [99].

Ureterointestinal anastomotic strictures treated with cold-knife endoureterotomy and stent placement showed success rates at 1, 2, and 3 year follow-up of 86, 67, and 60% respectively [109]. See Table 53.3.

### YAG laser

In a study of five patients treated with YAG laser endoureterotomy for anastomotic stricture in transplanted kidneys, 100% had resolution of stricture at a median follow-up of 52 months [111]. Gnessin et al. reported on 35 patients with benign strictures treated with YAG laser endoureterotomy: 14 had distal ureteral strictures at 27 months and 78% had resolution of stricture. Most failures occurred within less than 9 months of surgery [112]. Mano et al. treated nine patients with ureterovesicular strictures posttransplantation with either cold-knife or YAG endoureterotomy with a success rate of 83% at 44 months [50]. Han et al. reported a success rate of 76.5% out of 77 patients over a median of 19.6 months. Stone disease, positive presenting symptoms, and short length of the stricture were identified as variables with a good predictor [113].

## Summary and conclusions

The most essential aspect of endoscopic and endourologic management of distal ureteral stricture is an initial thorough assessment of cause, severity, length, and vascular

**Table 53.3** Endoureterotomy for benign ureteral strictures.

| Study | No. of strictures total (distal) | Technique | Success rate total (distal), % | Follow-up (months) |
|---|---|---|---|---|
| Lopatkin et al. [104] | 7 (4) | Cold knife | 86 (100) | 22 |
| Schneider et al. [110] | 12 (12) | Cold knife | 83 (83) | 15 |
| Chandhoke et al. [105] | 8 (5) | Acucise | 75 (80) | 4 |
| Cohen et al. [106] | 8 (5) | Acucise | 75 (80) | 29 |
| Preminger et al. [32] | 40 | Acucise | 55 (58) | 9 |
| Wolf et al. [64] | 38 (29) | Cold knife | 82 (78) | 28 |
| Singal et al. [107] | 10 (12) | Holmium laser | 67 (70) | 11 |
| Eshghi and Schwalb. [99] | 61 | Cold knife | 98 | 24 |

viability of the stricture. The coexisting risk factors and comorbidities will further define the path towards the treatment. An adequate training in endoscopic and interventional techniques along with a wide variety of instruments are basic requirements for treating challenging cases with altered anatomies. As a rule, once access has been secured across a stenotic area in most cases balloon dilation with 3–6 weeks of stenting provides an acceptable success rate. In more complicated cases staged procedures and use of dedicated instruments such as the cold-knife endoureterotome is recommended for better results. The dilemma is that, similar to other entities such as renal ureteropelvic tumors there are no standardized techniques or protocols to provide an adequate number of cases with level 1 evidence to allow definitive statements about some of these treatment modalities. With more time and expanded use of these techniques such recommendations will come to fruition.

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# 54

# Endoscopic Management of Ureteroenteric Strictures

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## Introduction

Ureteroenteric strictures (UES) represent an uncommon, but potentially devastating and difficult to treat complication of urinary diversion. UES may occur in 4–8% of cases [1, 2]. Open surgical repair is the gold-standard therapy, with reported long-term success rates of up to 80%, but it can be very difficult, with greater morbidity due to scarring and intra-abdominal adhesion formation [3–6]. The decreased morbidity of primary endoscopic management, as well as the continued refinement of endourologic equipment and techniques, has led to increased interest in this approach despite inferior outcomes compared to open revision. Uniformly, endoscopic treatments result in lower blood loss and length of hospital stay, as well as rapid recovery [7]. Initially felt to be suitable only for those unfit for open repair, endourologic management is now typically offered as first-line treatment. Due to the relatively low incidence of UES, most studies evaluating primary endoscopic therapy are small, which impairs direct comparison of modalities. Often, patients with UES are eliminated from larger studies evaluating the utility of endoscopic techniques for benign stricture disease. Additionally, no randomized studies comparing open and endoscopic management exist.

In this chapter we examine the current literature and published techniques pertaining to endoscopic management of UES.

## Background

Most nonmalignant strictures manifest within 2 years of the initial urinary diversion [8] and multiple factors are believed to contribute to their occurrence. Benign UES have been reported in all types of urinary diversions and are thought to be associated with ischemic changes in the ureter [9]. Multiple studies have noted an increased stricture rate on the left side, possibly related to the greater degree of ureteral dissection, as well as tunneling and kinking of the ureter through the mesentery [4, 8–11]. Several studies have investigated effects of technical variations at the time of diversion, although some are contradictory or provide results that do not reach significance due to a lack of subjects and statistical power. A running suture at the anastomosis may increase the incidence of strictures [12]. Use of a nonrefluxing anastomosis has been shown to raise the rates of stricture formation in comparison to a refluxing anastomosis [13]. The most studied technical consideration has been comparison of the Wallace (adjoined ureters implanted end to end) and Bricker (individually implanted) ureteral anastomoses, which has generally shown no difference in stricture frequency [10, 14]. The use of ureteral stents at the time of anastomosis is also controversial. Historically believed to assist in healing and alignment, and decrease the risk of urine leak, other studies have associated ureteral stenting with a greater likelihood of infection, and possible increased stricture formation [15–17]. Body mass index of $>30\,\mathrm{kg/m^2}$ and prior pelvic radiation [10] are also thought to influence the risk of developing a stricture.

## Presentation and diagnosis

Signs and symptoms of UES can include flank pain, malaise, failure to thrive, pyelonephritis, sepsis, hematuria, and worsening renal function [18, 19]. Some patients may develop strictures slowly and remain asymptomatic with only a rising creatinine level. This heterogeneity in

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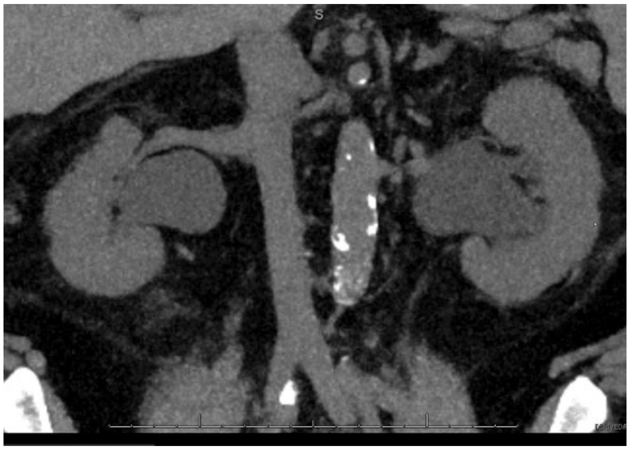

**Figure 54.1** Coronal CT scan showing bilateral hydronephrosis in a patient with bilateral uretero-ileal anastomotic strictures following radical cystectomy.

presentation necessitates routine laboratory and radiographic surveillance and close clinical follow-up [20]. Initial evaluation generally consists of serum chemistries and radiographic imaging. Renal ultrasound or computed tomography (CT) are most frequently utilized in the screening of hydronephrosis (Figure 54.1). Since reflux can mimic obstruction, it should be ruled out with other anatomic or functional studies. Free reflux of contrast into the ureter on loopography essentially excludes anastomotic stricture. If no reflux is seen on loopogram and renal function is adequate, renal scintigraphy can aid in the diagnosis of obstruction. Antegrade contrast studies such as intravenous urography, CT urography, and antegrade nephrostogram can also help diagnose a stricture and characterize its length and location as well as evaluate for filling defects that may herald recurrence of malignancy. Such a recurrence is relatively rare in comparison to benign etiologies of stricture, but should be considered if appearing at more than 6 months after initial diversion [21–23]. Urine cytology and biopsy may be indicated before definitive treatment of the stricture.

## Indications for therapy

Patients who develop symptomatic strictures generally require early relief of obstruction. Asymptomatic patients also benefit from decompression, as poorer treatment outcomes have been observed with an ipsilateral renal function of less than 25% [24]. Indications for urgent intervention include intractable flank pain, obstructive pyelonephritis, rising creatinine, and impending sepsis. Due to the inherent difficulty of retrograde approaches in patients with urinary diversions, percutaneous nephrostomy is most often utilized to relieve obstruction. Placing a nephrostomy tube also facilitates antegrade diagnostic studies to assist in stricture localization, characterization, and surgical planning.

## Endourologic techniques

Treatment of UES has largely developed from techniques used for ureteral stricture disease. Approaches can be retrograde, antegrade, or a combination of both. Because initial management of UES involves decompression of the collecting system with a percutaneous nephrostomy, this, in combination with the technical challenges of identifying the ureteral anastomosis in a conduit or neobladder, make an antegrade approach preferred.

Since the key manipulations required to treat UES occur in the distal ureter, it is important to have a percutaneous access which will allow easy passage of instruments to this area. Therefore, upper pole or upper interpolar renal access is preferable to lower pole access. If the patient has a lower pole nephrostomy tube that was previously placed simply to drain the kidney, strong consideration should be given to relocating the access to the upper or mid collecting system. If the patient does not have a nephrostomy tube at the time of definitive management, access is usually obtained with ultrasound guidance and confirmed with fluoroscopy. A urine culture should be obtained and any bacteriuria treated prior to definitive endoscopic treatment of a UES.

Video 54.1 demonstrates endoscopic treatment of UES in detail. After induction of general anesthesia, patients with ileal conduits are placed in flank position to provide easy access to the nephrostomy as well as the urostomy, and both the flank and abdomen are sterilely prepared and draped. For left-sided strictures, which are most common, the patient is placed in the right lateral decubitus position and for right-sided strictures the patient is positioned in left lateral decubitus. Standard cushioning done for flank approaches, including an axillary role, is utilized. Patients with neobladders are positioned prone with a urethral catheter in place. The technique used for a patient with a neobladder is similar to that used for a benign ureteral stricture treated with an antegrade approach, so the following description will be limited to the method used for patients with ileal conduits.

The procedure begins with antegrade injection of contrast through the nephrostomy to demonstrate the stricture (Figure 54.2) and the renal and ureteral anatomy, as well as to assess for any filling defects in the kidney and ureter. A 0.038 or 0.035 inch hydrophilic tip guidewire is passed through the nephrostomy tube into the collecting system and manipulated through the ureteropelvic junction and down the ureter. Various 4 or 5 Fr angle-tipped

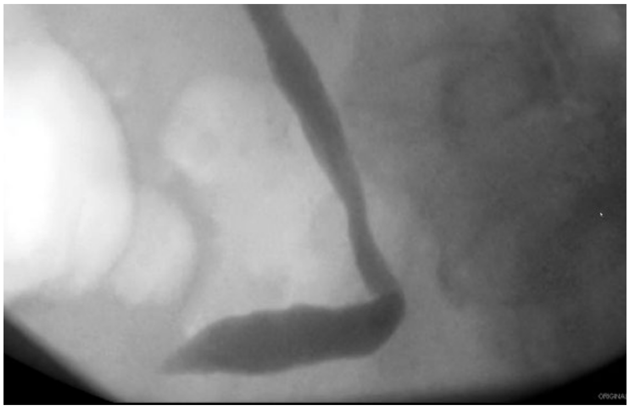

**Figure 54.2** Antegrade nephrostogram showing left ureter tapering to a stricture, with no contrast seen beyond the stricture.

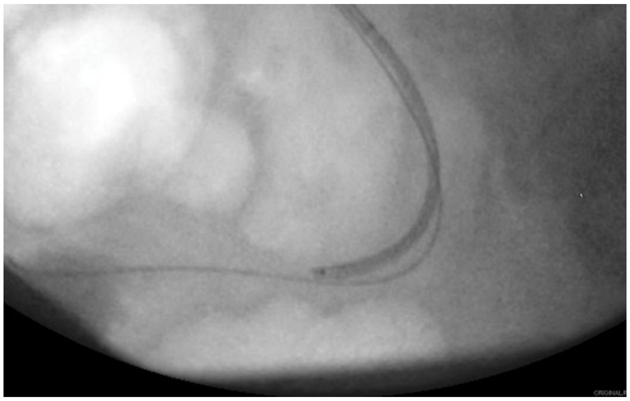

**Figure 54.3** Radiographic view of flexible ureteroscope examining left uretero-ileal anastomotic stricture. Guidewire is through the stricture into an ileal conduit.

catheters (Kumpe™, Cobra™) can assist in these manipulations. After incising the fascia along the wire with a scalpel, an 8/10 Fr coaxial dilator/safety wire introducer is passed over the working wire. A safety wire can then be placed down the ureter. Next, a 13 or 14 Fr short ureteral access sheath is advanced over the working wire. Further dilation or placement of a larger sheath is typically unnecessary. The renal collecting system and ureter can then be examined with a flexible fiber-optic or digital ureteroscope (Figures 54.3 and 54.4). Any suspicious lesions should be biopsied at this point. If the ipsilateral ureter happens to be very dilated, the tract can be upsized to a larger access sheath using an Amplatz dilating system, and an 18 Fr sheath can be placed in order to use a flexible cystoscope for subsequent manipulations. However, this is not typically necessary.

After establishing working access, any of the various treatment modalities reviewed herein can be employed. At the conclusion of treatment a ureteral stent is positioned to maintain patency during healing.

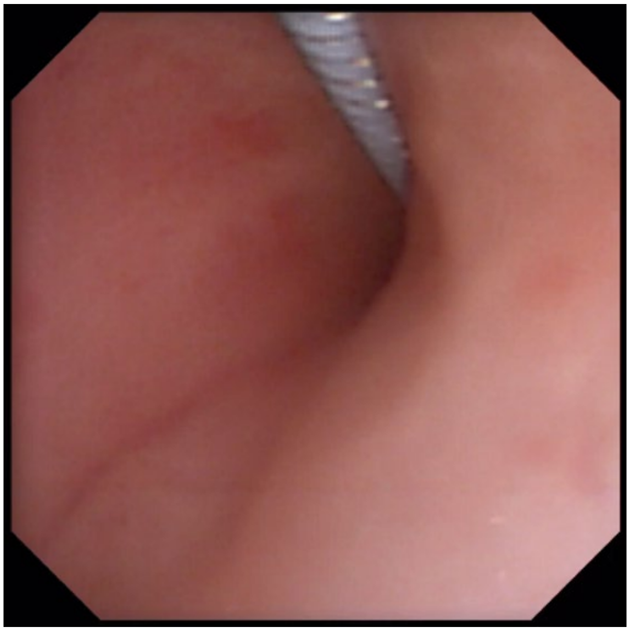

**Figure 54.4** Digital flexible ureteroscope view of uretero-ileal stricture with guidewire passing through the stricture. The area is too narrow to advance the ureteroscope close enough to perform laser endoureterotomy.

## Balloon dilation

The use of balloon dilation in urology was first described in the nineteenth century for the treatment of urethral strictures [25]. It was not until the 1980s that dilation was used in the treatment of ureteral strictures [26]. Since then, the use of ureteral balloon dilation has become commonplace in endourology. Balloon dilation may be used as primary endoscopic treatment, or in combination with other modalities. An advantage of balloon dilation when used as monotherapy is that it can be accomplished under local anesthesia and can be done by an interventional radiologist. The renal tract does not need to be dilated nor a working sheath placed. Once wire access is established, the dilation balloon is positioned under fluoroscopic guidance across the strictured area. The balloon is then slowly inflated with diluted radiographic contrast media until it assumes the typical hourglass shape caused by the stricture. Inflation continues until the hourglass shape gives way and the balloon is completely inflated (Figure 54.5). The dilation is then held for approximately 3–5 minutes before deflation. This cycle may be repeated as necessary until the entire stricture is treated. Figure 54.6 shows the endoscopic appearance of a UES immediately after balloon dilation.

## Endoureterotomy

Endoureterotomy, or incision of the ureter, was introduced due to the disappointing long-term success of

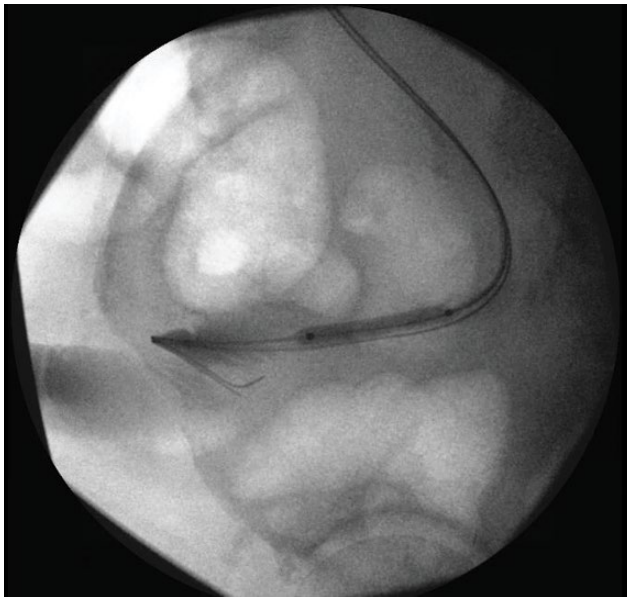

**Figure 54.5** Radiographic view of an inflated balloon catheter dilating a stricture.

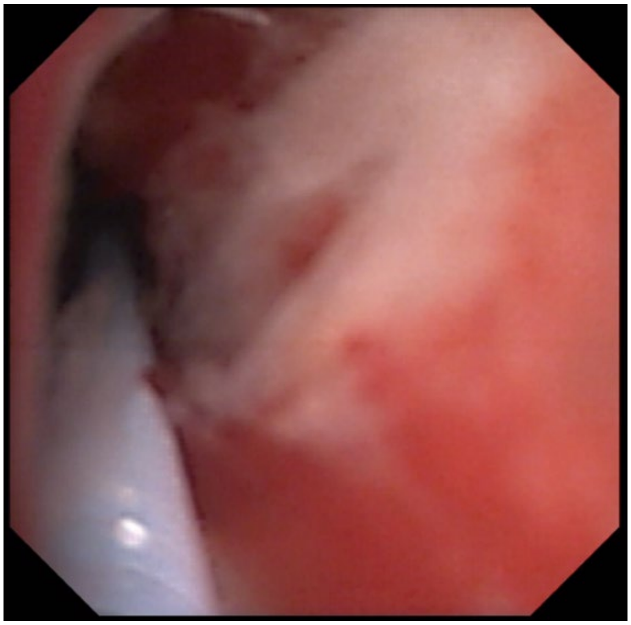

**Figure 54.6** Endoscopic view of a stricture after balloon dilation. The passage to the ileal conduit can be seen in the upper left quadrant.

balloon dilation. Endoureterotomy may be performed using a variety of instruments, including cold knife, electrocautery, or laser. Additionally, the Acucise™ cutting balloon catheter combines electrocautery with balloon dilation of the ureter. The primary goal of each modality is to create a full-thickness incision that extends approximately 1 cm beyond each end of the stricture and into peri-ureteral fat. This is confirmed by visualization of peri-ureteral fat or extravasation of contrast on fluoroscopy [27]. For dense strictures, endoscopic injection of 3–5 ml of 40 mg/ml triamcinolone into the incised stricture has been advocated to improve outcome [24, 28].

### Cold-knife endoureterotomy

Cold-knife treatment typically requires a semirigid ureteral resectoscope for retrograde incision of the stricture. Because of the larger diameter and lack of flexibility, the extent of narrowing that can be treated under direct vision is limited. An alternative method has been described in which a flexible wire-mounted cold knife is passed antegrade through a nephrostomy and then withdrawn to perform an endoureterotomy [29]. This may be performed under fluoroscopic guidance or visually in conjunction with a ureteroscope. Regardless, several incisions may be required. Cauterization of urothelial or mucosal bleeding is not necessary and should be avoided because of the risk of thermal damage [30]. Ureteral stents are typically utilized as the ureter heals.

### Electrocautery endoureterotomy

Electrocautery is typically performed under direct visualization through a semirigid or flexible ureteroscope. Safety wires should be insulated to avoid application of electrical current outside the target treatment area. A 2 or 3 Fr Greenwald electrode is advanced through the ureteroscope and incision is made on pure cutting current at a power of 75 W. Multiple controlled incisions into the fibrotic tissue may be made under direct visual control. It is challenging, but imperative, to maintain precise, linear, incision tracking with a flexible ureteroscope to avoid surrounding thermal damage. Lovaco and associates reported a method in which a guidewire is passed antegrade and a dilation balloon is passed retrograde, inflated at the stricture, and pulled down to intussuscept the stricture into the bowel segment. The stricture is thus well exposed and can be incised precisely from below [19]. This method seems to provide a theoretical advantage of decreased injury to retroperitoneal blood vessels and bowel, but no subsequent publications of this technique have been forthcoming.

### Acucise balloon catheter endoureterotomy

The Acucise™ cutting balloon catheter (Applied Medical, Rancho Santa Margarita, CA, USA), comprising a monopolar electrocautery cutting wire and a 24 Fr 3 cm balloon can be used to treat strictures throughout the ureter [31]. After identification of the stricture, the device is deployed over a guidewire and positioned so the radiopaque markers straddle the stricture. Special attention must be given to the location of the cutting wire after visual inspection to avoid any peri-ureteral vessels.

Treatment begins with inflation of the balloon with 2 ml of dilute contrast media along with simultaneous activation of the cutting wire at 75 for a maximum of 5 seconds. Similar to pure balloon dilation, Acucise balloon inflation may be maintained for 3–5 minutes. The manufacturer suggests no more than two treatments be undertaken at one time. Presence of a safety wire during electrocautery activation is not recommended because of potential conduction injury.

### Laser endoureterotomy

Laser endoureterotomy for UES may be performed with a variety of lasers, but the holmium:YAG laser is preferred because of its favorable safety characteristics with a depth of tissue penetration of only 0.4 mm [27]. Incision is performed visually through a flexible ureteroscope with a 200 µm fiber set at 1 J and 10 Hz (10 W) (Figures 54.7 and 54.8). Direct visual inspection prior to incision is necessary to avoid any pulsations representing peri-ureteral vessels and, afterwards can confirm the presence of fat. Again, care must be taken to make precise cuts to avoid thermal damage to a wide area of the ureteral circumference, which can be quite challenging with a flexible ureteroscope. After incision, contrast injection into the ureter should reveal extravasation (Figure 54.9).

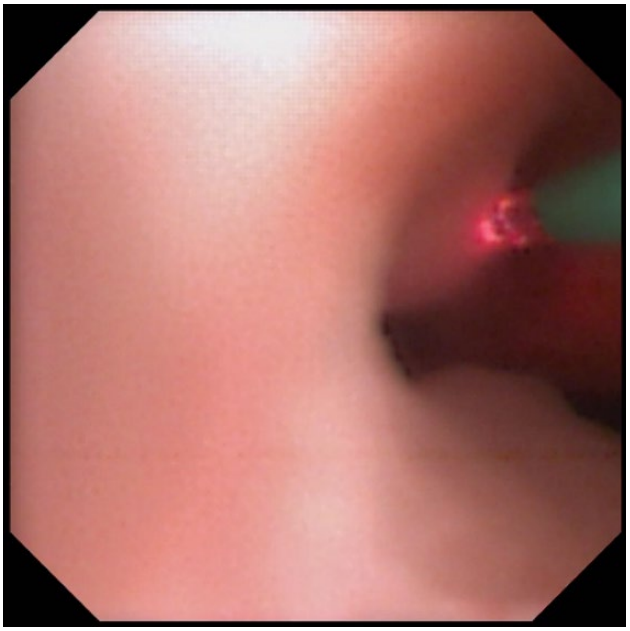

**Figure 54.7** A 200 µm holmium laser fiber poised to perform endoureterotomy. The laser is positioned just inside the conduit and drawn back through the stricture into the ureter (see Video 54.1).

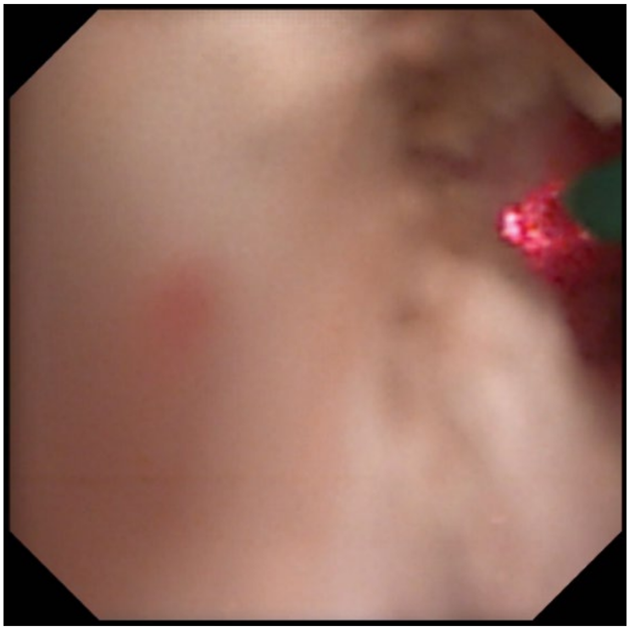

**Figure 54.8** View of incised stricture after first pass with the laser. Laser is positioned to start the second pass to deepen the incision.

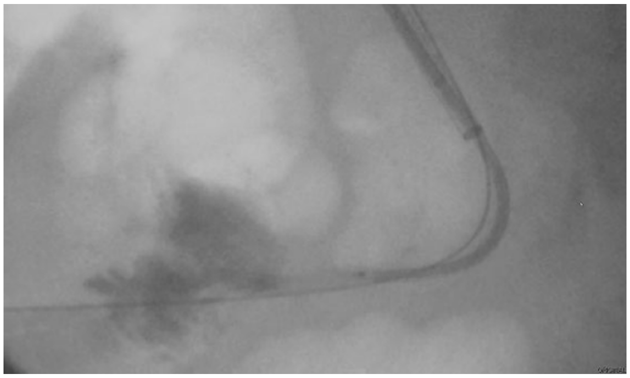

**Figure 54.9** Radiographic view of contrast media injection through ureteroscope resulting in extravasation, indicating full-thickness endoureterotomy.

## Post-treatment ureteral stenting

Regardless of the primary method used to treat UES, ureteral stenting is commonly employed to allow healing, limit extravasation of urine, and maintain patency. Ideal duration of stenting in the postoperative period is undefined, and four to six weeks may be reasonable. There is some evidence to suggest that prolonged stenting may be detrimental and lead to tissue overgrowth and fibrosis [27]. There is also disagreement as to the optimal stent diameter. Some recommend larger stents or even double stents, while others that argue an excessively large stent may induce ischemia and scarring [24, 32, 33].

Ureteral stents may be deployed either forward or retrograde in a through-and-thorough fashion over a guidewire with fluoroscopic assistance. Synthetic double-J stents are most commonly used. For patients with ileal conduits, a nephroureterostomy tube can be positioned in reverse fashion, with the distal pigtail in the renal pelvis and the proximal port in the urostomy bag [34].

For patients with severe comorbidities or those who do not want to attempt a definitive procedure, chronic ureteral stenting may be acceptable, despite the risk of encrustation, infection, and the need for frequent exchanges (every 3–6 months). This method is often successful in relieving obstruction but does not treat the underlying stricture.

To alleviate some of the problems with polymer stents, the use of metal stents has been investigated. Metal stents offer the benefits of resistance to compression and increased exchange interval [35]. Metal stents have been used previously in the setting of malignant obstruction with some success, but their use in benign stricture disease is controversial [36]. Their use in UES is even more limited. Many studies evaluate their use in the context of general ureteral obstructions, both benign and malignant, and report on only a handful of UES as a subgroup.

A variety of metal stents have been used: self expandable, balloon expandable, thermo-expandable shape memory, covered, and double pigtail stents [37]. Each type has its own manufacturer-provided deployment device and instructions. Many require dilation of the stricture before insertion. Details regarding the frequency of exchanges is device-specific. The following metal stents have been used primarily in ureteral strictures of both benign and extrinsic malignant obstructions, but have also been reported in UES in small numbers. There are few direct comparisons of these products in treatment of ureteral obstruction, and fewer in the setting of UES.

Resonance (Cook Medical, Bloomington, IN, USA) is made of a magnetic resonance imaging (MRI)-compatible nickel-cobalt-chromium-molybdenum alloy without a lumen and is similar in shape to a double-J stent. It is deployed through an 8 Fr sheath introducer. The Memokath 051 (Endotherapeutics, Epping, NSW, Australia) is a thermo-expandable shape memory stent made of nitinol and has a lumen. The stent is deployed over a guidewire with the provided sheath. The stent is then expanded *in situ* with the injection of normal saline at 65 °C [38]. The Allium URS stent (Allium Medical, Caesarea Industrial Park South, Israel) is a nickel-titanium alloy mesh invested with a biocompatible polymer to prevent tissue ingrowth and encrustation. It is available in two sizes, 30 and 24 Fr, and can be retrieved endoscopically. It is deployed over a guidewire in conjunction with the provided 10 Fr sheath [39]. The Uventa (TaeWoong Medical, Gyeonggi-do, South Korea) incorporates a triple-layer design consisting of a layer of PTFE between two nitinol layers in an expandable mesh capable of treating the entire length of the ureter. It is placed over a guidewire with a preloaded delivery system. The stent comes in 7, 8, and 10 Fr diameters.

## Novel techniques

Recently, there have been descriptions of novel endoscopic treatments of UES. These are typically technologies borrowed from other fields which have been adapted for experimental use in the ureter. Little or no comparative data exist, and publications have very limited follow-up.

In 2010, Boylu and associates reported use of a peripheral cutting balloon microsurgical dilator initially designed for use in coronary angioplasty. The balloon features four longitudinal microsurgical blades on a 2 cm-long balloon that dilates to 8 mm. In their study of only three patients with 12 month follow-up, improvement in hydronephrosis and serum creatinine were observed [40]. In 2007 Orsi and colleagues treated four UES with the Polar-Cath balloon dilator (Boston Scientific, Marlborough, MA, USA), requiring only one re-intervention during 12 months of follow-up [41].

## Surgical outcomes

The definition of success varies in the literature, but typically involves radiographic improvement in – or resolution of – obstruction, as well as absence of pain, infection, or stent, with recovery of normal activity.

### Balloon dilation

Balloon dilation is the oldest and most thoroughly evaluated endourologic treatment modality. Ten contemporary studies were reviewed comprising a total of 232 primary procedures. Success rates varied from 0 to 67% with a mean of approximately 22% [6, 18, 42–50] (Table 54.1). Follow-up ranged from 9 to 29 months. Larger contemporary series with mean follow-up of greater than 24 months demonstrate similar levels of success and reduced patency rates at longer-term follow-up [42]. There was great variability pertaining to balloon size, inflation pressure, time of inflation, and number of cycles needed to perform successful dilation. There was no standardization in the size of stent used postoperatively nor in the duration of stenting. When reported, stricture length was the parameter most predictive of treatment success or failure, with longer strictures having worse outcomes [6, 42, 43, 47].

**Table 54.1** Results following balloon dilation of ureteroenteric strictures.

| Study | Number of procedures | Mean follow-up (months) | Success rate (%) | Stricture location | Stricture length | Stricture diameter | Balloon size | Duration/cycles/ pressure | Stent size (Fr) | Stent duration (weeks) |
|---|---|---|---|---|---|---|---|---|---|---|
| Schöndorf et al. 2013 [42] | 84 | 29 | 25 | NS | >1 cm predicted failure | ND | DS | DS | DS | 4–6 |
| Nassar and Alsafa 2011 [43] | 16 | 47 | 50 | NS | >1 cm predicted failure | ND | DS | DS | 7 | 4–6 |
| Milhoua et al. 2009 [18] | 4 | 16 | 0 | NS | NS | NS | DS | DS | 6–16 | 1.5–9 |
| Tal et al. 2007 [44] | 6 | 26 | 0 | ND | ND | ND | DS | DS | DS | DS |
| DiMarco et al. 2001 [6] | 52 | 24 | 15 | NS | >1 cm predicted failure | NS | 8–10 | DS | DS | 3–6 |
| Kwak et al. 1995 [45] | 18 | 9 | 28 | ND | ND | ND | 8 | 45 s/3/15 atm | 10 | 4 |
| Aliabadi et al. 1990 [46] | 3 | 12 | 67 | ND | ND | ND | 6–8 | 10 m/DS/DS | 10 | 6 |
| Beckman et al. 1989 [47] | 5 | 22 | 60 | ND | >2 cm less successful | ND | 4–8 | DS | 7–10 | 4–8 |
| Shapiro et al. 1988 [48] | 37 | 12 | 16 | NS | ND | NS | 4–10 | 1–2 min/ DS/17 atm | 8–24 | 1–6 |
| O'Brien et al. 1988 [49] | 7 | 12 | 14 | ND | ND | ND | 4–6 | DS/DS/6–17 atm | DS | DS |

NS, predictor discussed but not significant; ND, predictor not discussed; DS, details not specified.

## Endoureterotomy

Due to the poor outcome and long-term durability of balloon dilation, endoureterotomy has become the initial endoscopic treatment of choice [18]. Regardless of the energy source used, incision of the ureter, with or without concomitant balloon dilation, appears to be more effective than balloon dilation alone. In the 15 studies included in this review (Table 54.2), 215 individual procedures were captured. Success rates were reported between 33 and 100% (mean of 60%) with a follow-up ranging between 10 and 60 months [3, 7, 18, 19, 24, 28, 29, 42, 43, 50–58]. Studies of cold-knife incision were the least common, and the lack of new publications over the past several years indicates this technique has largely been abandoned. Wire-mounted cold-knife incision achieved a patency rate of 60.5% with 3 year follow-up in the largest and most recent study of this technique in 2003 [29].

Electrosurgical and holmium laser endoureterotomy are more commonly cited in the literature and have similar success rates (70 and 64%, respectively), although the former group had longer follow-up [3, 7, 18, 19, 28, 42, 56–58]. These techniques are advantageous because they allow direct visual inspection and incision of the ureter. Additionally, these modalities utilize instruments commonly used in other urologic procedures.

Acucise incision has demonstrated superiority to balloon dilation with a mean success rate of 35%, which is lower than the methods which use direct visualization [18, 24, 42, 52–55]. Head-to-head comparison of each modality is difficult. Even in the study by Schondorf and associates [42], in which patients underwent balloon dilation, Acucise, or holmium laser endoureterotomy, patients were not randomized and the choice of modality used was not explained. Despite this, as well as different patient numbers in each group, Acucise and holmium laser incision had similar success rates of 33%. Electroincision and cold-knife incision were not evaluated in this study.

As with balloon dilation, all procedures were concluded with stent placement, but no consensus on stent size (6–22 F) or duration (1.5–28 weeks) was noted. Six weeks was the most commonly cited duration of stenting [7, 19, 50, 52–54, 56]. When assessed, stricture length less than 1 cm and ipsilateral renal function greater than 25% were the strongest predictors of success. As would

**Table 54.2** Results of endoureterotomy techniques for ureteroenteric strictures.

| Study | Number of procedures | Mean follow-up (months) | Success rate (%) | Stricture location | Stricture length | Stricture diameter | Balloon size | Duration/ cycles/pressure | Stent size (Fr) | Stent duration (weeks) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Cold knife** | | | | | | | | | | |
| Nassar and Alsafa 2011 [43] | 21 | 47 | 52 | NS | >1 cm less success | ND | DS | DS | 7 | 4–6 |
| Poulakis et al. 2003 [29] | 43 | 38.8 | 60.5 | NS | >1.5 cm predicted failure | ND | NA | NA | 8–12 | 6–12 |
| Bierkens et al. 1996 [50] | 2 | 12 | 100 | ND | ND | ND | NA | NA | 12 | 6 |
| Schneider et al. 1991 [51] | 2 | 15 | 100 | ND | ND | ND | NA | NA | 14 | 3–6 |
| **Electrocautery** | | | | | | | | | | |
| Lovaco et al. 2005 [19] | 25 | 51 | 80 | NS | Greater length, likely failure | ND | DS | DS | 6–7 | 6 |
| Meretyk et al. 1991 [28] | 14 | 28.6 | 57 | ND | ND | ND | 6–12 | DS | 8–27 | 3–28 |
| Kramolowsky et al. 1988 [3] | 7 | 13.5 | 71 | ND | ND | ND | 10–12 | DS | 7–18 | >2 |
| **Electro-incision (Acucise)** | | | | | | | | | | |
| Schondorf et al. 2013 [42] | 9 | 29 | 33 | NS | >1 cm predicted failure | ND | DS | DS | DS | 4–6 |
| Milhoua et al. 2009 [18] | 2 | 23.2 | 50 | NS | NS | NS | DS | DS | 6–16 | 1.5–9 |
| Touitiet al. 2002 [52] | 6 | 16 | 50 | ND | ND | ND | NA | NA | 8–12 | 6 |
| Lin et al. 1999 [53] | 10 | 24 | 30 | NS | NS | NS | NA | NA | 10 | 6 |
| Kabalin et al. 1997 [54] | 4 | 22 | 10 | ND | ND | ND | NA | NA | 10 | 6 |
| Wolf et al. 1997 [24] | 9 | >36 | 39 | left more likely to fail | NS | NS | NA | NA | 7–16 | variable |
| Preminger et al. 1997 [55] | 9 | DS | 33 | ND | ND | ND | NA | NA | 6–7 | 3–11 |
| **Holmium laser** | | | | | | | | | | |
| Schondorf et al. 2013 [42] | 3 | 29 | 33 | NS | >1 cm predicted failure | ND | DS | DS | DS | 4–6 |
| Milhoua et al. 2009 [18] | 15 | 23.2 | 33 | NS | NS | NS | DS | DS | 6–16 | 1.5–6 |
| Hibi et al. 2007 [56] | 3 | 60.5 | 100 | NA | NA | NA | NA | NA | 12 | 6 |
| Watterson et al. 2002 [7] | 24 | 22.5 | 71 | Left tended to fail | >1 cm tended to fail | NS | 6 | DS | 6–12 | 6 |
| Laven et al. 2001 [57] | 19 | 20.5 | 57 | Left tended to fail | ND | ND | NA | NA | 7–14 | 4–6 |
| Singal et al. 1997 [58] | 9 | 10.8 | 89 | ND | ND | ND | 6–8 | DS | 6–12 | 4–6 |

NS, predictor discussed but not significant; ND, predictor not discussed; DS, details not specified.

Table 54.3 Results of stenting for ureteroenteric strictures.

| Study | Number of strictures | Type of stent | Time to exchange | Mean follow-up (months) | Success rate (%) | Secondary procedure (%) | Worsening renal failure (%) | Stent migration (%) | UTI (%) |
|---|---|---|---|---|---|---|---|---|---|
| **Synthetic** | | | | | | | | | |
| Tal et al. 2007 [44] | 20 | 17 10.2 Fr NU/ 3 double-J | q3m | 26 | 45 | 41 | 15 | 5 | 0 |
| **Metal** | | | | | | | | | |
| Campschroer et al. 2014 [61] | 56 | 8 mm Wallstent | DS | 39.2 | 41.1 | 22.4 | DS | 1.8 | DS |
| Liatsikos et al. 2010 [62] | 6 | 6 Fr Resonance | DS | 6.8 | 50 | 50 | 0 | 0 | 0 |
| Liatsikos et al. 2007 [63] | 24 | 6–8 mm self-expanding | NA | 21 | >50 | 62.5 | 0 | 0 | 0 |
| Rapp et al. 2004 [64] | 6 | 8 mm Wallstent | NA | 10 | 100 | 0 | 0 | 0 | 0 |
| Wakui et al. 2000 [65] | 1 | 6 mm Palmaz stent | NA | 11 | 100 | 0 | 0 | 0 | 0 |
| Palascak et al. 2001 [66] | 10 | 8–10 mm Wallstent | NA | 22.4 | 100 | 10 | 0 | 0 | 0 |
| Daskalopoulos et al. 2001 [67] | 3 | 6–10 mm Wallstent | NA | 9 | 100 | 0 | 0 | 0 | 0 |
| Barbalias et al. 1998 [68] | 6 | 8 mm self-expanding | NA | 12 | 100 | 25 | 0 | 0 | 0 |
| Pollak et al. 1995 [69] | 6 | 10 mm Wallstent | NA | 6 | 16.7 | 0 | 0 | 0 | 25.6 |
| Reinberg et al. 1994 [70] | 2 | 8 mm Wallstent | NA | 12.5 | 100 | 0 | 0 | 0 | 0 |
| Sanders et al. 1993 [71] | 2 | Palmaz stent | NA | 7 | 100 | 0 | 0 | 0 | 0 |

NS, predictor discussed but not significant; ND, predictor not discussed; DS, details not specified; NU, nephroureterostomy; UTI, urinary tract infection.

be expected, some investigators demonstrated lower success rates for left-sided strictures.

## Chronic stenting as long-term management

Chronic stenting (Table 54.3) is most often utilized for patients who are too ill for definitive intervention, have a limited life expectancy, or wish to be less aggressive with treatment. Despite the use of chronic stenting in other ureteral obstructive processes, little data is available for its use in management of UES. Only one study reported long-term data for chronic stenting [44]. Success was only 45% at 26 months and periodic exchanges were necessary. Although stent exchange in patients with ileal conduits is not typically complicated, sometimes the altered anatomy can make exchanges difficult [59, 60].

Interest in metal stents is growing and several small studies have evaluated their use. Because of heterogeneity in metal stent designs, assessing them as a single group may not be appropriate. As described previously, there are a variety of metal stents (self-expandable, balloon expandable, thermo-expandable shape memory, covered, and double pigtail stents) for UES. The most studied are the Wallstent self-expandable stent (Boston Scientific), the Palmaz balloon-expandable stent (Palmaz Scientific, San Antonio, TX, USA) and the Resonance stent (Cook Medical). The Wallstent and other self-expandable stents are the best reported with 108 procedures. Overall success was 62% (range of 16.7–100%) [61–70]. However, most studies are small and have limited follow-up (6–39 months). In the single largest and most contemporary study of 56 procedures, success was 41.1% with mean follow-up of 39.2 months [61]. Balloon expandable stents such as the Palmaz stent have similarly reported success rates of 100%; however, this is in only three reported procedures with mean follow-up of 10.3 months [63, 65, 68, 71]. Resonance double-J metal stents were also reported; however, success was only 50% at a mean of 6.8 months [62]. Newer thermo-expandable shape memory stents like the Memokath 105 are being used, but both short- and long-term data are lacking [72, 73]. Clearly, more research with larger cohorts and longer follow-up is needed.

## Complications

Complications of endourologic management of UES include pyelonephritis, sepsis, and bleeding. In the most contemporary series of 96 interventions, there were a total of nine infectious complications [42]. Overall, balloon dilation had the fewest side effects and complications. Endoureterotomy is known to have increased risks compared to balloon dilation. The most serious complications involve vascular injury. In the series of 30 endoureterotomies of Wolf and colleagues, there was one reported laceration of the common iliac [24]. More recent series using direct visualization techniques do not report any serious bleeding complications [7, 19, 42]. Overall, it appears that as the techniques become more refined, the likelihood of complications decreases.

Complications related to stenting are primarily infection, encrustation, and obstruction [44]. Even use of metal stents has risks. Because of the heterogeneity of devices, it is again hard to group them as a whole. The resonance stent, most notably, was found to have a migration rate of 90% in one study [74], however most investigators have not encountered such a high incidence [62]. As many of the studies involving metal stents included strictures other than UES, complications specifically pertaining to UES are hard to ascertain. Based on the literature, there does appear to be a risk of tissue ingrowth [75]. Tables 54.1–54.3 summarize outcomes pertaining to complications of endoscopic management of UES.

## Postoperative follow-up

Due to the high failure rate of endourologic treatment methods, close monitoring is imperative. While there are no standard guidelines on surveillance schedules, follow-up should include serum chemistries to monitor electrolytes and renal function, and routine imaging to assess for hydronephrosis or stability of renal morphology [18, 19, 29, 57]. Because UES are rare and can present in a heterogeneous fashion, and because multiple endoscopic treatment modalities exist, surveillance needs to be tailored to individual patients. Many UES patients will have a history of urothelial carcinoma and will be monitored routinely for recurrence of malignancy with computed tomography, which can also serve to monitor for return of UES. A reasonable follow-up protocol for UES may include serum chemistries as well as periodic imaging with ultrasound at intervals beginning at 3 months and increasing at the clinician's discretion. Any suggestion of recurrent obstruction, such as flank or abdominal pain, pyelonephritis, rising serum creatinine, or worsening hydronephrosis on imaging, should prompt a renewed investigation into the cause, using the same methods as described for initial evaluation.

## Conclusion

UES are a relatively uncommon but difficult to manage complication of urinary diversion. At this time, there are few if any definitive technical considerations at time of anastomosis to eliminate the risk of strictures. Initial management remains a dilemma, and advances in endoscopic technology have led to a variety of approaches. Despite inferior long-term success compared to open repair, endoscopic treatment remains a reasonable first-line approach in appropriately selected patients, and does not seem to greatly complicate matters should later open surgical revision become necessary. Balloon dilation is the safest and most easily accomplished procedure, but has disappointing durability. Endoureterotomy, with or without concomitant dilation, seems to have become the minimally invasive treatment of choice regardless of incision method, but has a slightly increased risk of complications. Generally, success is more likely in patients with right-sided strictures and satisfactory ipsilateral renal function. Stricture length less than 1 cm also appears to be a significant factor predicting success. Long-term stenting still remains a viable option for those willing to undergo periodic exchanges, and refinement of metal stent technology may lead to additional therapeutic choices. Since UES are relatively rare and tend to be treated at tertiary referral centers, an international collaborative registry gathering data on large numbers of patients may be the only rigorous way to evaluate these methods and advance techniques and outcomes.

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# 55

# Ureterorenoscopy: Ureteral Stents and Postoperative Care

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Ureteroscopy is commonly used to treat urolithiasis and has become a standard endoscopic technique replacing open stone surgery of the past. This chapter will discuss analgesia and other medications utilized in the postoperative period. The use of ureteral stents and new and future technologies will also be discussed. Finally, the use of postoperative imaging following ureteroscopy will be examined.

## Ureteroscopy: outpatient versus inpatient management

The overwhelming majority of patients undergoing flexible or semirigid ureteroscopy and intracorporeal lithotripsy are treated on an outpatient basis. Common indications for unplanned admission postprocedure include flank or bladder pain not manageable with oral analgesics, fever, urinary retention, or significant hematuria. In addition, management of the uncommon procedural complications of ureteral perforation or avulsion account for a small percentage of admissions. In common with other planned outpatient procedures, late procedure start times and social circumstances precluding early discharge may result in overnight admission [1]. Box 55.1 lists techniques to increase the likelihood of maintaining ureteroscopy as an outpatient procedure. Emergency admission for renal colic with subsequent emergent ureteroscopy can increase the likelihood of ongoing hospital stay postprocedure [1].

## Prescriptions

Following any surgery, physicians typically prescribe medications for the postoperative period consisting of an antibiotic and/or analgesic. Following ureteroscopy, there are many types of analgesics that can be prescribed and there is very little evidence for antibiotics in the postoperative period. In addition, there are two other types of medication that can be prescribed to patients with urolithiasis. In the case of uric acid stones, patients may be prescribed a urinary alkalinizing agent to dissolve any remaining fragments. The second are alpha-antagonists which have been utilized to facilitate passage of fragments by relaxing ureteral smooth muscle [2, 3] and to help alleviate postoperative ureteral stent symptoms [4–7].

### Antibiotics

Patients are often prescribed antibiotics following surgical cases to prevent infection. The decision on whether to prescribe antibiotics should balance the risk of infection with the risk of adverse effects of antibiotics and the induction of antibiotic-resistant bacterial strains. In cases where the risk of infection is high, the risk of complications such as *Clostridium difficile* colitis and inducing bacterial resistance is justified. In cases where there is a low risk of infection, then the utility of postoperative antibiotic prophylaxis becomes less clear.

There is good evidence to give antibiotics at the time of surgery. A randomized trial of 113 patients were administered either levofloxacin 250 mg by mouth 60 minutes prior to ureteroscopy or no antibiotics [8]. The rate of bacteriuria in the control group was 12.5% compared to 1.8% in those receiving levofloxacin. They did not examine the use of antibiotics in the postoperative period.

The current American Urological Association guidelines (2016) recommend preoperative antibiotic prophylaxis in all patients undergoing ureteroscopy administered within 60 minutes of the start of surgery. It can be a single oral or intravenous dose of antibiotic that covers

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**Box 55.1 Technique to increase likelihood of outpatient ureteroscopy.**

1) Thorough discussion with patient and family preoperatively regarding postureteroscopy clinical course and expectations
2) Operative start time during morning or early afternoon
3) Prompt surgical intervention in patients presenting emergently with renal colic
4) Dose of nonsteroidal anti-inflammatory drug such as Ketorolac at completion of procedure
5) Bladder drainage at completion of procedure
6) Avoidance of routine ureteral stenting for uncomplicated ureteroscopy
7) Appropriate stent length and diameter
8) Consideration of anticholinergic medications for stent-related bladder spasms
9) Consideration of alpha-blocker medication for stent discomfort

both Gram-positive and Gram-negative uropathogens. Local antibiograms should be consulted for selecting an appropriate antibiotic to prevent antimicrobial resistance and ensure the best patient outcomes. There is no good evidence in the literature for using antibiotic prophylaxis in the postoperative period.

## Analgesics

### Analgesics for renal colic and passage of fragments

The options for treating postoperative pain range from the commonly used analgesics which target pain at the central nervous system to medications that target specific receptors in the urothelium. The literature is lacking in suggestions for analgesics specifically after ureteroscopy, but the passage of fragments after intracorporeal lithotripsy can be accompanied with pain very similar to that found in renal colic.

### Alpha-antagonists for stone expulsion

Alpha-antagonists inhibit smooth muscle contraction and have been used extensively in the treatment of benign prostatic hyperplasia. In the endourological world, they have found two further purposes: as medical therapy to facilitate stone expulsion and to relieve ureteral stent symptoms. The theory underlying these observations is relaxation of ureteral smooth muscle to allow ureteral stones to pass and, in the case of stents, to prevent ureteral spasm. This is done by inhibiting selective alpha$_1$-adrenergic receptors and reducing ureteral contractility [9, 10].

Medical expulsive therapy has been found to increase the stone passage rate as well as hasten the time to stone passage and reduce pain, narcotic requirement, and hospitalizations for renal colic [11, 12]. A Cochrane systematic review of 32 studies (5864 participants) found significantly higher stone-free rates in the alpha-blocker group compared to standard therapy (risk ratio 1.48, 95% confidence interval [CI] 1.33–1.64). Reductions were found in stone-expulsion time, number of pain episodes, need for analgesic medication, and hospitalization with alpha-blockers. However, patients experienced more adverse effects with alpha-blocker therapy than standard therapy or placebo [13]. Another meta-analysis evaluating 693 pooled patients found a greater likelihood of stone passage than those given placebo when given an alpha-blocker or calcium channel blocker with steroids [3]. The number needed to treat in this analysis was only four, indicating that this is a worthwhile and effective treatment for ureteral stones. Some studies have produced an even higher rate of stone expulsion in patients administered tamsulosin [14].

A more recent large, multicenter clinical trial randomized 1167 patients with a single ureteral stone 10 mm or less to tamsulosin, a calcium channel blocker (nifedipine), or placebo [15]. The primary end point was need for intervention by 4 weeks after randomization. Participants, clinicians, and trial personnel were blinded to treatment assignment. There was no difference in stone passage rates between tamsulosin, nifedipine, or placebo groups, as 80–81% of patients did not need further intervention in all three groups. No differences were found between the trial groups for visual analogue pain scores at 4 weeks, number of days of analgesic use, or time to stone passage. Criticisms of this study include the fact that the need for surgery was used as a surrogate end point rather than radiologic testing. Additionally, since more than 75% of the stones were 5 mm or less, one could argue that these stones were likely going to spontaneously pass anyway and that the alpha-blockers were unable to show a difference.

### Analgesics for stent-related pain

Phenazopyridine and oxybutynin have been administered orally in an attempt to relieve stent-related symptoms. A randomized trial involving 60 patients randomized to phenazopyridine, oxybutynin, or placebo was performed and the following measures were recorded: narcotic use, flank pain, suprapubic pain, urinary frequency, urgency, dysuria, and hematuria [16]. There was a trend, although statistically insignificant due to the small group numbers, for a reduction in narcotic usage in the oxybutynin group. Phenazopyridine significantly reduced the amount of hematuria patients had on postoperative day 1 compared to placebo. Perhaps a larger study would discern if either of these medications would be helpful in relieving stent symptoms. A meta-analysis of 1408 patients showed reduction in stent-related symptoms, as measured by the International Prostate Symptom Score, visual analogue pain scale, and quality of life instruments, for alpha-blockers (alfuzosin or tamsulosin) alone and antimuscarinics (tolterodine or solifenacin) alone compared to control. The combination of alpha-blockers and antimuscarinics provided even greater reduction in stent-related symptoms [17].

#### Alpha-blockers and stent-related pain

Patients randomized to alfuzosin following ureteroscopy and stent insertion had significantly less narcotic use, less overall pain in the back and groin area, less flank pain during urination, and less urinary frequency compared to patients given placebo [18]. Tamsulosin also produced similar significant results in other placebo-controlled prospective trials of patients undergoing ureteral stent placement following ureteroscopy [4, 7, 19]. In a network meta-analysis, tamsulosin and alfuzosin were shown to have significant reduction in the urinary symptom scores and body pain scores of the Ureteric Stent Symptoms Questionnaire when compared to placebo. However, no significant difference was found between tamsulosin and alfuzosin with respect to these measures [20]. It would appear that alpha-blockers administered postureteral stent insertion is an excellent way to prevent and relieve symptoms.

### To stent or not to stent? That is the question

The decision must be made at the end of each ureteroscopy on whether or not a ureteral stent should be placed. The absolute indications to leave a ureteral stent are listed in Box 55.2 [21]. The evidence on whether to stent a patient following ureteroscopy is controversial. There is good evidence from randomized clinical trials suggesting that patients without ureteral stents experience fewer symptoms than those who receive a ureteral stent [1, 22–25]. In unstented patients postureteroscopy, few patients require surgical intervention for ureteral obstruction with the majority managed by improved pain control. In addition, the vast majority of patients treated on a "stent-less" basis have no obvious preprocedure predictor of subsequent flank pain or obstruction. Although the avoidance of a postprocedure ureteral stricture is commonly encountered in the literature as a justification for ureteral stenting, the meta-analysis of randomized controlled trials by Nabi et al. indicates no difference in stricture rate between those stented and nonstented [26].

**Box 55.2 Indications for ureteral stenting postureteroscopy [21].**

1) Ureteral perforation intraoperatively
2) Ureteral dilation greater than 10 Fr (either coaxial or balloon dilator)
3) Significant ureteral edema due to stone (e.g. impacted stone)
4) Failure to advance the ureteroscope due to a narrow ureter or ureteral orifice and in preparation for a subsequent ureteroscopy after 7 days
5) Infected urinary system with an obstructing system
6) Large stone burden with many fragments remaining to pass
7) Solitary kidney

Supporting the role of postprocedure ureteral stenting is the study by Borboroglu et al. in which the authors reported a risk for admission for flank pain postureteroscopy of 7.4% in the unstented group versus a 0% re-admission rate in the stented group [27]. However, the overall cohort of unstented patients had substantially less flank pain. While some studies have shown fewer symptoms and less pain in those patients without a stent, a metaanalysis found a trend towards fewer urologic complications in patients who received a stent following ureteroscopy [28]. Some of the trials included in this analysis did not find a difference in complication rates between stented and unstented patients, but there was an overall 4.5% reduction in rate of complications in those patients who underwent placement of a stent following ureteroscopy ($P = 0.001$, 95% CI 1.8–7.3%). When a more stringent random effects model was applied, however, this difference was not statistically significant (4.1% risk difference, 95% CI 1.8%–10.1%, $P = 0.175$). At present in the literature, there is no significant difference in outcomes between patients who receive a ureteral stent compared to those who do not receive a ureteral stent following ureteroscopy.

When a ureteral access sheath is used during ureteroscopy, there is good evidence to place a stent afterwards. A retrospective comparison of 51 patients stented and 51 patients not stented after flexible ureteroscopy with a ureteral access sheath found that stented patients had significantly lower postoperative pain scores and were less likely to seek medical attention for pain compared to unstented patients [29]. In another retrospective review, the rate of return to the emergency department of nonstented patients after ureteroscopy was significantly higher in those who had a ureteral access sheath (37%) compared to those treated without a ureteral access sheath (14%) ($P = 0.04$) [30].

## Which stent is most comfortable?

Once a decision to place a stent is made, the question becomes which stent to use. There are no conclusive data as to which commercially available stent is the most comfortable for patients. There are a variety of factors that are taken into consideration including the softness (durometer) of the stent, its design, and its size both in length and diameter.

Intuitively, one would think that softer stents would be more comfortable than harder stents; however, randomized trials have shown no difference between soft and hard stents in terms of urinary symptoms, pain, time away from work, or sexual dysfunction utilizing the Ureteral Stent Symptom Questionnaire (USSQ) [31], the only validated tool for evaluating ureteral stent symptoms [32, 33]. In one trial, patients randomized to a "stiffer" stent that was greater than 64A durometer in stiffness (Percuflex® stent; Boston Scientific, Natick, MA, USA) were compared to patients who received a softer stent of less than 64A (Contour™ stent, Boston Scientific) [32]. No differences between groups were seen at 1 and 4 weeks in terms of urinary symptoms, overall body pain, work performance, or general health index. Lennon et al. randomized patients to firm polyurethane stents or a softer Sof-Flex™ stent [33]. Patients with firmer stents had a higher rate of dysuria, and renal and suprapubic pain; however, there was no significant difference in the degree of bladder inflammation, stent encrustation, urgency, frequency, nocturia, or hematuria. The only shortcoming of this study is that patients were not evaluated with a validated stent symptom questionnaire, the USSQ.

More recently, Lingeman et al. and the Comfort Study Team utilized the USSQ to assess whether patient comfort was best in a short loop tail stent, a long loop tail stent, or a Percuflex Plus stent (Boston Scientific) or Polaris stent (Boston Scientific) [34]. All kidney curls were identically composed of a 6 Fr pigtail curl and the Percuflex Plus stent consists of the same material and coil in the bladder end. The distal ends differed in the other three stents: the short loop tail stent (5 cm long, 3 Fr diameter) and long loop tail stent (8 cm long, 3 Fr diameter) consisted of two loops and the Polaris stent was a dual durometer stent with a stiffer renal curl to prevent migration but a softer curl in the bladder in an attempt to decrease bladder irritation and symptoms. The 236 patients were randomized to receiving one of the stents following uncomplicated ureteroscopy and were administered the USSQ at baseline, 4 days after stent placement, and 5 days after stent removal. There were no statistically significant differences in pain scores between any of the stent groups. There was decreased use of narcotics in the first 1–3 days after stent placement in the short loop tail stents, but this was insignificant at 4 days. Most notably, the USSQ may not have been administered at the correct time as all patients had the most severe discomfort symptoms on postoperative day 1. By day 4, all symptoms had subsided when the USSQ was administered, thus there may have been a significant difference if it was measured at day 1. It also goes to support the theory that stent symptoms occur from irritation of the trigone of the bladder. Having softer material that also has less mass in the bladder may help alleviate ureteral stent-related symptoms.

## Stent length relating to discomfort

Even though there are no clear data to support the use of one type of stent over another, there are good data that longer stents that protrude into the bladder produce more symptoms. Choosing the correct length of stent will significantly reduce patient stent symptoms. Stents that cross the midline of the bladder result in significantly more dysuria, urgency, and irritative voiding symptoms and more impaired quality of life than stents that do not cross the midline [35, 36]. Giannarini et al. found significant association between the distal stent loop crossing the midline of the bladder and the urinary symptoms, body pain, general health, work performance, and sexual matters domains of the USSQ [37]. Long stents are associated with excess material in the bladder – and, therefore, presumably with more bladder irritation – but do not result in excess stent length in the kidney [35]. Fluoroscopic studies of stented patients show that, with motion, the stent tends to bow in the mid and proximal ureter and the excess length slides in and out of the bladder at the ureterovesical junction, with relatively little motion seen in the kidney [38]. Flank pain was not affected by stent length, but there is good evidence that negative bladder symptoms are increased in patients with longer stents compared with those who are stented with the correct length stent.

However, more recent studies have not been able to consistently support the association between excess stent length and urinary symptoms. In one study, patients completed the USSQ before stent removal and were categorized by X-ray into three groups with contralateral, tangential, or ipsilateral stent position. While the ipsilateral stent group showed lower USSQ scores, these differences were not statistically significant between groups for the USSQ total score ($P = 0.35$) and subgroup scores [39]. A multicenter randomized trial between multilength 6 Fr × 22–30 cm Contour VL and 6 Fr × 24 cm Contour ureteric stents also found no significant difference in the same USSQ subgroup scores, adding ambiguity to the question of whether excess stent material in the bladder adds to stent-related symptoms [40].

How is the correct stent length chosen? This question has baffled many a urologist and numerous methods have been described including measuring patient height, torso length, intravenous urography, and direct ureteral measurement. One study found that direct intraoperative measurement of ureteral length was better than patient height at correlating with the correct stent length [41]. Another study evaluated several anthropometric factors, including patient height, body mass index, and distances from the acromion process (shoulder) to the head of the ulna (wrist), olecranon process (elbow) to the head of the ulna, xiphoid process to pubis, umbilicus to pubis, and anterior iliac spine to anterior iliac spine [42]. They measured ureteral length intraoperatively with a 5 Fr ureteral catheter and found that height, xiphoid process to pubis distance, and the shoulder to wrist distance all correlated with ureteric length. Ho et al. recommend a 22 cm stent for patients 149.5–178.5 cm in height, but did not study patients outside this height range [36]. To date, there is no standard accepted method of determining the most appropriate length of ureteral stent.

## Stent coatings

In an effort to reduce bacterial infection related to indwelling material, antimicrobial peptides have been proposed to reduce bacterial adhesion and biofilm formation, thus preventing infection. Antimicrobial peptides have been shown to substantially improve the infection resistance of biomaterial surfaces using polymer brushes to increase the density of the antimicrobial peptides [43]. Antimicrobial activity was observed for both Gram-positive and Gram-negative organisms. Antimicrobial peptides may be used in the future to reduce systemic antibiotic administration for ureteral stent-related infections and thus prevent the induction of antibiotic resistance.

## Biodegradable ureteral stents

Ureteral stents typically require a secondary procedure for removal if a suture tether is not used. This can add cost, inconvenience, and patient discomfort. In addition, if a patient is lost to follow-up and if there is any miscommunication about the patient having a stent, a "forgotten" stent may result, potentially requiring several surgeries for removal or even loss of the renal unit [44–46]. There have been case reports of mortality stemming from forgotten ureteral stents [47]. Attempts to reduce retained stents have included a stent registry [48, 49]. A stent without a suture tether that does not require cystoscopic removal has also been developed using a high-powered magnet catheter that is inserted into the bladder to bind a steel bead attached to the distal end of the stent for removal [50]. This low-cost alternative to cystoscopy offers a safe "blind" removal of the ureteral stent in any type of setting under local anesthetic.

Perhaps the holy grail of preventing a retained stent is one that would degrade over time. The ideal biodegradable stent must function to provide drainage like a plastic stent, be easy to deploy, be radiopaque, and maintain its integrity for at least a certain amount of time in order for ureteral edema etc. to subside, but not overstay its welcome and take too long to degrade. Furthermore, it should be comfortable, biocompatible to surrounding tissues, and degrade in a fashion that does not obstruct the distal ureter.

Lingeman et al. performed a phase I clinical trial to evaluate the Temporary Ureteral Drainage Stent (TUDS, Boston Scientific) in 18 patients [51]. All stent material was extruded within 4 weeks with only one stent prematurely migrating into the bladder at day 1. A phase II trial of the TUDS stent evaluated 88 patients following ureteroscopy and the stents were eliminated from the ureter at a median time of 8 days and eliminated completely from the body at a median of 15 days [52]. By 30 days, 84% (74/88) of the stents had completely degraded. Unfortunately, three patients retained stent fragments at 3 months and required surgical intervention for removal. For the majority of patients (78.2%), the stent was effective at providing upper tract drainage for at least 48 hours postoperatively: the targeted time to define success. Due to the manufacturer's concerns about retained fragments, the TUDS stent is no longer commercially available.

A more recent degradable stent composed of ʟ-lactide, glycolide, and copolyester components similar to those found in absorbable sutures has been developed and tested in a porcine model (Uriprene™, Poly-Med, Greenville, SC, USA) [53]. It has been developed to degrade within 2–3 weeks with 90% of stents being completely eliminated from the body by week 4 in a porcine model [54], with one pig retaining three small fragments less than 1.5 cm in the bladder. The biodegradable stent was biocompatible on histology, with fewer abnormal histological findings, and resulted in significantly less hydronephrosis in comparison to the control biostable stents. Drainage was equivalent to control stents as seen by excretory urogram. The safety of this stent has been tested and proven in animal model of ureteral stenting. Human trials will determine its true degradation time and if there is any improvement in comfort. Hopefully, the development of biodegradable stents will aid in reducing stent symptoms and infection, and avoiding the forgotten stent syndrome.

## Postoperative imaging following ureteroscopy

Routine imaging postoperatively remains controversial despite over a decade of studies reported in the era of small-diameter semirigid and flexible ureteroscopes. Multiple authors, in the setting of either a randomized controlled trial of stented versus unstented ureteroscopy, or as a retrospective case series, have demonstrated a low risk of postureteroscopy obstruction [22, 55–69] (Table 55.1).

Given the high stone-free rate for ureteroscopy of upper tract calculi, the major indication for postprocedure imaging is the detection of a ureteral stricture, with a risk in uncomplicated cases of less than 5%. Predisposing factors for ureteral stricture postureteroscopy include preoperative factors such as chronic stone impaction, reduced renal function, coexistent ureteral stricture on the treated side, and complete ureteral obstruction [65, 70, 71]. In addition, intraoperative factors such as significant ureteral edema, ureteral trauma, or ureteral perforation are established risk factors for ureteral stricture and mandate close long-term radiologic follow-up [70, 71]. Indeed, the retrospective case series of Roberts et al. [71] reported a 24% incidence of ureteral stricture in patients with chronic ureteral stone impaction greater

**Table 55.1** Ureteroscopy: follow-up imaging.

| Study | *N* | Stone location | Ureteroscopy type | Imaging modality | Mean duration follow-up | Postoperative hydronephrosis | Postoperative stricture | Postoperative surgical interventions |
|---|---|---|---|---|---|---|---|---|
| Gokce et al. 2016 [66] | 116, pediatric | Renal and ureter | R&F | US or NCCT | At least 3 weeks | 27.6% | 0% | – |
| Barbour et al. 2015 [68] | 324 | Renal and ureter | R&F | US or CT | 6–7 weeks | 15% | 0.6% | – |
| El-Abd et al. 2014 [67] | 1980 | Ureter | R&F | KUB, US, CT-IVU | 42 months | – | 0.6% | – |
| Schatloff et al. 2010 [56] | 60 | Ureter | R | US or CT | 1 month | – | | 1.7% |
| Manger et al. 2009 [64] | 289 | Renal and ureter | R&F | US | 1 month | 9.3% | 0.3% | 2.8% |
| Breda et al. 2009 [69] | 51 | Renal | F | US | 1 month | – | 0% | – |
| Adiyat et al. 2009 [65] | Complicated ureteroscopy ($n = 158$) | Renal and ureter | R&F | NCCT | 16 months | 10.7% | 5.3% | – |
| | Uncomplicated ureteroscopy ($n = 56$) | | | | 10 months | 5.6% | 0% | |
| Elashry et al. 2008 [61] | 4512 | Distal ureter | R | US, IVP | 7.6 months | – | 0.2% | – |
| Ibrahim et al. 2008 [22] | 220 | Distal ureter | R | US, CT | 25 months | – | 1.4% | – |
| Karadag et al. 2008 [62] | 268 | Ureter | R | IVP, US | 27.4 months | 1.1% | 0.7% | – |
| Portis et al. 2006 [59] | 58 | Renal and ureter | F | NCCT | 1 month | – | 1.7% | – |
| Geavlete et al. 2006 [60] | 2436 | Ureter | R | – | 56 months | – | 0.1% | – |
| Weizer et al. 2002 [57] | 241 | Renal and ureter | R&F | IVP, CT, or US | 5.4 months | 12.3% | 1.2% | – |
| Sofer et al. 2002 [58] | 330 | Renal and ureter | R&F | IVP, US | >1.5 months | – | 2.4% | – |

Numbers of patients, where reported, consists of patients with upper tract urolithiasis undergoing ureteroscopic intervention. R, semirigid ureteroscope; F, flexible ureteroscope; US, ultrasound; CT, computed tomography; IVP, intravenous pyelography; IVU, intravenous urogram; KUB, kidney–ureter–bladder; NCCT, noncontrast computerized tomography.

than 2 months. However, previous iatrogenic ureteral perforation from previous stone manipulation was encountered in the majority of stricture cases. Regardless, the more contemporary series of Beiko et al. [70] reported that all four cases of ureteral stricture postureteroscopy occurred in patients with risk factors.

Adiyat et al. [65] retrospectively compared the incidence of ureteral stricture between a high-risk group of complicated ureteroscopy cases ($n = 56$) compared to a cohort of uncomplicated ureteroscopy patients undergoing routine stone surveillance imaging ($n = 158$) (Table 55.1). In common with other authors, complicated ureteroscopy, consisting of cases with encountered impacted stone, need for ureteral balloon dilation, or ureteral perforation, demonstrated a substantial risk of ureteral stricture of 5.3%. In contrast, long-term radiologic surveillance in the uncomplicated ureteroscopy group (mean follow-up of 10.2 months) revealed no ureteral strictures. This evidence further supports selective imaging in patients with known risk factors for postoperative ureteral stricture development. The predisposition of a ureteral stricture from ureteral balloon dilation remains controversial with some authors suggesting this a risk factor [65, 70] while others do not [1, 68]. In one study, the rate of stricture in patients who underwent ureteral balloon dilation was 1 in 107 patients reviewed (0.9%) [72].

Multiple authors advocating limited radiologic evaluation in the early postureteroscopy period have based this recommendation on the presence or absence of pain as an indication for imaging [62]. The majority of studies assessing the etiology of pain after ureteroscopy demonstrate a substantially greater likelihood of a retained stone fragment rather than a stricture being responsible [65, 73]. Barbour and Raman [68] studied 324 patients following ureteroscopy and found a 48-fold greater risk of abnormal imaging postureteroscopy for patients with symptomatic presentation. They also found that of those with symptomatic presentation and hydronephrosis on subsequent imaging, 43% were due to ureteral obstructing residual fragments and thus recommend directly proceeding to stone protocol CT for symptomatic patients. Other factors that were found to increase risk of abnormal imaging included larger stone size (5 mm increments, odds ratio 5.1, $P = 0.008$), longer operation duration (30 minute increments, odds ratio 1.01, $P = 0.001$), and prior ipsilateral ureteroscopy, and thus a CT or renal ultrasound was recommended for this population. Bugg et al. [73], as advocates of limited postureteroscopy imaging, reviewed the chance of postoperative obstruction when pre-operative obstruction and postoperative pain are combined. The authors reported that patients with preoperative obstruction and postoperative pain had a 67% chance of having residual fragments and a 50% chance of residual obstruction. In contrast, 96% of patients without preoperative obstruction and no postoperative pain had no persistent obstruction or residual fragments. However, the risk of missing silent obstruction remains as 25% of asymptomatic patients had residual stone fragments or obstruction.

The correlation of pain with postureteroscopy ureteral obstruction has been questioned by Weizer et al. [57], who caution urologists regarding the risk of silent hydronephrosis. In this retrospective case series, the absence of pain was noted in seven patients who presented postoperatively with silent hydronephrosis out of a total 241 patients. This translates into a 3% risk of renal functional impairment in patients undergoing ureteroscopy if relying on only symptoms to prompt imaging. Similarly, Manger et al. [64], in a retrospective case series of 289 patients with available postureteroscopy sonography, reported that 27 (9.3%) had sonographic evidence of hydronephrosis (14 asymptomatic). From this series, the risk of silent obstruction is significant (4.8%), with the number needed to diagnose of 18 asymptomatic patients postureteroscopy to diagnose one case of hydronephrosis. Further, the negative predictive value and positive predictive value of ipsilateral flank pain for hydronephrosis were 94 and 35%, respectively. In conflict with this large percentage of patients with postureteroscopy hydronephrosis (providing evidence for routine postureteroscopy imaging) is the small number of patients in this series with asymptomatic hydronephrosis who eventually required surgical intervention.

Sutherland et al. [74] compared the economic costs of routine imaging after ureteroscopy with selective imaging in only symptomatic patients after ureteroscopy. They considered the costs of complications following ureteroscopy, including postoperative pain, stricture, and silent obstruction with subsequent renal loss due to silent obstruction causing chronic kidney disease, end-stage renal disease, and cardiovascular disease. Taking these complications into account and assuming a rate of silent obstruction of 1.9%, the authors found the cost of ureteroscopy with routine postoperative imaging to be US$5326 per patient whereas with selective imaging it was $5196 per patient. Despite a modest $130 cost savings per patient under a selective imaging model, Sutherland et al. recommended routine postureteroscopy imaging to offset the patient risk of loss of kidney function due to silent obstruction.

The majority of studies assessing imaging postureteroscopy have relied on intravenous pyelography or CT scans to rule out obstruction. In contrast, Manger et al. [64] demonstrate the value of renal ultrasound postureteroscopy as a screening study. Given the increasing recommendations to limit medical radiation exposure in our urology patients [75, 76], combined with ready availability of sonography, the authors recommend renal ultrasound as the imaging study of choice postureteroscopy in asymptomatic patients to rule out obstruction.

## Residual fragments after ureteroscopy

The management of residual stone fragments after urologic stone procedures is controversial. These stone fragments have the potential to grow, cause obstruction or infection, and contribute to recurring stone episodes. A retrospective study from six centers in North America of 232 patients with residual stone fragments found a 44% rate of stone-related complications, with 15% not requiring intervention and 29% requiring intervention [77]. Stone fragments greater than 4 mm were more likely to grow ($p < 0.001$), cause complications ($P = 0.039$), and require re-intervention ($P = 0.01$). The authors suggest pre-emptive treatment of residual fragments greater than 4 mm to prevent complications based on these findings.

## Summary

Postoperative use of ureteral stents is not supported for every routine, uncomplicated ureteroscopy. If a stent is to be left, however, the proper length stent should be inserted to reduce stent symptoms. Ketorolac, oxybutynin, or an alpha-antagonist may help reduce stent-related symptoms. Alpha-antagonists may also be prescribed postoperatively in an attempt to facilitate spontaneous expulsion of stone fragments. Postoperative imaging following ureteroscopy remains controversial following uncomplicated cases.

See Video 55.1.

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# 56

# Ureteroscopy Complications

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## Introduction

Miniaturization of instruments, improved technique, and developing safety principles have led to ureteroscopy (URS) being a safe, effective option for stone therapy. With smaller-diameter ureteroscopes, less traumatic tips, and improved techniques, iatrogenic complications have declined and are now less common. To avoid intraoperative complications from URS, the surgeon should be familiar with the various complications, their incidence, associations, and the appropriate treatment. We review the various complications associated with URS and the strategies for safe URS.

## Classification

The definition and reporting of complications varies widely. Commonly employed reporting systems segregate complications either by severity (minor and major) or by chronology (intraoperative and postoperative). No standardized classification has been adopted specifically for endoscopic complications. Many investigators utilize the Clavien-Dindo classification; however, this system struggles to correlate the particulars of endoscopy. The Satava classification system attempted to address this deficit, with complications predicated on the intensity of management (Table 56.1) [1]. Several grading systems have emerged that are specific to the severity of ureteral wall injuries, which will be discussed later.

## Intraoperative complications

The incidence of intraoperative ureteroscopic complications ranges from 0.5 to 20%, with 1.5–5% being major complications [2]. The majority of complications are minor and managed conservatively.

### Bladder distention

Intraoperative overdistention of the bladder can lead to postoperative urinary retention and, on rare occasions, bladder perforation. Surgeons should note prostatic enlargement and pre-existing outlet obstruction as contributing factors to postoperative retention. A small-caliber Foley or red rubber catheter may be placed alongside the ureteroscope for bladder drainage. Monitoring bladder volume is particularly important for longer procedures performed without a ureteral access sheath (UAS). UAS use can mitigate this concern by creating a continuous irrigation flow system and bypassing the bladder.

### Failure to access the upper tract

Accessing the ureter or kidney can be difficult. Failure to access the upper tract has been reported at 1.6–1.8% with flexible URS and up to 8% with semirigid ureteroscopy [1, 3, 4]. Associated risk factors are stones >15 mm and proximal stones [4]; anatomic features also contributing to operative difficulty include patient body habitus, intrinsic or extrinsic ureteral narrowing, stone impaction, ureteral edema or lesions (iatrogenic or pathologic),

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**Table 56.1** Clavien-Dindo and Modified Sativa classification systems for surgical complications.

| Clavien-Dindo | Satava, Modified |
|---|---|
| Grade I: any deviation from normal postoperative course | Grade 1: incidents without consequences for the patient |
| Grade II: requiring pharmacologic therapy with drugs other than those allowed in Grade I | Grade 2a: managed intraoperatively with endoscopic maneuvers<br>Grade 2b: managed with retreatment (additional surgery) endoscopically |
| Grade III: requiring surgical, endoscopic, or radiological intervention:<br>a) without general anesthesia<br>b) requiring general anesthesia | Grade 3: managed with open surgery or laparoscopy |
| Grade IV: life-threatening complication requiring intensive/critical care management:<br>a) single organ failure<br>b) multiple organ failure | |
| Grade V: death<br>Suffix “d” may be added for disability, indicating follow-up is needed after discharge to fully evaluate the complication | |

or genitourinary anatomy. Specific genitourinary anatomy that contributes to difficulty includes a cystocele, enlarged prostate, large intravesical median lobe, generalized edema, trabeculations, cellules, and abnormalities related to the ureteral orifice location, such as re-implanted, ectopic, or duplicated ureters. Perhaps the safest option for the management of failed access is to abort the procedure with ureteral stenting if possible.

## Techniques for difficult ureteral access

### Tight ureteral orifice

Numerous difficulties can arise when attempting to access the ureteral orifice. Several techniques exist for orifice identification or cannulation. These include telescoping the wire through a ureteral catheter to improve direction and stability, converting to a straight or curved hydrophilic wire, emptying/filling the bladder, and manually reducing a cystocele or vaginal prolapse (e.g. vaginal packing). Ancillary instruments for complex access include a ureteroscope, flexible cystoscope, Albarran bridge with 70° lens, or specialty ureteral catheters (Figure 56.1). In the absence of complete ureteral obstruction, Methylene blue or Fluorescein can be administered intravenously to endoscopically visualize the effluxing ureteral orifice, and intravenous contrast can illuminate the distal ureter radiographically. Furosemide administration will expedite this process.

If the ureteral orifice is narrow or stenotic, it may not accommodate the ureteroscope. Dilation may be accomplished with tapered dilators or dilating balloons. Such dilation can be associated with perforation, stone extrusion, and avulsion [5]. To prevent such injury from unknown ureteral anatomy or ureteral stone, the ureter should be visualized using retrograde pyelography before dilating maneuvers. Prestenting the ureter (staged approach) is also an option.

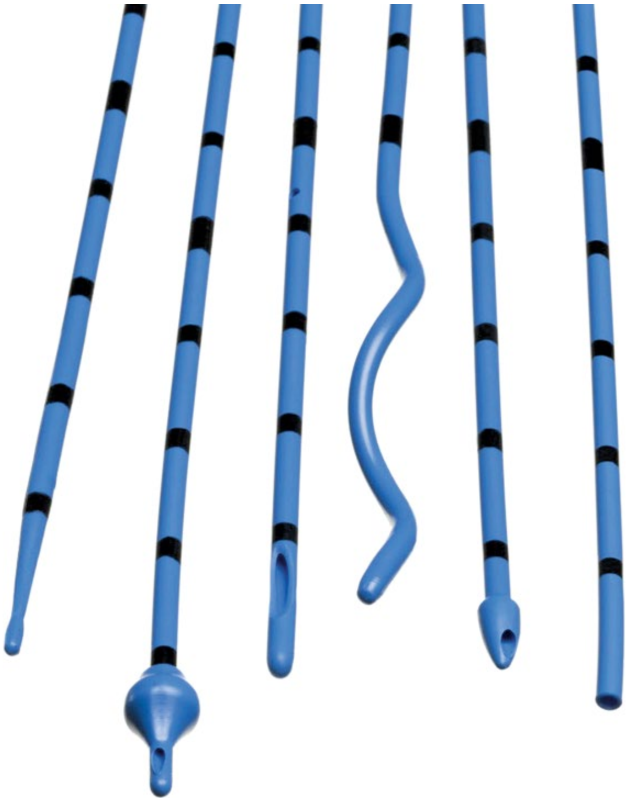

**Figure 56.1** Ureteral catheters. *Source:* Boston Scientific Corporation, Massachusetts, USA. Reproduced with permission of Boston Scientific.

#### Difficult ureter

If difficulty is encountered passing a wire, several techniques may be employed. Retrograde ureterography can opacify the challenging anatomy and guide maneuvers. Telescoping the wire through a ureteral catheter and/or converting wires (e.g. combination polytetrafluoroethylene (PTFE)/hydrophilic wire, straight or curved hydrophilic wire) may be beneficial. If an obstruction or impacted stone is present, lubricating lidocaine jelly can be injected through a ureteral catheter positioned 1–2 cm beneath the stone/obstruction in an attempt to relax the ureteral smooth muscle and create separation between the stone and ureteral wall. To fluoroscopically visualize this maneuver, contrast agent can be mixed into the jelly. However, excessive injection force/pressure may injure the ureter, producing extravasation. Lastly, URS can be performed to endoscopically visualize the difficult ureteral segment and advance the wire under direct vision.

If wire access is achieved but URS remains difficult, entering a narrow ureteral orifice and negotiating a difficult ureter can be accomplished using two wires (safety and working wire) and by maintaining maximal distance between the wires opening the ureter to “shoehorn” the scope (railroad technique). The scope should be rotated, as needed, to maintain scope orientation between the wires.

If a stricture is encountered distal to a stone, it may be tapered or balloon-dilated followed by case resumption. If the stricture is incised, a stent should be placed with stone treatment later to prevent stone fragments migrating into the disrupted ureteral wall. When deciding between the two techniques, the surgeon should note that balloon dilation provides faster, less forceful access through a narrowed ureter [6]. Because ureteroscopes have decreased in size, incidence of balloon dilation has decreased; however, UAS utilization has been reported to increase balloon dilation use [7]. Failure to advance UAS after balloon dilation is rare but merits termination of case and stenting [7]. Repeat URS can be performed 1–2 weeks later. An antegrade approach remains an option should retrograde fail.

### Equipment failure

Equipment failure can preclude ureteroscopic success, with procedure abortion reported at a suspected underestimated 0.8% [1], while scope failure necessitating repair can be expected every 9–50 cases [8–11]. Most ureteroscope damage is iatrogenic, such as improper handling during instrumentation [12]. Most commonly, damage occurs to the working channel, especially the distal tip. The primary mechanism is passing instruments with the scope deflected or firing the laser within the scope’s working channel. The use of lithotrite alone predicts ureteroscope damage [12]. A major risk from laser use in a maximally deflected scope is damage to the channel at the point of maximum deflection due to energy released through microfractures in the quartz core material [13]. Stones should be repositioned to more favorable calyces prior to laser treatment. Backloading the ureteroscope over the stiff portion of a wire also risks internal channel punctures and flap creation.

The most fragile portion of the scope is the active deflection unit. Excessive force/stress on the deflection mechanism expedites deterioration, typically occurring when the deflection circumference is greater than the renal pelvis size [9, 13]. Newer scopes with exaggerated active deflection may therefore shorten the interval between major repairs [14]. Duration of scope use inside the patient and patient’s body mass index were correlated with loss of downward deflection during use [15]. Lastly, applying excessive torque on the semirigid scope shaft leads to image distortion and scope failure [16].

To improve longevity, handling is critical: this includes maintaining the scope loosely coiled in transit, holding the handpiece with tip relaxed in a dependent position, straightening the scope into neutral position before advancing instruments through the channel, and using jelly or silicone lubricants to reduce frictional forces within the working channels. Ensuring both proximal and distal sections of the scope are synchronized mitigates torque-twisting damage. Other recommendations include using UAS, nitinol devices, smaller holmium laser fibers, and laser tip visualization during use [17].

### Stone migration

#### Ascending/proximal migration

Proximal stone migration occurs in 3.5–12.2% of URS cases [1, 3, 4, 18, 19]. This increases operative/anesthesia time and may prevent case completion, subjecting a patient to additional anesthetic. Risks of proximal stone migration include initial proximal stone location, degree of ureteral dilation, pneumatic or electrohydraulic lithotrites, laser settings, and increased fluid irrigation. Antiretropulsion products are available to prevent proximal stone migration [1].

#### Ureteral stone extrusion

Stone migration into the ureteral wall occurs <1% in URS [20, 21]. Stone removal is technically difficult after extrusion, and further action should be done with caution and care.

#### Intramural stone extrusion

Intramural stone migration (“submucosal stone”) is stone extrusion through the ureteral mucosa, injuring the inner ureteral lining. This usually occurs during stone

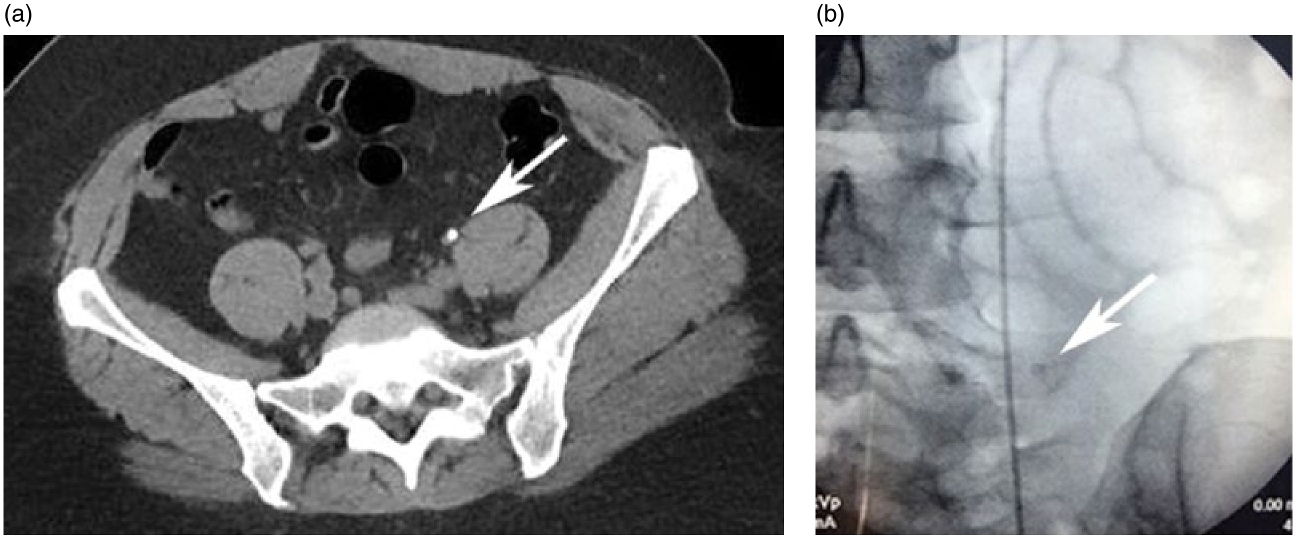

**Figure 56.2** Misdiagnosed ureteral stone. CT scan shows stone appearing to be in the mid left ureter; however; URS shows stone external to the ureter.

treatment and often with an impacted stone. Submucosal stones have been identified as predisposing to stricture formation and may become a nidus for stone growth [20, 21]. Stone fragments embedded within urothelium stimulate inflammation that may result in stone granuloma [22]. This raises concern during stone dusting techniques performed after ureteral perforation. Fragments may imbed within perforations as they pass down the ureter. Submucosal stones are typically diagnosed endoscopically as bulges from the inner ureteral wall, but can also be diagnosed with computed tomography (CT).

Therapeutic approach is controversial because with observation a granuloma or stricture may occur, but extraction remains difficult and may result in further ureteral injury with worse long-term sequelae. If a submucosal stone is identified during atraumatic URS (presumed chronic) laser excision followed by ureteral stent placement is recommended. Failure to remove stones requires long-term follow-up to ensure that a stricture does not occur.

### Extramural stone migration: complete extrusion

Extramural stone migration ("lost stone") extruding past full thickness of the ureter is rare. This was more common prior to holmium, when higher power lithotrites were used. Risk factors for complete extrusion include improper endoscopic techniques, ureteral edema, poor blood supply of the ureteral segment, microtrauma to the ureteral segment, high intraluminal pressure from fluid irrigation, and outward compressive force on the stone into the ureteral wall from scope or instrument. The most serious sequelae are stricture and fluid extravasation, and retroperitoneal abscess can occur rarely if urinary tract infection (UTI)/bacteruria is present [23]. Stone retrieval should not be attempted [23, 24], but a ureteral stent should be placed due to perforation. Stone location should be documented, as future imaging studies may falsely diagnose ureteral calculus (Figure 56.2). Follow-up upper tract imaging is indicated to exclude stricture formation and document extramural calculus position.

## Ureteral injury

### Classification

Ureteral injury is the most frequent complication; however, it is typically managed with a ureteral stent. Delayed sequelae of significant ureteral injury and urine extravasation include prolonged ileus, urinary obstruction, urinoma, azotemia, fever, persistent flank pain, fistula formation, and sepsis [25]. Several validated classification systems have been developed for ureteral injuries (Table 56.2) [26–28].

### Management

Failed conservative management or high-grade injuries require reconstruction. Timing of repair is either within first 5 days or deferred at least 6 weeks until resolution of acute periureteral inflammation. With a nephrostomy tube in place, retrograde and antegrade radiographic studies may be performed (Figure 56.3). Cystogram should also be performed prior to any potential bladder involvement in reconstruction. The optimal repair is based on injury location, degree of ureteral loss, and surgeon comfort/training (Table 56.3).

**Table 56.2** Classification of ureteral injuries.

| | Grade | Description | Management |
|---|---|---|---|
| AAST[a] | 1 | Contusion or hematoma without devascularization | Ureteral stent |
| | 2 | <50% transection | Ureteral stent (or nephrostomy), may require surgical reconstruction |
| | 3 | >50% transection | Ureteral stent (or nephrostomy), may require surgical reconstruction |
| | 4 | Complete transection with <2 cm devascularization | Surgical reconstruction |
| | 5 | Avulsion with >2 cm devascularization | Surgical reconstruction |
| | | Note: advance one grade for bilateral up to grade 3. | |
| Traxer and Thomas | 0 | No lesion found or only mucosal petechiae | No Intervention required, consider ureteral stent 1–2 weeks |
| | 1 | Ureteral mucosal erosion without smooth muscle injury | Ureteral stent 1–2 weeks |
| | 2 | Ureteral wall injury involving mucosa and smooth muscle (periureteral fat not seen) | Ureteral stent 3–6 weeks |
| | 3 | Ureteral wall injury involving adventitial perforation (periureteral fat seen) | Ureteral stent and/or nephrostomy, may require surgical reconstruction |
| | 4 | Total ureteral avulsion | Surgical reconstruction |
| PULS[b] | 0 | No lesion or insignificant mucosal abrasions: contusions with minimal hematoma, mucosal moulding via guidewire | No intervention required |
| | 1 | Superficial mucosal lesion and/or significant mucosal edema/hematoma: superficial bleeding/tears of the mucosa and/or mucosal edema or hematoma | No intervention required, consider ureteral stent (<1 week) |
| | 2 | Submucosal lesion: deep tear of the mucosal and submucosal layer (ureteral integrity, no extravasation) | Short-duration ureteral stent (1–2 weeks) |
| | 3 | Perforation <50% (partial transection) | Moderate-duration ureteral stent (3–4 weeks) |
| | 4 | Perforation 50–99% (partial transection) | Long-duration ureteral stent (6–12 weeks) (remaining tissue bridge enables conservative therapeutic attempt); likely to require surgical reconstruction |
| | 5 | Complete transection | Ureteral stent or nephrostomy to temporize; surgical reconstruction is mandatory |

[a] American Association for the Surgery of Trauma.
[b] Post-Ureteroscopic Lesion Scale.

## Mucosal abrasion

Mucosal abrasion can occur to varying degrees in all URS procedures, especially with UAS use (Figure 56.4). Postoperatively, these abrasions may result in ureteral obstruction from edema or clotted blood [29]. Incidence of mucosal abrasion has decreased with newer, smaller endoscopes [27]. Multiple passes through the ureter increases the likelihood of mucosal abrasion [16].

## False passage/mucosal flap

Mucosal perforation without full-thickness involvement occurs in 1.1–2.8% of cases [1]. This can occur when attempting to pass a wire past an impacted stone or during semirigid scope advancement into the ureteral wall. Passing wire without smooth advancement up the ureter or the appearance of abnormal anatomy on fluoroscopy should alert the surgeon to the possibility of false passage. Alternatively, the wire may follow the path of the ureter and collecting system within a flap (Figure 56.5) and radiographically appear to be in position. This presents a subtle but very dangerous situation, which if not recognized can lead to major ureteral injury. Immediately, the wire should be withdrawn and repositioned. Contrast enhancement of the ureter or direct-vision endoscopy can aid in correcting the misguided wire. Peri-adventitial extravasation confirms the false passage or mucosal flap. If minimal injury exists, case termination is not always necessary, but a stent should be placed at the conclusion. If injury seems more extensive immediate stenting is always a prudent decision.

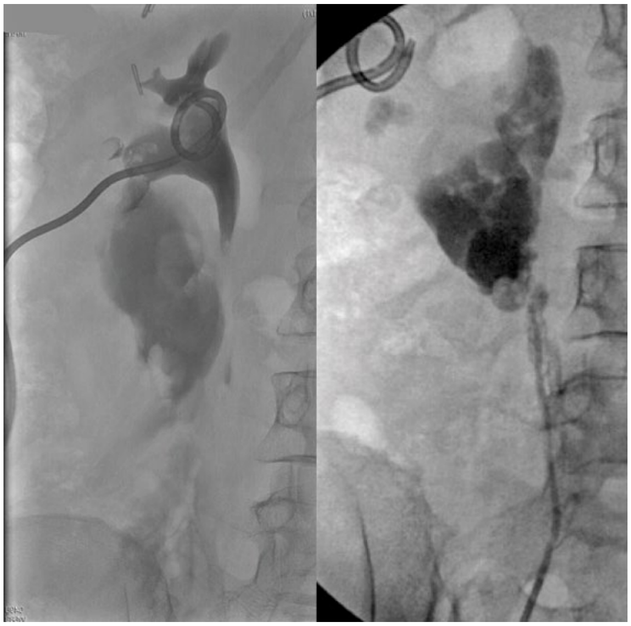

**Figure 56.3** Antegrade and retrograde fluoroscopic studies help to identify and quantify ureteral injury in preparation for repair.

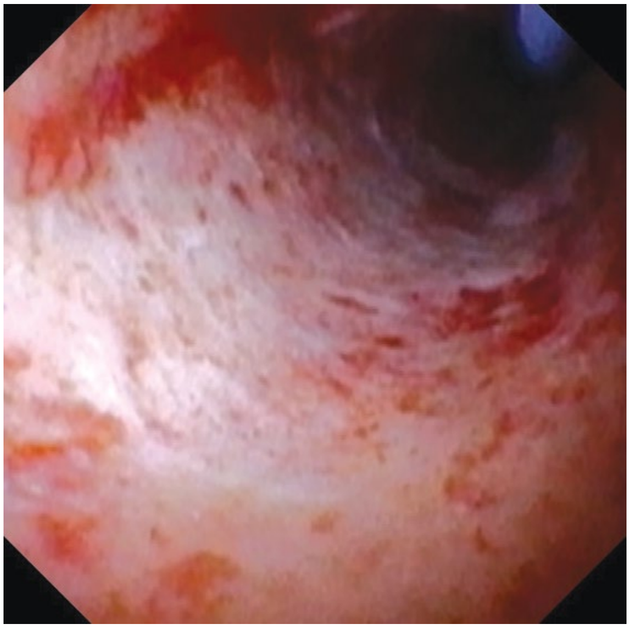

**Figure 56.4** Mucosal abrasion of ureter after removal of access sheath.

**Table 56.3** Principles of ureteral reconstruction.

| Ureteral injury | Reconstructive options |
|---|---|
| **Proximal ureter** | |
| Small defect (<2 cm) | Ureteropyelostomy (dismembered pyeloplasty)<br>Ureteroureterostomy<br>Ureterocalycostomy |
| Large defect (>2 cm) | Renal pelvis flap (Scardino-Prince vertical flap, Culp-DeWeerd spiral flap)<br>Ureterocalycostomy (with renal mobilization)<br>Ureteroplasty with gastrointestinal segment (buccal, appendix)<br>Ureteral interposition with gastrointestinal segment (buccal, appendix, ileum)<br>Ureteroneocystotomy with Boari flap (Long) |
| **Mid ureter** | |
| Small defect (<2 cm) | Ureteroureterostomy |
| Large defect (>2 cm) | Ureteroneocystostomy with Boari flap<br>Ureteroplasty with gastrointestinal segment (buccal, appendix)<br>Ureteral interposition with gastrointestinal segment (buccal, appendix, ileum)<br>Transureteroureterostomy |
| **Distal ureter** | |
| Small defect (<2 cm) | Ureteroneocystostomy (reimplant): refluxing or nonrefluxing |
| Large defect (>2 cm) | Ureteroneocystostomy with psoas hitch<br>Transureteroureterostomy |
| **Complete** | |
| Defect >10 cm | Ileal interposition graft<br>Renal autotransplantation |

- Debridement of necrotic/fibrotic tissue
- Wide spatulation of ureteral ends
- Watertight mucosa-to-mucosa anastomosis (interrupted or running)
- Absorbable suture
- Bridge anastomosis with internal stent
- Consideration for external drain
- Isolation of reconstructed ureter with peritoneum or omentum

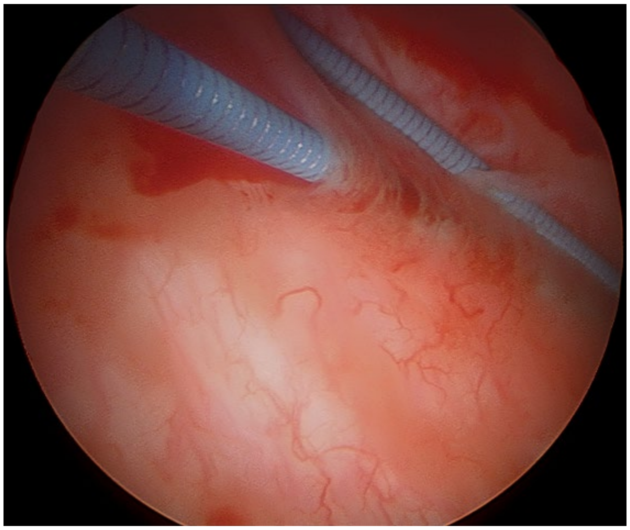

**Figure 56.5** Mucosal flap created with advancing second wire. Radiographically, this wire follows the path of the ureter and can be mistaken as being intraluminal.

## Perforation

Large-cohort studies of stone-related URS cases have reported ureteral perforation at 0–18% [2, 30]. Perforations occur from passing wires, ureteral dilation, ureteroscope passage, instrument manipulation, lithotripsy, and unexpected patient movement [7]. Increased operative time and procedure difficulty are independent risk factors [2]. Additional risks include ureteral tortuosity, periureteral fibrosis, stone impaction, ureteral stenosis/stricture, and patient movement.

These injuries are typically recognized endoscopically, with visible disruption of the ureteral wall or visible fat (Figure 56.6). The diagnosis can also be made radiographically with contrast extravasation. Small perforations do not necessarily merit immediate cessation of a case but do require stenting. Large perforations do require immediate termination and stenting. Percutaneous nephrostomy tube placement is indicated if a stent cannot be successfully placed. Large urinoma requires percutaneous drainage. A ureteral stent is typically maintained for 2–4 weeks to facilitate healing of the perforated segment. A bladder catheter should be considered for maximum drainage if perforation is significant with large extravasation. Follow-up imaging is obtained to assess healing and drainage [31, 32]. These patients carry long-term risk of stricture [33].

## Ureteral access sheath

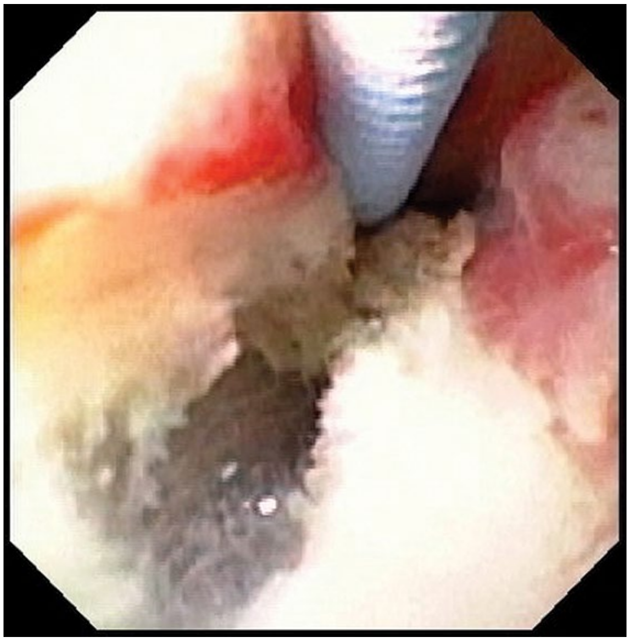

**Figure 56.6** Ureteral perforation recognized endoscopically.

Evidence supports that access sheaths provide the benefit of decreased operative time, simplified re-entry into the ureter, decreased operative costs, and improved stone-free rate [34, 35]. UAS further provides lower intrarenal pressure by facilitating continuous flow irrigation and subsequently reduces the risk of systemic infection [36].

Ureteral injury can occur with UAS placement, but these are typically low-grade and self-limiting. Traxer and Thomas reported 47% ureteral wall lesions following UAS placement, of which 85% were low grade [27] but long-term sequelae were not reported. A retrospective review of 71 patients undergoing endoscopy with UAS found only one patient developing a stricture; however, this patient had recurrent stones and stricture developed proximal to placement of the 12/14 Fr UAS [37].

To avoid significant unnecessary complications, retrograde ureterogram should be performed prior to UAS placement to rule out ureteral stone or stenosis. If the UAS does not pass easily under fluoroscopy, the inner tapered dilator portion should be used independent of the sheath to predilate the ureter before passing the combined dilator and sheath. If still unsuccessful, sequential tapered dilation or radial balloon dilation may be performed in ureteral dilation. We do not recommend dilation of proximal ureter due to higher risk of major ureter injury. Prestenting in cases of difficult UAS placement is reasonable but routine prestenting for all cases is not supported. UAS larger than 12/14 Fr should not be used without prior stenting or dilation to avoid inadvertent ureteral damage.

## Ureteral avulsion

Ureteral avulsion is widely considered the most devastating complication of URS and is fortunately rare 0.1–0.5% [3, 19].

It is an extensive degloving injury to the ureter, resulting in full- (mucosal and muscularis) or partial-thickness (mucosal) discontinuity of the ureter. This typically results from overstretching the ureter, most commonly after difficult manipulation of an impacted ureteral stone or forceful basketing [31, 32]. The proximal one-third of the ureter is most prone because it is less muscular. Some patients may be predisposed to injury due to loss of ureteral elastic fibers and chronic ureteritis or fibrosis, which may result from prior endourologic procedures or previous trauma [38]. Avulsion may occur during attempted removal of a stone fragment too large for the ureter to accommodate and can also occur as the ureter is initially instrumented, such as advancing a ureteral dilator, access sheath, or ureteroscope in a retrograde fashion. Avulsion can occur during withdrawal of basket with unrecognized tissue entrapment. This is often recognized only after a portion of ureter is withdrawn into the bladder or out of the patient (Figure 56.7) along with the basket often attached to the stone. If retrograde pyelography is performed, complete avulsion will demonstrate extravasation of contrast, without opacification of ureter and collecting system proximal to the disruption.

The distal ureter may be avulsed upward with scope advancement if the distal segment has extensive edema, inflammation, stenosis, or tortuosity usually caused by impacted stones [39–41]. This may also occur without initial recognition because avulsion occurs behind the tip of the scope. Recognition of injury occurs with scope removal and long intussuscepted ureter tissue, known as "scabbard" injury, as seen with a sword in a scabbard. The earliest point of recognition is the haptic sensation of a tight ureter that requires additional force to advance or withdraw the scope. The semirigid ureteroscope has a tapered shaft, and although the tip may appear to be passing adequately through the ureter, the proximal shaft may be too large to pass a narrow segment. Scabbard injury results in the loss of a large ureteral segment that typically requires autotransplantation or bowel interposition. Thus, clipping the proximal ureter and placing a nephrostomy drain would be helpful in the acute setting to prepare for definitive treatment.

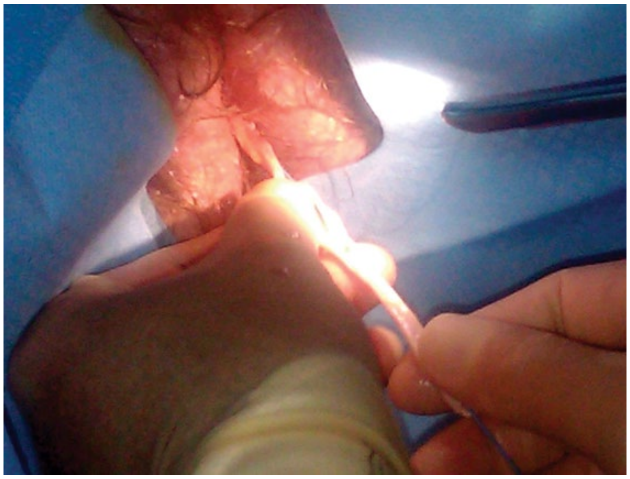

**Figure 56.7** Ureteral avulsion recognized after removing the ureteroscope from the patient. Surgeon is advancing wire up the prolapsed ureter attempting to temporize injury with stent placement.

To reduce risk of avulsion, stones should be removed and instruments manipulated under direct vision, ensuring stone fragments are smaller than the lumen before removal. *Increased resistance may be the only sign that impending injury is about to occur*. UAS can be protective but the urologist should be mindful that as a stone is drawn into the access sheath, urothelium may become entrapped resulting in injury at this site. Proponents of the stone dusting technique cite the decreased risk of ureter injury as it avoids basket use altogether.

#### Incomplete (urothelial) ureteral avulsion/intussusception

Incomplete ureteral avulsion occurs similar to complete avulsion; however, only the inner urothelial layer of the ureter is disrupted and stripped, leaving behind the outer muscularis layer. This occurs in the direction of the scope's (or instrument's) movement and can occur in either direction. Urothelial stripping often arises at a narrowed ureteral segment and is often associated with extraction of a large calculi or polypoid urothelial lesion. Retrograde pyelogram demonstrates containment of contrast inside a ragged, irregular-looking lumen. Without the urothelial layer, these ureters most often scar with large segment stricture and become nonfunctional. Immediate sequelae are less severe than with complete avulsion. Initial management involves placement of a stent (or percutaneous nephrostomy tube and attempting antegrade stent) followed by close monitoring for 6 weeks. Only rarely is ureteral healing over a stent successful. Usually, staged ureteral reconstruction is necessary.

### Lithotrite injury

Lithotrite use can mechanically or thermally injure the ureter, causing bleeding, perforation, or tissue ischemia. Bleeding is typically minor and self-limiting, but even minimal bleeding can reduce visibility. Moderate-to-severe bleeding may require procedure termination. Reduced visibility from hemorrhage has been reported as the most frequently encountered reason for a repeat or staged endoscopic procedure [42]. Patients remaining on anticoagulation therapy during surgery intrinsically have greater bleeding risk; however, these patients are at no increased risk of adverse events related to URS with laser lithotripsy [43]. Lithotripsy near the crossing of the iliac artery should be performed with extreme care. Endoscopic bleeding involving an iliac vessel is exceedingly rare but is a potential source of catastrophic hemorrhage.

Thermal injury from lithotripsy may result in various lesions from small mucosal defects to large necrotic areas. Rate of complication is significantly higher with pneumatic over laser lithotripsy [44, 45]. The neodymium-doped (Nd):YAG holmium laser penetrates 5–6 mm when in contact with the urothelium. This contact laser produces energy that is absorbed by water; thus, thermal lesions are produced 0.5–1 mm deep [46]. Higher energy settings in newer-generation laser units (>1 J) can produce greater thermal injury. Injury is avoided by limiting urothelial contact, which is achieved by constant visualization of the laser tip, maintaining a short working distance, and keeping the laser fiber parallel to the ureteral wall. If urothelial contact is intentional (for bleeding control or upper tract urothelial tumor ablation), the urologist should be judicious about the amount of thermal injury induced, ensuring it doesn't exceed that needed for therapy. These patients also require close follow-up with imaging to rule out stricture development.

### Stone basket entrapment

Entrapment of a basket device on a stone occurs in approximately 0.5% of cases where a basket is used [21]. This is attributed to grasping a stone or fragment too large for removal through the ureter, resulting in a stone entrapped by the basket or snaring of the urothelium. Forced retraction of an entrapped basket is often the preceding event to severe ureteral injury. If a basket has engaged a stone that becomes stuck or does not easily pass down the ureter, the first maneuver is to gently advance the stone more proximal and disengage the stone using the basket mechanism. The next maneuver should be to cut the basket wiring with scissors just beyond the handle or basket disassembly if basket preservation is necessary (Video 56.1). Once cut or disassembled, the ureteroscope can be withdrawn from the ureter removing the basket from the working channel. This permits re-introduction of the ureteroscope with a vacant working channel and the ability to perform laser lithotripsy. One or two of the nitinol wires can be fractured with laser to disengage an entrapped stone. It is important to spare some of the basket wires or discontinuity of the basket and foreign body deposit into the upper urinary tract will occur. Nitinol baskets are easily withdrawn after being lasered because of their soft nature. Steel baskets have the potential to cause ureteral injury during removal and may potentially require delayed, staged removal, or even an open procedure for safe removal.

### Pressure-related injury

High intrapelvic pressure, from a retrograde pyelogram or URS, can lead to pressure-related kidney injury. This fluid pressure can produce urinary extravasation, urinoma, and sepsis (if bacteriuria present) [16]. High intrapelvic pressure, from an iatrogenic or obstructing source, may lead to pyelosinus extravasation from the calyceal fornices. Extravasation frequently exits the renal hilus and resides in the retroperitoneum, which is visualized with contrast around the ureter, simulating a ureteral rupture, and may accumulate outside the contour of the kidney. Extravasation decreases immediately after addressing the source. Recurrent extravasation of this nature may lead to parapelvic pseudocyst or – less commonly – periureteral pseudocyst, the formation of a urinoma at the site of the extravasation. To avoid iatrogenic forniceal rupture, decreased irrigation fluid pressure and/or UAS are recommended.

## Early postoperative complications

### Residual stone

Although complete stone-free status is the optimal outcome, residual stones are fairly common after these procedures. Providing appropriate preoperative patient expectation is important. Patients should always understand the possibility of requiring multiple procedures. Adjunctive alpha-blocker therapy may facilitate passage of residual fragments. Post-URS obstruction from stone fragments can be prevented with ureteral stenting. If obstruction occurs, a stent or nephrostomy tube should be placed in patients with severe symptoms or compromised renal function. Repeat URS or shock-wave lithotripsy provides a definitive treatment.

### Urinary extravasation/urinoma

Urine extravasation, occurring in 0.6–1% cases, may occur subsequent to ureteral wall or collecting system disruption with potential for retroperitoneal urinoma formation [18]. This reporting may be underestimated since retrograde pyelography is always performed at the conclusion of ureteroscopic procedures, and a small amount of urine extravasation into the retroperitoneum usually has no clinical significance. Risk is associated with an impacted stone, ureteral perforation, and laser injury [16]. Intraoperative extravasation of irrigation can potentially enter the retroperitoneum and undergo

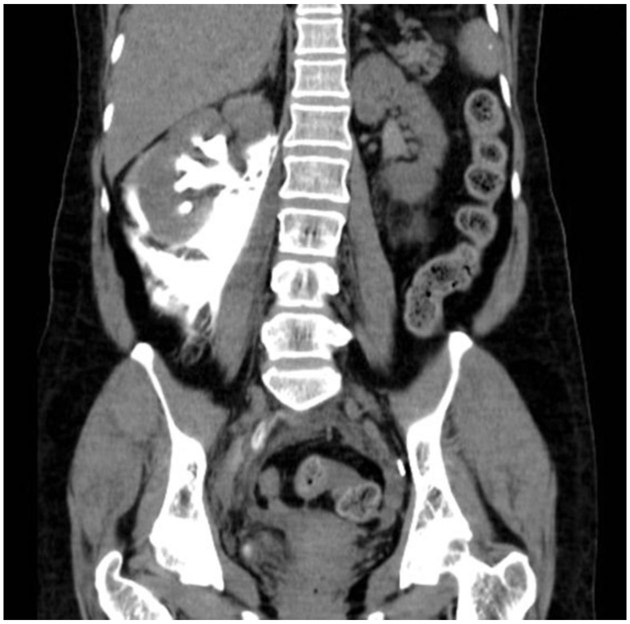

**Figure 56.8** Large extravasation of urine seen on noncontrasted CT performed after a previously contrast-enhanced study.

reabsorption resulting in fluid overload, hyponatremia, and hemolysis; therefore, saline solution is recommended. A urinoma may become infected, requiring drainage and antibiotics, which presents with pain, fever, or ileus. If urine extravasation is suspected, diagnostic studies (e.g. retrograde pyelography, intravenous pyelography, or CT urography) are required to determine further management.

Management involves urinary drainage with stent and/or nephrostomy tube. Significant extravasation (Figure 56.8) may require ureteral stenting and nephrostomy tube drainage for maximal urinary diversion. A foley catheter may be considered as adjunct. Often times with maximum drainage of the ureter and collecting system, appropriate healing will occur without sequelae. If the urinoma is symptomatic, suspected to be infected, or persists despite adequate renal drainage, a percutaneous drain should be placed by interventional radiology, and fluid culture should be obtained. Antibiotics should be administered to reduce the risk of infected urine and abscess formation. A ureteral stent should remain in place 2–6 weeks with scheduled follow-up imaging to ensure proper healing and adequate draining [31, 32].

## Urinary obstruction

With instrumentation of the upper tract, the delicate ureter undergoing intraluminal maneuvers is inevitably subject to iatrogenic trauma, which can result in local edema, ureteral spasms, and bleeding with clot formation. This may result in ureteral obstruction causing post-URS renal colic and hydronephrosis, with the incidence ranging 4–9% [47, 48]. Obstruction is typically self-limiting and managed conservatively. Often, patients can be managed with alpha-blockade and steroid or nonsteroid anti-inflammatory agents, with symptom resolution within several days. Persistent or refractory pain warrants imaging to identify other potential diagnoses or to confirm obstruction, determine its degree, and establish its precise location. Definitive treatment is ureteral stent placement. The need for replacing a ureteral stent after removal has been reported as high as 2.6% [6].

## Neuromusculoskeletal complications

Proper positioning and appropriate padding of pressure points is imperative to mitigate neuromuscular damage. Appropriate dorsal lithotomy positioning involves the anterior-superior iliac spine aligned with the lower break, with hips flexed 80–100° and abducted 30–45°. If boots are used, heels should be well supported, and the pressure on the calves and lateral knee should be minimized. Special attention is necessary for obese or contracted/stiff patients. The most common injury is to the common peroneal nerve, which would clinically manifest as foot drop. Risk factors include maintaining this position >4 hours, body mass index >20 kg/m$^2$, and smoking. Other less common nerve injuries related to position include obturator, posterior tibial, and pudendal nerves, which warrant neurology and/or physical therapy consultations.

## Hemorrhage

Hemorrhage from URS is typically minor and self-limiting and rarely warrants monitoring or intervention. Mild bleeding has been reported as the most common intraoperative complication at a rate of 1.4%, and the most common reason for requiring repeat URS [3, 49]. Innate bleeding risks should be screened using patient history and labs seeking to identify underlying coagulopathy or anticoagulant use. These patients should be counseled prior to procedure, and measures should be implemented to reduce risk, such as holding medications prior to surgery. URS is the preferred surgical option in those with bleeding diathesis. These authors prestent patients whose risks of thromboembolic event precludes cessation of anticoagulants.

Intraoperative bleeding is managed by aborting the procedure, stent placement, and fluid hydration. Profuse or pulsatile intraoperative bleeding could indicate iliac vessel injury. Significant postoperative bleed, especially with drop in hematocrit, warrants immediate workup with contrasted imaging studies or interventional arteriogram. Ureteral balloon placed in the distal ureter can temporize bleeding until interventional or vascular repair is achieved. Perinephric (subcapsular) hematoma is suspected with flank pain out of proportion and subsequently diagnosed with imaging. This is a rare complication attributed to laser misfiring, wire perforation, high-pressure irrigation, and forceful retrograde pyelogram and is managed with observation, reassurance, and analgesia. Occasionally, a ureteral stent is warranted and, rarely, a transfusion.

### Venous thromboembolism

Deep vein thrombosis is a rarely encountered surgical complication. It carries the potentially fatal sequel of pulmonary thromboembolism, which is exceedingly rare (0.02%) [3]. Pulmonary thromboembolism is one of the most common causes of nonsurgical death in patients undergoing urologic surgery and is associated with significant long-term morbidity [50]. The American Urological Association (AUA) Best Practice Statement does not specify URS procedures; however, all patients should be provided mechanical compression modalities and encouraged for early ambulation, and high-risk patients should be considered for pharmacologic prophylaxis [50].

### Urinary tract infection

Complicated UTI and pyelonephritis have a post-URS incidence of 1–3.7% [3, 51]. General risks of infectious complications include older age, obesity, female gender, nutrition or immune system impairment, diabetes mellitus, smoking, coexisting bodily infection, and increased bacterial load [52]. Increased bacterial load is associated with history of urogenital infections, preceding or recent hospitalization, urinary obstruction, large urinary stone, or long-term urinary drainage tubes [52]. The AUA recommends antibiotic prophylaxis for all patients undergoing URS; however, the European Association of Urology (EAU) only recommends prophylaxis for select URS cases of proximal or impacted stones and patients with risk factors associated with infectious complications [52, 53].

Martov retrospectively reviewed the Clinical Research Office of the Endourological Society (CROES) database identifying that in patients having negative baseline urine culture, the rates of post-URS UTI and fever were not reduced by preoperative antibiotic prophylaxis; moreover, female patients or those with impaired immunity (such as Crohn's disease) and higher American Society of Anesthesiologists (ASA) grades were at greatest risk of post-URS fever or infection. However, antibiotic use was not controlled, and conceivably higher risk patients were provided antimicrobial prophylaxis [51]. Although several randomized controled trials have reported that antibiotic prophylaxis significantly decreased bacteriuria following URS [54, 55], Ramaswamy and Shah demonstrated that a course of prophylactic antibiotics following an uncomplicated ureteroscopic procedure provided no benefit in preventing infectious complications, and is therefore not recommended [56]. A study reviewing the CROES data showed a significantly reduced incidence of postoperative infectious complications with a UAS (fever 28 vs. 39%, UTI 18 vs. 24%, and sepsis 4 vs. 15%, for UAS vs. non-UAS groups, respectively) [57].

A urine culture or urinalysis should be obtained prior to URS, and bacteriuria or positive culture should be treated prior to surgery. If frank pus or pyonephrosis is encountered intraoperatively, especially in the setting of obstruction, the case should be terminated with placement of stent or nephrostomy tube and antibiotics tailored towards cultures.

### Infection/sepsis

Sepsis is an uncommon but life-threatening complication of URS, reported at 0.3% [3]. Retrograde seeding of bacteruria or infected calculi are contributory factors. The surgeon should be cognizant of fluid pressure transmitted to the upper tracts, especially in patients with chronic indwelling urinary drainage tubes or urinary stasis. Additional antibiotics may be used postprocedure for higher-risk patients. Renal urine aspirate and stone culture can be obtained intraoperatively to guide antibiotic administration if infection does manifest. A significantly reduced incidence of infectious complications (specifically >50% reduction in sepsis) has been reported in patients treated using a UAS [51].

## Late postoperative complications

### Ureteral stricture

The miniaturization of technology and improved technique has led to dramatic decrease in stricture rates. Contemporary studies suggest stricture incidence of 0.5–4% [32, 58, 59] with some reporting a consistently infrequent rate of <1% [3, 6, 60–62]. Strictures (Figure 56.9) develop secondarily to inflammatory processes following devascularizing or ischemic injury to the urothelium, usually from direct mechanical trauma, iatrogenic mucosal lesions, perforation, submucosal dissection, relative ischemia, dilation, thermal lesions, radiation, impacted stone, and periureteral fibrosis [63]. However, some strictures develop without an identifiable precipitator. Presentation can be either symptomatic or asymptomatic ("silent obstruction").

Stone impaction >2 months carries a greatly increased incidence of stricture [63]. Ureteral perforation increases

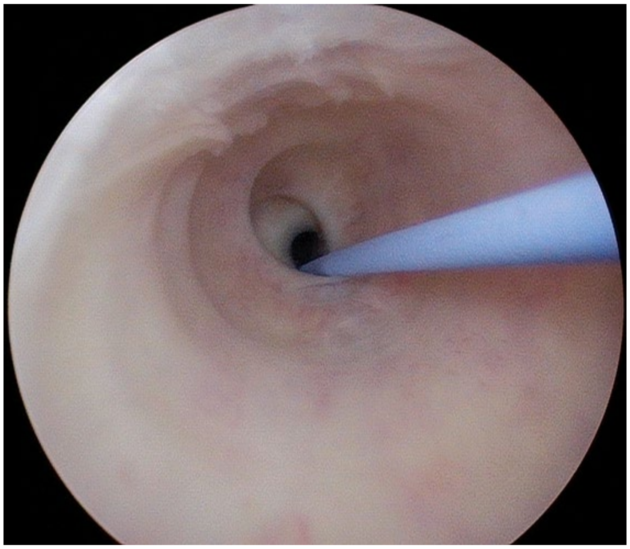

**Figure 56.9** Ureteral stricture recognized endoscopically.

stricture formation simply as an ischemic event; however, ureteral perforation at the site of stone impaction was identified as the greatest primary risk factor for stricture formation [33, 63, 64]. If perforation is identified, stenting for 2–3 weeks may decrease the risk of stenosis [33]. Some investigators suggest ureteral balloon as a precipitating event to stricture formation but a multi-institutional study showed only one stricture (0.9%) developed in 151 patients who underwent balloon dilation [7]. The use of UAS does not seem to significantly increase the risk of stricture formation [37].

In order to prevent missing the rare but potentially catastrophic silent obstruction the AUA Guideline Panel recommends routine postoperative ultrasound (±kidney, ureter, and bladder) imaging after URS. The relatively low cost and lack of ionizing radiation with ultrasonography justifies its use.

Management of ureteral stricture is discussed in other chapters in this volume. Briefly, short (<1 cm) diaphanous strictures typically can be treated endoscopically, while long (>2 cm) typically require more invasive procedures for a durable outcome. Those intermediate length strictures (1–2 cm) require a balanced assessment of patient acuity and durability of technique; e.g. younger, healthier patients likely needing more durable procedure and older, less healthy patients perhaps benefiting from less invasive procedures.

### Urethral stricture

Any transurethral procedure has the potential to injure or scar the segments of the urinary tract undergoing instrumentation. As such, URS procedures performed in a retrograde fashion are typically transurethral. The incidence of urethral stenosis in women is extremely rare, but it is more commonly observed in males. This complication should be suspected in any patient with a history of transurethral instrumentation who has new onset voiding symptoms, split stream, or change in urinary flow pattern. This diagnosis can be worked up with uroflowmetry and followed with cystoscopy and surgical management, as needed.

### Persistent vesicoureteral reflux

Vesicoureteral reflux may be present after URS even if ureteral dilation was not performed. Its incidence has been reported as high as 10% within the first 24 hours post-URS. Resolution of vesicoureteral reflux is typically observed within 2 weeks; however, 5–10% of these patients (mostly those having undergone ureteral dilation, incision of the ureteral orifice, or excised lesions at the intramural ureter) demonstrate persistent vesicoureteral reflux 3–20 months after their procedure [33]. Theoretically, persistent vesicoureteral reflux can increase the risk of upper tract infections in the presence of lower tract bacteriuria, but indication for surgical correction is rare. Grades 1–3 sterile reflux typically have no consequences in adult populations, and therefore radiographic vesicoureteral reflux evaluation after URS is not routine [65]. If treatment is required because of recurrent upper tract infections or high-pressure voiding, bulking agents are injected at 6 o'clock beneath the ureteral orifice and are usually sufficient to reduce the reflux. Formal antirefluxing reimplantation can be performed but is exceedingly rare.

## Conclusion

- Adherence to general safety rules for endourology will help minimize perioperative complications: a safety wire is essential to maintaining access. Always visualize ureteroscope advancement, working instruments, and energy sources. When unsure or encountering difficulty during a procedure, the urologist should continue with extreme caution, using fluoroscopy for orientation.
- Patient selection, appropriate procedure selection, and surgical planning are critical to successful outcomes.
- Complications can typically be conservatively managed, with opportunities for staged and successful outcomes using either a repeat or alternative approach.
- Forced maneuvers must be avoided with low threshold for stenting and staging a procedure, if difficulty is encountered.

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# 57

# Retrograde Intrarenal Surgery in the Future: Robotics

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## Introduction

As the world enters the fourth industrial revolution, there will be rapid evolution in the areas of artificial intelligence (AI), robotics, three-dimensional (3D) printing, nanotechnology, genetics, and biotechnology. "Robots" have been part of human society since before Leonardo Da Vinci described gears, wheels, and pulleys to animate a robotic knight for a Milan pageant in the 1490s. *Robot*, a derivation of the Czech word "robota" from a 1920 play entitled *R.U.R.* (*Rossumovi Univerzalini Roboti*) by Czech author Karel Capek, meant forced labor or serf. Capek described fictional human-like machines that continuously performed repetitive hard, dull, or dangerous complicated tasks for their human counterparts without feeling. The machines eventually became "resentful," rebelled, and killed all the humans. Consequently, over time, the word "robot" has encompassed several meanings including that of a brutal human being who has become insensitive or machine-like because of overwork and mistreatment. In 1939, after meeting Ernest and Otto Binder at the Queens Science Fiction Society, who had published a story entitled *I, Robot* about a sympathetic misunderstood robot called Adam Link (who was motivated by love and honor), and following a conversation a year later with John W. Campbell, Isaac Asimov introduced his Three Laws of Robotics in a short story called "Runaround."

1) A robot may not injure a human being or, through inaction, allow a human being to come to harm.
2) A robot must obey the orders given it by human beings except where such orders would conflict with the First Law.
3) A robot must protect its own existence as long as such protection does not conflict with the First or Second Laws.

A fourth law was later added:

4) A robot may not harm humanity, or, by inaction, allow humanity to come to harm.

Since then, robots have been remade in mankind's image, and popularized by the televisual industry. Before Azimov, Edgar Allen Poe (1839) related the story of a wounded soldier whose body was rebuilt with synthetic parts. During the early part of the space race (1960) this was termed a cybernetic organism, for it was envisaged that blending technology with astronauts' bodies could help endurance and survival in space. This led to a plethora of medical technologies such as pacemakers, insulin pumps, cochlear implants, prosthetics, and exo-suits, all of which are already integrated into human society.

In today's world, the real issues regarding robots' future roles center over debate as to whether they will primarily augment or replace current human functions. Autonomous robotic technology has increasingly replaced traditional tedious repetitive industrial human manufacturing roles, performing dull, dirty, and dangerous tasks, leaving their human counterparts in the shade for both accuracy and efficiency. Simultaneously, programmable and master/slave-controlled drone technology, automated driverless vehicles (cars and airplanes), and crop spraying and seed dispersal farming drones have all begun to impact different aspects of daily human life, while also replacing humans in situations of inherent task-associated danger. Where sustained precision, reliability, reduced costs, and greater productivity are desired, advanced sensor robotic technology can

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easily augment or supplant human performance without fatigue. More human functions are or will be threatened in the coming years, and some have even predicted that the ultimate supremacy of robotic over human development will be reached in only two more decades. It is a potential revolution akin to the Internet, where robots can fulfill diverse roles in society as human substitutes, companions, and partners (co-bots).

For medical applications, a key issue is whether robotic machines are better, or simply enhance human performance by lacking or reducing fatigability, allowing greater precision and efficiency over longer durations. This is particularly true for master/slave devices where expensive development costs can be offset by time saved, greater task performance precision, and increased productivity, and perhaps also consistency, particularly in repetitive or endurance-based tasks. Ideally, a master/slave human–robot partnership should enhance the capability of each individual component part provided the master can maintain concentration throughout the task. In interventional urology, robotics has already made great inroads through the use of devices that are master-independent, such as the PUMA560 [1] (1988; arm with six degrees of freedom used for brain biopsy and later for transurethral resection of prostate) and, more recently, the Cyberknife for precision radiotherapy. Zeus and Aesop (US Food and Drug Administration [FDA] approved in 1990; Computer Motion, Santa Barbara, CA, USA), were bought and quashed by Intuitive Surgical (Sunnyvale, CA, USA) in favor of their Da Vinci™, a next-generation master/slave console-controlled robotic device with endo-wrist technology (FDA approved in 2000) [2, 3]. It and the Sensei-Hansen device (Hansen Medical, Mountain View, CA, USA) [4, 5] were their urological successors, incorporating console-based 3D optical visualization with magnification, motion control and scaling, tremor reduction, and a greater range of movement and ergonomics compared to traditional instruments. Although it is beyond the scope of this chapter to examine cost-benefits, this aspect of all new technologies will be amplified in an era of economic austerity coupled to higher healthcare demands from chronic illness, fueled by obesity and ageing pandemics, and falling birth rates in the world's developed nations.

Rupel and Brown's endourological legacy of cystoscopic nephroscopy for renal stones at open surgery in 1941 [6] has been the evolution of a wide range of extracorporeal, ureteroscopic, percutaneous, and laparoscopic procedures, all embraced by urologists worldwide. The dominant large/branched renal stone treatment remains percutaneous nephrolithotomy (PCNL). Nevertheless, after two decades of evolution, classical retrograde intrarenal surgery (cRIRS) is now the most dominant endourological stone treatment modality overall. Expertise and allied technological growth has projected cRIRS to the mainstream of complex endourological stone and soft tissue treatment in the upper urinary tract. For the first time, cRIRS rightly challenges the dominant alternative of PCNL treatment of larger intrarenal calculi [7–12]. However, cRIRS for large stones remains a technically challenging procedure requiring specific expert endo-skill sets, real-time problem solving capabilities [13–15], and both physical and mental endurance. Even when ureteral access sheaths (UAS) are used (almost mandatory in this setting), and the stone(s) can be accessed and completely laser-fragmented, the single-sitting stone-free rate is limited by the operator's stamina during long dusting and "pop-corning" procedures, and the size and number of stone fragments that can safely be removed down the ureter in a safe, timely manner (in turn dependent on stone composition and hardness, and collecting system anatomy). Additional limiting factors are current flexible ureterorenoscope (FUR) design, a moving target (renal respiratory excursion) during fragmentation, and awkward calyceal anatomy, particularly if several such cases are scheduled per day. This has resulted in ≥50% secondary procedure rates to render patients stone-free. Furthermore, the surgeon depends on assistants for key task performance, to activate lasers (standby-ready and energy-rate settings adjustments), deploy nitinol baskets and capture fragments, maintain and enhance irrigant flow, aspirate, and to draw/inject contrast, while manipulating and targeting the ureterorenoscope tip. All operating room staff are exposed to radiation over a longer period (range of 1.7–56 μSv [16–18]). Meanwhile, less invasive evolutionary PCNL techniques (mini, ultra-mini, super-mini, and micro-PCNL [19–24]) have also evolved to challenge cRIRS, to gain parity or ascendancy in the current larger renal stone treatment paradigm, particularly in Asia, so further technological and technique evolution is mandated.

During the last two decades, significant changes in both semirigid and FUR design, specifically tip and shaft size reduction along with configuration changes, have facilitated easier natural orifice access into the upper urinary tract for the majority of users (albeit at the cost of increased fragility and repair costs). Greater direction and range of tip deflection (both single and dual active flexion/extension motion range) has made navigation through the intrarenal collecting system easier, allowing more urologists to reach and inspect >95% of the entire collecting system (the most challenging part being the lower antero/medial calyx, especially in a dilated pelvicalyceal system which limits use of both active and secondary passive deflection).

In 2012, ELMED (Ankara, Turkey) started developing a procedure-specific robot-assisted RIRS (RA-RIRS) device [25]. The IDEAL (idea, development, evaluation, assessment, long-term study) framework for surgical innovation stages was embraced from prototype to the commercially available Avicenna Roboflex (IDEAL stage 1), and early clinical experience with treatments performed by different experienced endourologists (IDEAL stages 2–4) was reported as follows.

## Device development

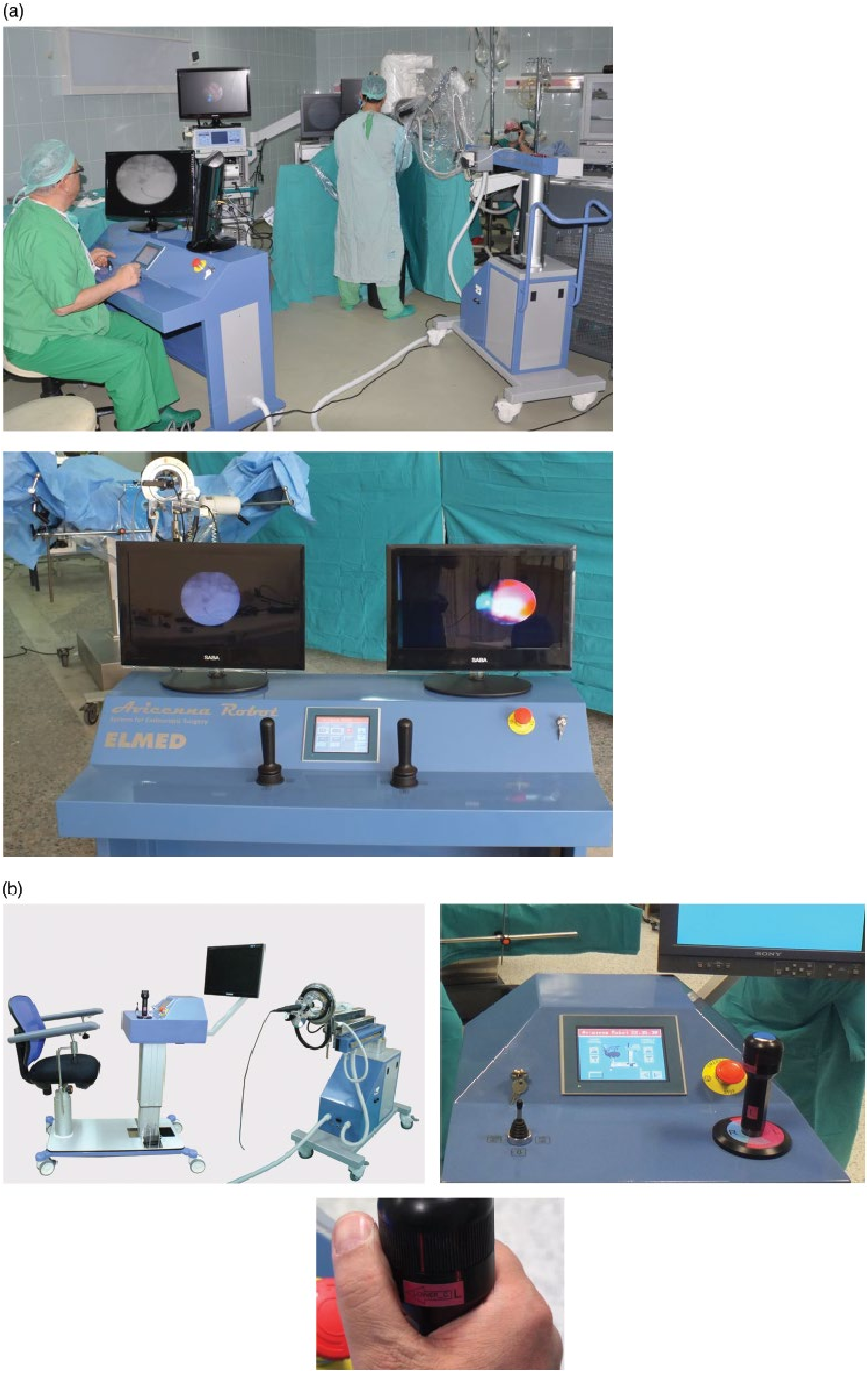
The basic Avicenna Roboflex design from prototype (Figure 57.1a) to successive versions (Figure 57.1b–d) consisted of a master control console (MCC) seating the surgeon and a manipulator arm (MA), which can now be coupled to any standard commercially available FUR using a custom-made model-specific adapter. During the early developmental phase, incremental improvements were made to the size and design of the MCC, the joysticks to control advancement, rotation, and tip deflection, and to develop a system to remotely advance-retract the laser fiber.

### Master control console design features

The current Avicenna Roboflex (version 5) MCC (Figure 57.2a) is connected to the MA unit, and its monitor is connected as a slave to the operating room stack monitor. It has key-control on-switch, with separate red push-button emergency stop (Figure 57.2b). The MCC reclining seat has adjustable height, head, and armrests. Six users can store individual seat positions and all preferred custom deflection-scaling settings in the system memory (Figure 57.3). The comfortably seated surgeon activates wheel locks, selects endoscope type, brightness, time, background screen color (one of six options), rotation precision and direction, deflection precision, and horizontal plane movement speed via the set-up menu. Moreover, they can also select low- (0.5×) or high-precision (1.5×) modes, timer stopwatch start or reset options, and define target kidney side (right or left) on the touch-screen panel (also displayed on the center right of the monitor screen). The MCC touch screen also allows control of laser fiber actuator, irrigation flow rate, short bursts of flush, and abdominal compression belt inflation to reduce renal respiratory movement (Figure 57.4). Below this on the monitor screen is the endoscope deflection and rotation icon, and above it are laser fiber and irrigation flow rate indication bars (Figure 57.5). The rotation display circle containing the endoscopic view is in the center. The surgeon controls two joysticks (with adjustable padded wrist support) to manipulate the FUR, which is mounted on the MA component. The right-hand vertical joystick bulb's "magic wheel" controls fine tip deflection akin to the handpiece of any standard FUR (Figure 57.6a), but with additional tenfold motion scaling. The deflection direction (upwards, downwards) can be programmed for logical deflection (down = tip down and up = tip up) or counterintuitive deflection (down = tip up and vice versa). The new horizontal left joystick (Figure 57.6b) allows clockwise and counterclockwise MA rotation, as well as advancement and retraction of the endoscope shaft with millimeter per second adjustment, using +/– buttons. The rotation speed, scale (2, 1, 0.5×) and MA rotation direction (clockwise or counterclockwise), and advancement can be regulated by console touch-screen control. Warning display box alerts inform the user about rotating the MA to the mounting position (90° clockwise), continuing from a particular position, or returning to the neutral position.

→

**Figure 57.1** (a) Avicenna Roboflex version 1 prototype for RA-RIRS: simple circular holder for FURS control and laser fiber movement, controlled from console with two small four-way joysticks (left for forward/backward and laser fiber in/out, right for rotation clockwise/counterclock wise, and deflection up/down). The joysticks were later modified with bigger, thicker handles. (b) Similar manipulator arm with longer horizontal movement (forward/backward movement) for easier basket application, and smaller control console with height adjustable seat. Control of the left joystick movements were unchanged, but right joystick had a thick, rotatable handle to control FUR rotation and there was another individually rotatable disk incorporated into the top of the joystick handle to control up/down deflection. (c) Version 3: new manipulator arm design (with high-precision robotic components) with open-type endoscope holder and new master control console (MCC). Rotation movements over 440° were designed for smooth precision following hand movement. Special endoscope holder was designed for easy docking with deflection control unit. A force-torque deflection mechanism sensing system was developed to protect the device against high-deflection torsion. Horizontal movement (forward/backward) was set to a speed of 22 mm/second (adjustable from 0.5 to 22 mm/second). The MCC was designed with two joysticks to control rotation and forward/backward movement (left joystick), and deflection movement on the right joystick. Laser fiber movement and vertical movement (according to patient tabletop position) were controlled from the touch screen. Later, a central precision control cylinder was added to the center of the MCC for fine tip deflection control as a modification of that version. (d) Version 4 incorporating a new interchangeable endoscope holder system to accommodate all FUR brands/models. The right joystick controlled rotation and two-stage speed control for forward/backward movements and incorporated a thumb wheel ("magic wheel") for tip deflection. Precision or scale of all rotation and tip deflection movements were selectable from the MCC touch screen. A new MCC foot-pedal unit was incorporated to control any laser or fluoroscopy foot pedals. Additional visual guidance was provided on the video monitor screen to indicate the spatial position of the FUR (such as horizontal distance, rotation angle, and deflection angle).


(a)
SABA
SABA
Avicenna Robot
System for Endoscopic Surgery
ELMED
(b)
SONY

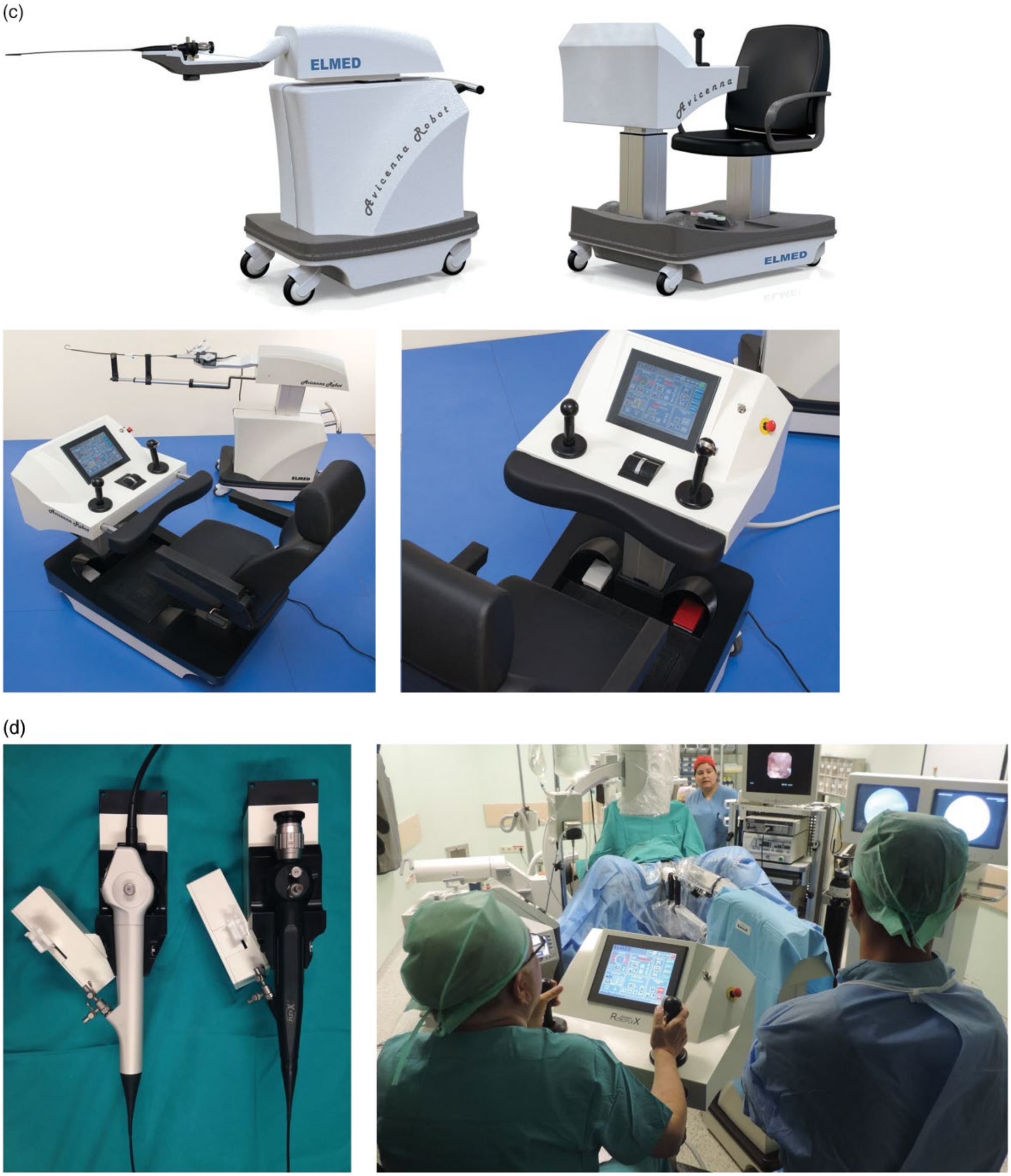

(c)
ELMED
Avicenna Robot
Avicenna
ELMED
(d)

**Figure 57.1** (Continued)

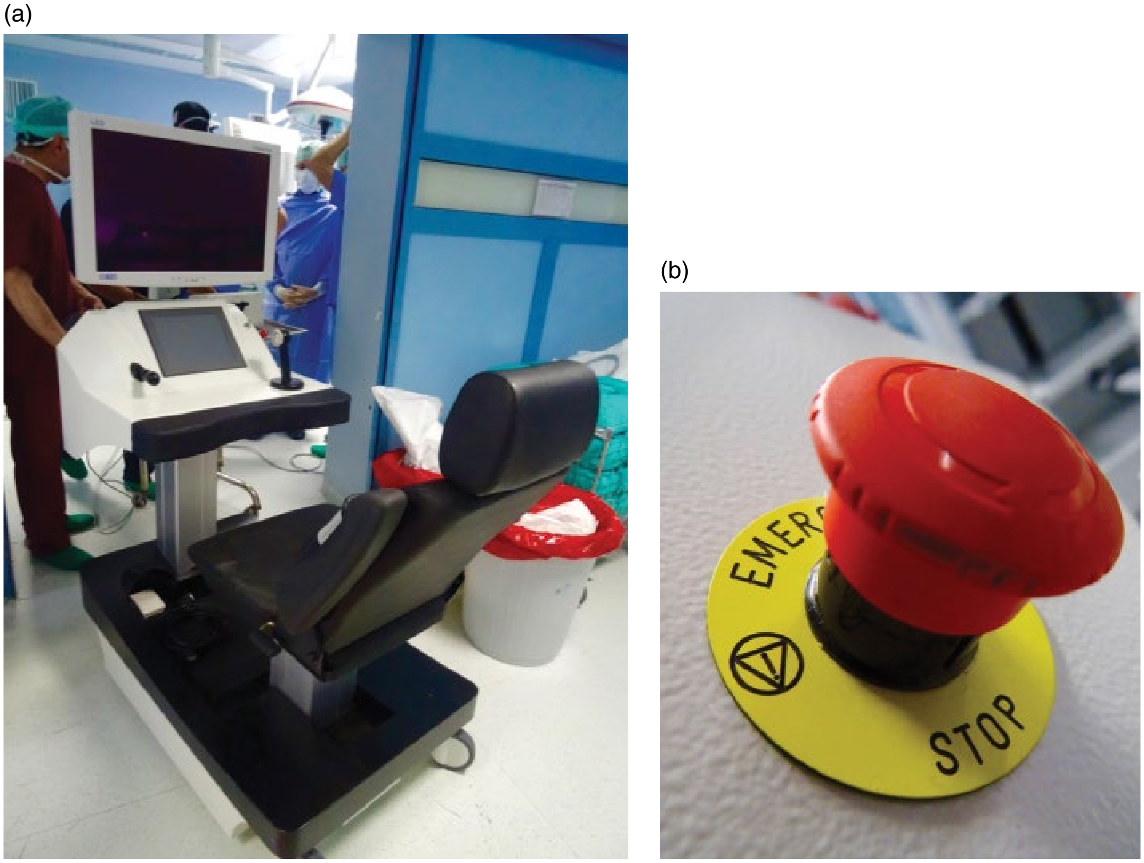
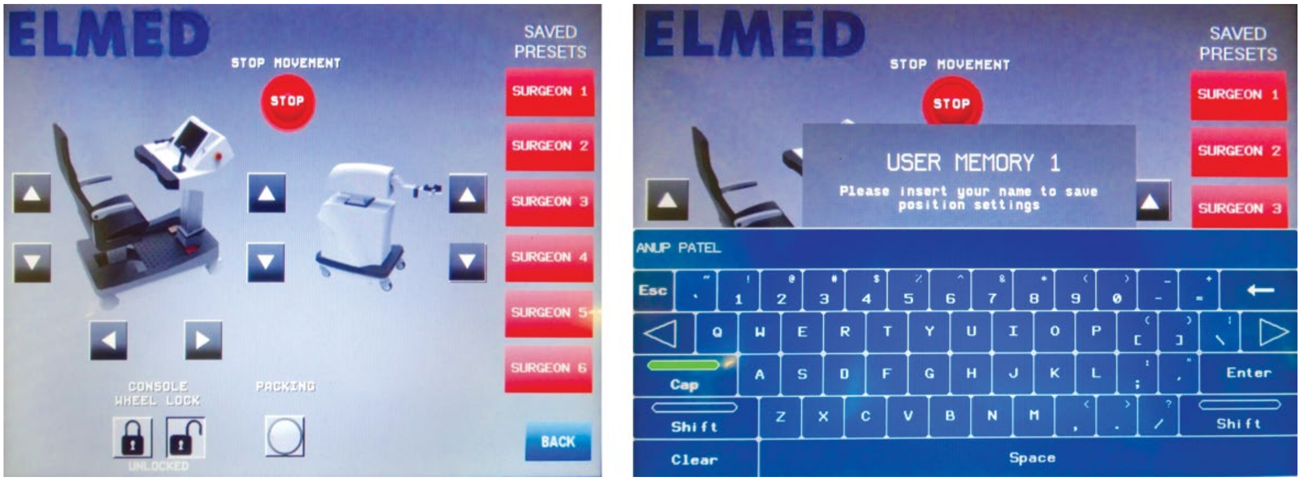

(a)
(b)
EMERG
STOP

**Figure 57.2** (a) Version 5 MCC unit with key control start, and improved adjustable seat design, headrest, and wrist support bar as an ergonomically sound comfortable surgical workstation. Horizontal left joystick for horizontal and rotational movement control, and right vertical joystick with magic wheel to control fine tip deflection (all with adjustable precision from MCC touch screen). (b) Red emergency stop button.

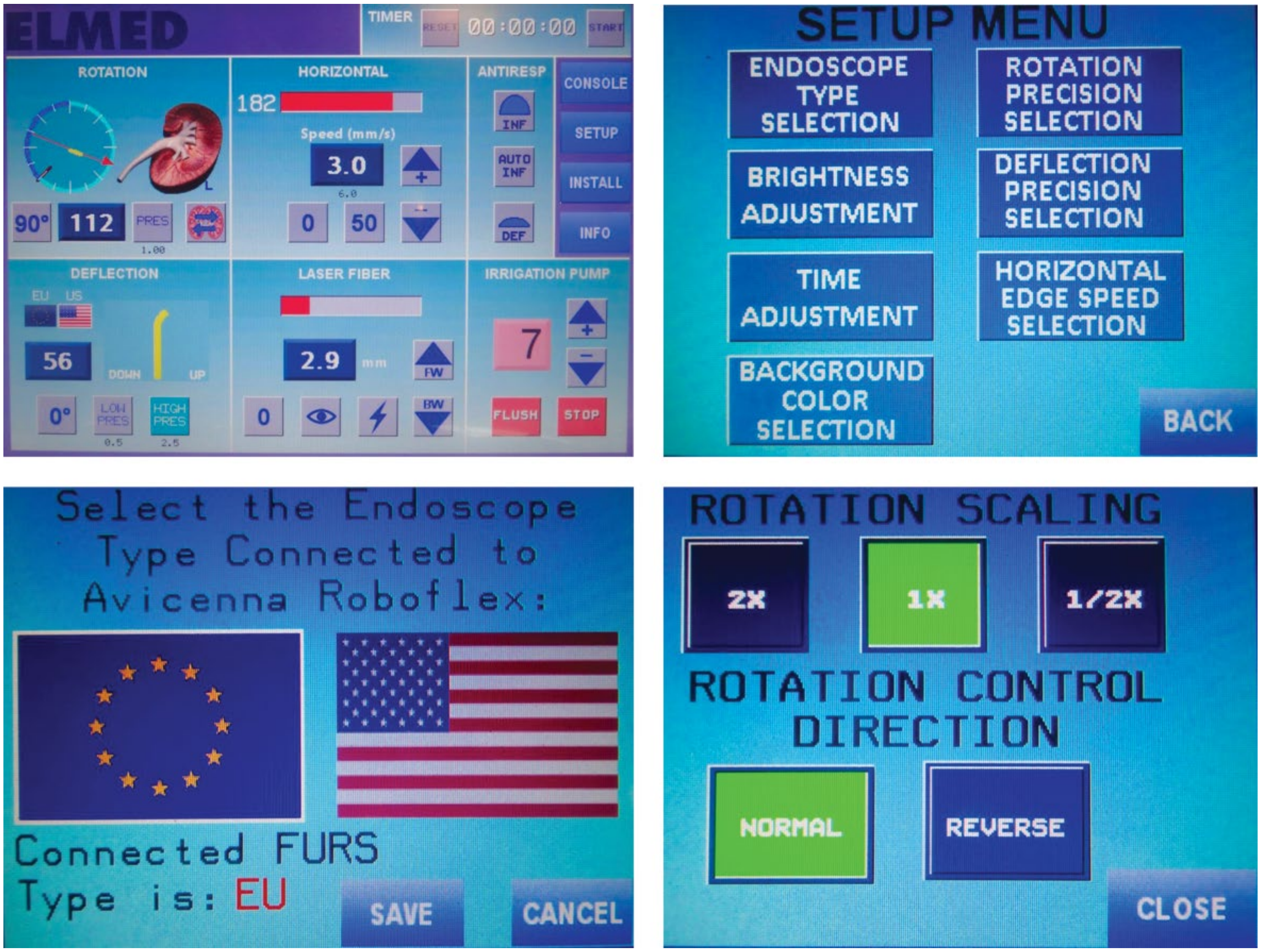

ELMED
STOP MOVEMENT
STOP
SAVED PRESETS
SURGEON 1
SURGEON 2
SURGEON 3
SURGEON 4
SURGEON 5
SURGEON 6
CONSOLE WHEEL LOCK
PACKING
UNLOCKED
BACK
Esc
Cap
Shift
Enter
Clear
Space

USER MEMORY 1

Please insert your name to save position settings

ANUP PATEL

**Figure 57.3** System memory for six users.


ELMED
TIMER
RESET
00:00:00
START
ROTATION
HORIZONTAL
182
Speed (mm/s)
3.0
6.0
ANTIRESP
INF
AUTO INF
DEF
CONSOLE
SETUP
INSTALL
INFO
90°
112
PRES
1.00
0
50
DEFLECTION
EU US
56
DOWN
UP
0°
LOW PRES
HIGH PRES
0.5
2.5
LASER FIBER
2.9
mm
FW
BW
0
IRRIGATION PUMP
7
FLUSH
STOP
SETUP MENU
ENDOSCOPE TYPE SELECTION
ROTATION PRECISION SELECTION
BRIGHTNESS ADJUSTMENT
DEFLECTION PRECISION SELECTION
TIME ADJUSTMENT
HORIZONTAL EDGE SPEED SELECTION
BACKGROUND COLOR SELECTION
BACK
SAVE
CANCEL
ROTATION SCALING
2X
1X
1/2X
ROTATION CONTROL DIRECTION
NORMAL
REVERSE
CLOSE

Select the Endoscope Type Connected to Avicenna Roboflex:

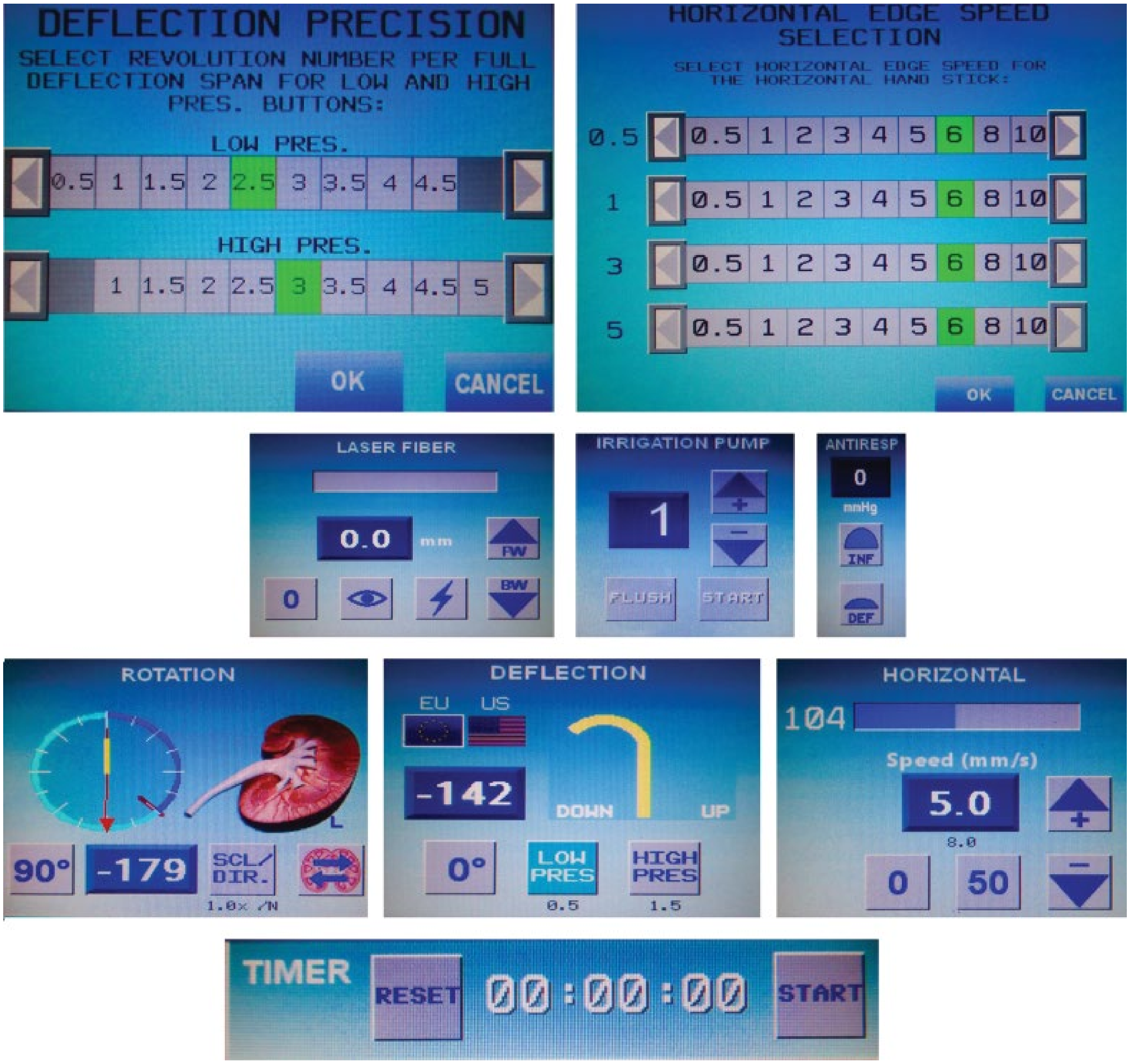
Connected FURS Type is: EU

**Figure 57.4** The MCC touch screen with various functions in the set-up menu: adaptation to FUR mode (i.e. American or non-American), change of rotation, deflection precision, horizontal advancement/retraction speed, laser fiber advancement and retraction, irrigation flow rate adjustment, compression belt inflation-deflation, and degree of rotation, deflection, and horizontal insertion display, along with timer and stop watch.

The assistant introduces the laser fiber at the start with the endoscope tip in a “0” straight position, with the tip cladding just visible endoscopically, and the touch-screen “eye button” in the laser fiber box is pressed. The zero button is then activated to level the fiber tip with the work-channel exit point. The endoscope can now be safely maneuvered to the stone before advancing the fiber tip 1.8 mm for safe firing. The MCC floor-mounted red right foot pedal controls laser firing, while the white left pedal controls the fluoroscopy (Figure 57.7a), both aided by compressed air cabling to a foot-pedal coupler unit (Figure 57.7b). The laser fiber foot pedal is automatically disabled when the fiber tip is within 1.6 mm of the endoscope tip (the red warning bar is a useful safety feature).

## Manipulator arm design

The MA consists of computer-controlled motor systems, a robotic arm, which holds and moves the endoscope, and the lower stabilizing arm to which vertical supports are attached in two places. The arm height can be adjusted according to the patient’s anatomy. The endoscope hand piece with appropriately placed deflection lever is fixed into the arm’s customized coupler housing and secured by double clip holders after draping (Figure 57.8). The distal vertical stabilizer is fixed to the preplaced UAS hub, while the proximal one stabilizes the straight endoscope shaft approximately 5 cm further back (Figure 57.9a). A UAS is virtually mandatory for Avicenna Roboflex procedures, due to lack of haptic



DEFLECTION PRECISION

SELECT REVOLUTION NUMBER PER FULL DEFLECTION SPAN FOR LOW AND HIGH PRES. BUTTONS:

HORIZONTAL EDGE SPEED SELECTION

SELECT HORIZONTAL EDGE SPEED FOR THE HORIZONTAL HAND STICK:

LOW PRES.
0.5 1 1.5 2 2.5 3 3.5 4 4.5
HIGH PRES.
1 1.5 2 2.5 3 3.5 4 4.5 5
OK
CANCEL
0.5
1
3
5
0.5 1 2 3 4 5 6 8 10
OK
CANCEL
LASER FIBER
0.0
mm
FW
BW
0
IRRIGATION PUMP
1
FLUSH
START
ANTIRESP
0
mmHg
INF
DEF
ROTATION
L
90°
-179
SCL/ DIR.
1.0x /N
DEFLECTION
EU
US
-142
DOWN
UP
0°
LOW PRES
HIGH PRES
0.5
1.5
HORIZONTAL
104
Speed (mm/s)
5.0
8.0
0
50
TIMER
RESET
00:00:00
START

Figure 57.4 (Continued)

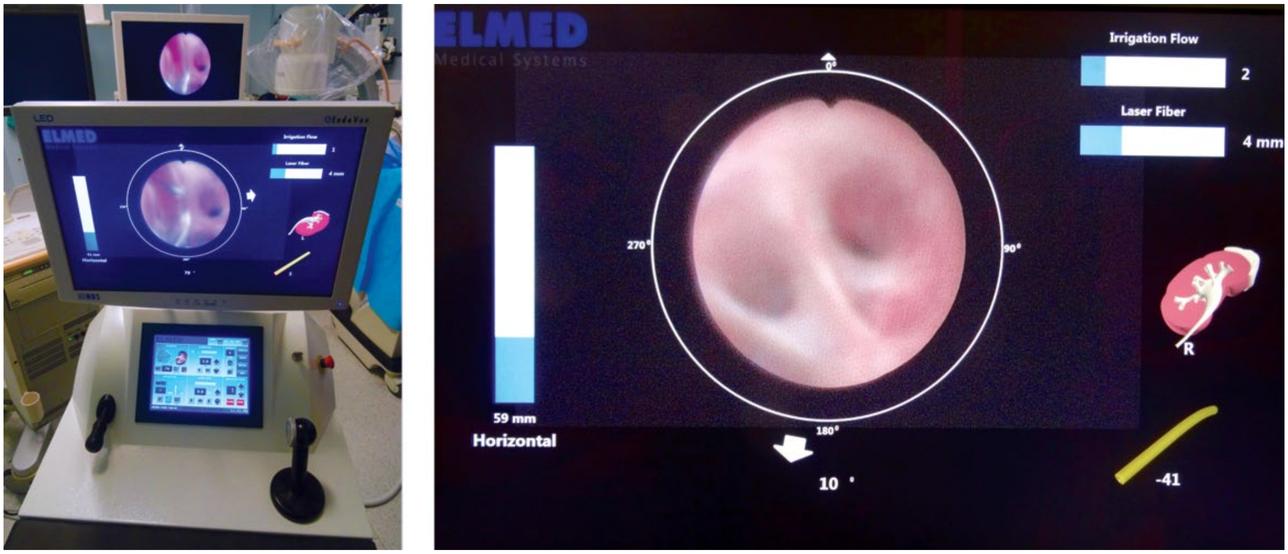

ELMED
Medical Systems
Irrigation Flow
2
Laser Fiber
4 mm
0°
90°
180°
270°
R
59 mm
Horizontal
10 °
-41

Figure 57.5 MMCC with slave monitor screen for endoscopic image within central rotation indicator circle, progress bars for irrigation flow rate and laser fiber extrusion distance from tip (mm) on right upper, side of kidney right central, FUR tip deflection indicator right lower, and insertion rate progress bar left of center.

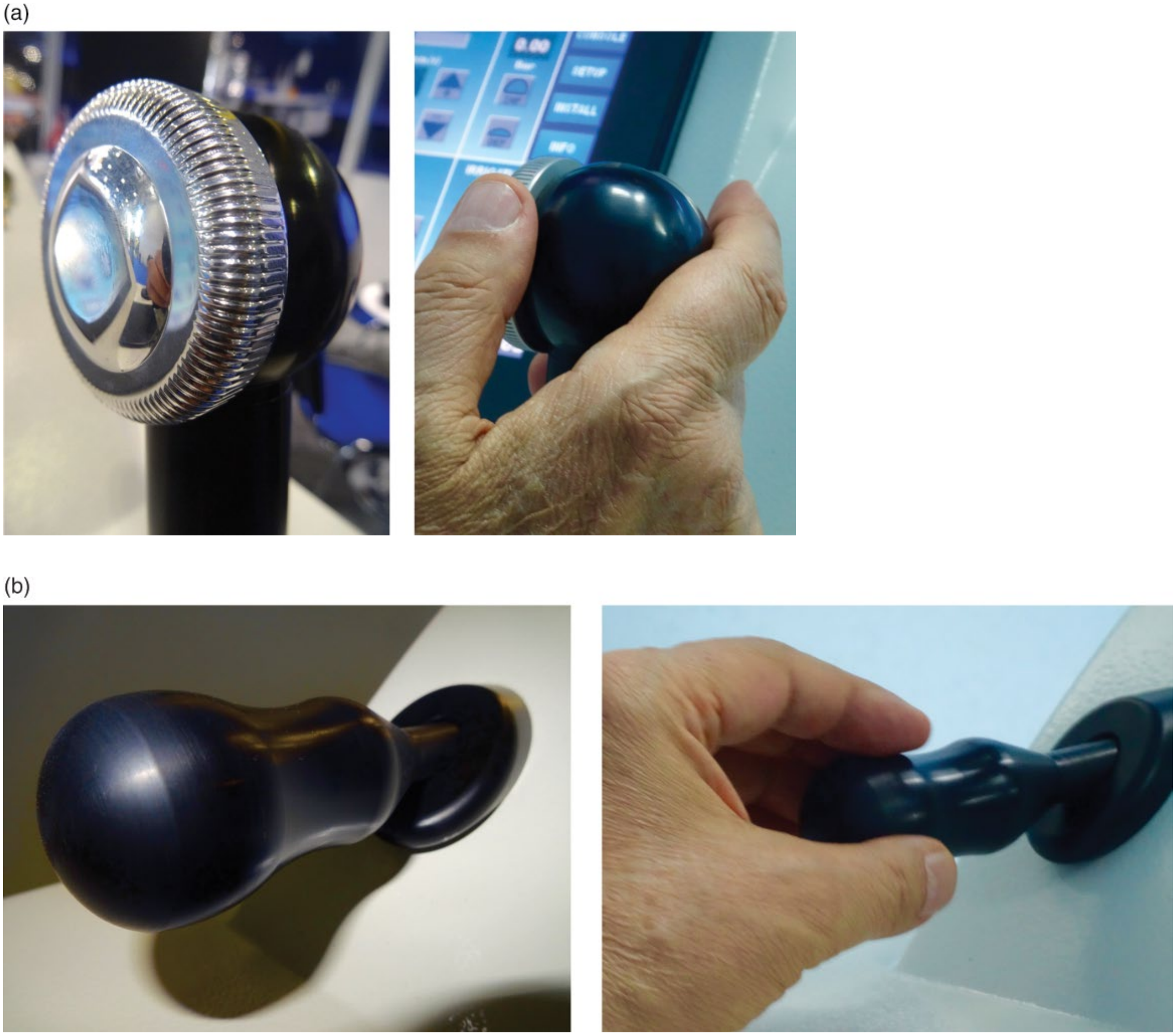
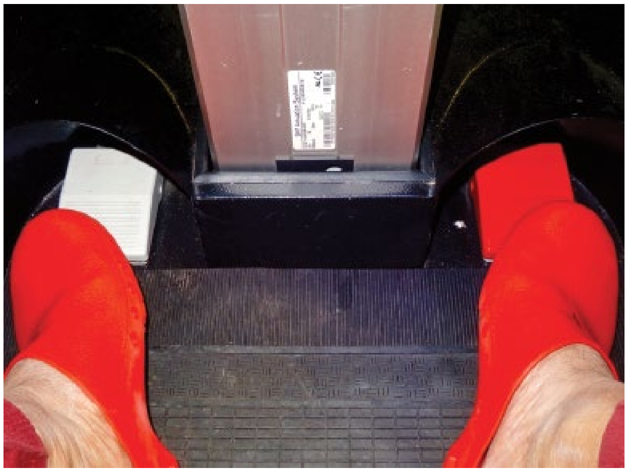


**Figure 57.6** (a) Magic wheel atop bulb of right-hand MCC control joystick for fine scaled up-and-down endoscope tip deflection. (b) Left-hand horizontal control joystick of MCC for clockwise and counterclockwise rotation, and in-and-out endoscope movement.

feedback, reducing risk of inadvertent ureteral injury. The custom-made coupler accepts any FUR, although initial development was made using a digital instrument (Flex-XC; Karl Storz, Tuttlingen, Germany). The MA can be rotated bidirectionally by 210° allowing overlap for a total 440° compared to 120° for humans. Miniaturized hand-piece adaptor motors allow endoscope steering lever movement for deflection and enable motion scaling of the cable-based endoscope tip movement mechanism. Due to FUR design and cabling inertia, a short lag period between robot control and endoscope tip reaction exists. This is vital for the user to understand and remember, for there is a tendency to continue MCC deflection if no immediate visible screen reaction is seen, leading to delayed deflection overshoot. The same lag occurs for the same reason when switching deflection direction. Normally, a 10° manual lever deflection moves the tip 60°. With Avicenna Roboflex, FUR tip control precision is eightfold greater than manual operation. The thumbwheel scaling precision, which can be low or high, or on a scale of 1–10 as set on the MCC, allows 10° of thumb movement to result in 3–30° of tip deflection. The applied forces were limited to 1 N/mm$^2$ for safety to minimize the risk of collecting system and endoscope injury.

Moreover, the coupling hand-piece adapter accepts placement of a micromotor-driven actuator system, which is connected to the instrument's working-channel for precise laser fiber advancement (Figure 57.9b).

(a)



(b)

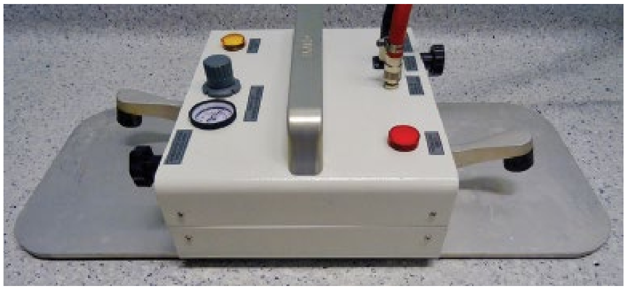


**Figure 57.7** (a) MCC floor-mounted red right foot pedal (for laser firing control) and white left pedal (for fluoroscopy control). (b) Compressed air cable activated foot-pedal coupler unit.

## Experimental evaluation

For all MCC steering, and movement reliability functions, the Avicenna Roboflex was tested in a validated flexible ureterorenoscopy *in vitro* training model (Minnesota University Kidney Model [25]) containing artificial stones. This enabled safe prototype(s) simulations to evaluate key parameters and all device functions. It was also used for hands-on training of all participating surgeons.

### *In vitro* studies

Avicenna Roboflex showed safe, stable maneuverability, with easy translation of MCC functions when in both bench training models and pig ureters. Prototype ergonomics were already good, but incremental improvements to wrist movements, and fine-tuning of deflection were made.

## Surgical technique

With the patient under general anesthesia, supine in lithotomy, intravenous diuretic (lasix) and antibiotic prophylaxis are given, and manual cystoscopy, retrograde pyelography, and placement of a safety guidewire can be performed. The ureteral orifice is accessed with a semi-rigid ureteroscope, inspecting the ureteral lumen up to/beyond the ureteropelvic junction, thereby achieving maximal optical ureteral orifice and ureteral dilation, leaving behind a working wire as needed. A suitable size (10–12/12–14 Fr) and length (35–46 cm) UAS is then advanced into the upper ureter under fluoroscopic control as needed, confirming ureteral integrity postplacement with further pyelography via the access sheath obturator.

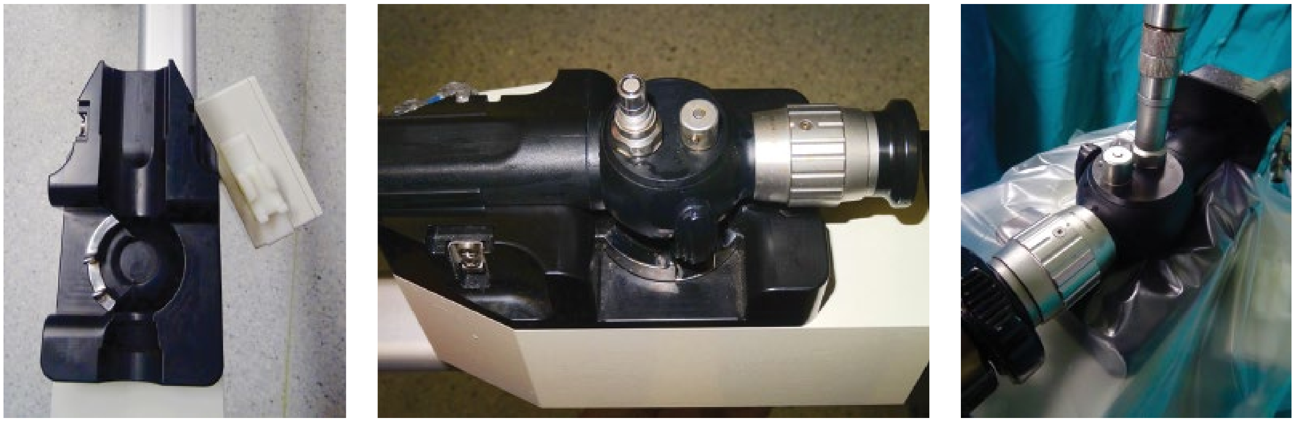


**Figure 57.8** The MA custom endoscope coupler and motorized actuator housing, with FUR hand piece fixed in the manipulator coupler and stabilized by double clip holder after draping.

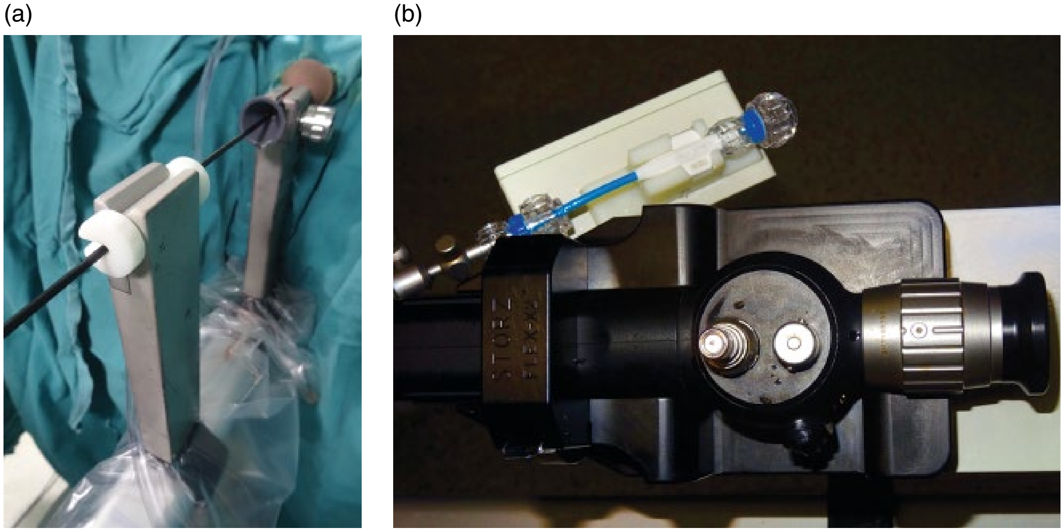


**Figure 57.9** (a) The proximal stabilizer supports the straight endoscope shaft, while the distal stabilizer fixes the UAS shaft in the same plane. (b) The laser fiber (and irrigation tube) is attached to the endoscope by a motorized actuator for fine laser fiber movements.

Next, the FUR is inserted into the UAS lumen and its hand piece is fixed in the sterile plastic-draped robotic-arm coupling adaptor, where it is securely locked with securing clips. Thereafter, checks are made for a stable, secured, straight FUR shaft, before console steering can begin. Using the MCC touch screen and control levers, the target stone(s) is endoscopically visualized and recorded with fluoroscopic snapshot (master console floor left foot pedal). If the laser fiber was not inserted at the start, the endoscope is placed in a neutral straight retracted position with the console zero button to guarantee safe laser fiber insertion without risking work channel damage. The MCC provides a memory function to guide the scope back to its previous position near the stone surface after laser fiber insertion. The inserted laser fiber tip with cladding should be just visible near the endoscope tip and the eye button on the master control laser fiber box is activated for memory entry. Only then can the fiber be retracted to a position level with the scope tip (zero button) and advanced from there by the console touch screen controls using the actuator device fitted to the endoscope work channel. The fiber cannot be retracted inadvertently into the scopes working channel and energy activated, where it might damage the instrument. Once the fiber is advanced (as shown by bicolored bar in MCC laser fiber panel) with precision to the optimal distance from the stone surface, laser-induced lithotripsy can be initiated, ideally "dusting" the stone surface with meandering rotation and small up-and-down deflection movements of the laser fiber tip in the millimeter range using the left hand rotation control lever and/or the right hand pin-wheel control, or by fragmentation (various techniques). Any commercially available holmium:YAG laser unit can be used, but one that allows higher-frequency application at low energy is recommended for optimal dusting. Smaller fiber sizes allow sufficient scope tip deflection with lowest risk of fiber fracture in the work channel at maximum energy and frequency. Once fragmentation has started, higher energy frequency gives a "popcorn effect" for fragment pulverization when dusting is not possible. Sometimes, with fiber tip in the calyx lumen center, this can even be done "hands-free" if time-consuming (see Video 57.1). Fiber tip erosion must be monitored, as it reduces energy transfer over time, and judicious appropriate cleaving with fiber re-introduction is undertaken as required. To introduce nitinol baskets for fragment retrieval at the end, the laser actuator has to be driven back to its preset zero position with the endoscope tip straight, and the fiber exchanged for the basket, once the laser console is on standby (assistant). This might be time-consuming especially if there are multiple fragments, and hence ablation by stone dusting is preferred until a suitably sized fragment is retrieved at the end for stone analysis. The need for JJ stent placement at the end of the procedure is not mandated, but left to the operator's discretion.

## Published clinical experience

### Patients and outcomes

In the first peer-reviewed study, Ankara Medical School ethics commission approval was secured, and 81 patients were treated (IDEAL stage 2) (Table 57.1). Inclusion criteria were aged >6 year, single or multiple stones with a 30 mm total diameter ceiling, absent active urinary tract infection, and no previous ureteral surgery. All patients or minors' parents were informed about Avicenna

**Table 57.1** Baseline RA-RIRS demographic and outcomes data ($n = 81$).

| Criteria | Value | Range | SD | Comment |
|---|---|---|---|---|
| Age (years) | 42[a] | 6–68 | 25.4 | According to inclusion criteria |
| Male/female | 56/25 | – | – | – |
| Left/right | 35/46 | – | – | – |
| Single/multiple calculi | 29/52 | – | – | – |
| Upper calyx | 62 | – | – | – |
| Middle calyx | 23 | – | – | – |
| Lower calyx | 62 | – | – | – |
| Renal pelvis | 26 | – | – | – |
| Stone diameter (mm) | 13[a] | 5–30 | 5.3 | Multiple calculi: sum of lengths |
| Stone volume ($mm^3$) | 1296[a] | 432–3100 | 544.3 | Calculated based on preoperative computed tomography |
| Treatment time (minutes) | 74[a] | 40–182 | 31.8 | Inclusive of UAS and double-J stent placement |
| Robot docking time (seconds) | 59.6[a] | 35–124 | 45 | 46 seconds after 42 cases |
| Stone visualization time (minutes) | 3.7[a] | 2–8 | 1.4 | Including complete inspection of collecting system |
| Fragmentation time (minutes) | 46[a] | 18–115 | 21.7 | Depending on stone size/hardness |
| Fragmentation speed, ($mm^3$/minute) | 29.1[a] | 18–46 | 6.1 | Increasing to 32.7 $mm^3$/min after 42 cases |
| Console time (minutes) | 53[a] | 23–135 | 23.2 | Depending on stone size and learning curve |
| Complications | 1 | – | – | Endoscope failure (case 42), cRIRS not possible; double-J stent placement |
| **Ergonomic scores** | | | | |
| cRIRS | 31.3[a] | 16–40 | 7.8 | Based on last 10 cases performed by each surgeon at own institution |
| RA-RIRS | 5.6[a] | 3–10 | 2.4 | Based on immediate subjective evaluation |
| Re-treatment | 2 | – | – | cRIRS |
| Robotic failure | None | – | – | – |
| 3-month stone-free rate | 65 (80%) | – | – | 16 patients (20%) with clinically insignificant residual fragments ≤3 mm |

UAS in 72 patients; nine patients with tight ureters (six children and three females) had optical rigid ureteroscopic dilation, placement of safety guidewire, and FUR without UAS. Seven experienced surgeons (5–16 years' individual cRIRS experience) with all MCC Avicenna Roboflex functions learned in the *in vitro* training model.

SD, standard deviation.

[a] Mean value.

*Source:* [26]. Reproduced with permission of Elsevier.

Roboflex use and provided informed consent. Primary end points included RA-RIRS safety and reproducibility based on successful fragmentation data, second sessions, auxiliary measures, complications (Clavien-Dindo classification), and any FUR-related/robot malfunction. Secondary end points were robot docking time, stone location time, fragmentation time, and speed (cubic millimeters per minute) based on computed tomography (CT) stone volume evaluation [27–29], console, and treatment time. Numerical data were expressed as mean with standard deviation (SD) including range; categorical data were expressed as numbers. SPSS v.15 (IBM Corp, Armonk, NY, USA) was used for data analysis. Categorical variables were analyzed using the $\chi 2$ test (or Fisher exact test). The Mann–Whitney U test was used for numeric variables. $P$ values <0.05 were considered statistically significant.

79 patients (97%) had complete stone disintegration. One patient with a large lower calyceal stone (2.5 cm) had intraoperative digital FUR failure (case 42; broken video system); cRIRS conversion did not allow procedure completion due to complicated access plus stone burden, and interval cRIRS was needed 5 days later. Another patient required secondary cRIRS for significant residual fragments. All patients had DJ stents, with removal after a median 7 day interval (range 5–10 days). Three-month stone-free rates were judged by plain X-ray and ultrasound.

## Ergonomics

Based on a published questionnaire comparing laparoscopic and robot-assisted laparoscopic surgical ergonomics [30], the operator's discomfort during RA-RIRS was subjectively compared to their last 10 home institution cRIRS cases. All participating surgeons preferred standing-position cRIRS. A significant difference existed when comparing classic and RA-RIRS ergonomics for all questionnaire domains (Table 57.2; total questionnaire score 31.3 vs. 5.6 respectively; $P < 0.01$).

## Radiation safety

Operating room personnel are at X-ray exposure risk in RA-RIRS (fluoroscopically guided stone procedure). Hence, fluoroscopic radiation exposure was measured during RA-RIRS for patient, anesthesiologist, and urologist, using RANDO phantoms, 19 thermoluminescent dosimeters (TLDs), and 21 TL ring dosimeters (TLRDs). The patient RANDO phantom with upper abdominal TLDs to measure the surface dose was placed on the operating table. The anesthesiologist and surgeon mannequins

**Table 57.2** Ergonomic comparison of classic and RA-RIRS using a validated endourology questionnaire.

| Surgeon | B.E. | A.Y.M. | K.S. | R.S. | Z.T. | J.J.R | O.T. | Mean |
|---|---|---|---|---|---|---|---|---|
| Age (years) | 51 | 52 | 50 | 67 | 40 | 59 | 46 | 52.14 |
| RIRS experience (years) | 16 | 7 | 10 | 5 | 5 | 16 | 15 | 10.57 |
| RIRS workload (hours/week) | 10 | 12 | 15 | 7 | 10 | 6 | 18 | 11.14 |
| **cRIRS, complaints (0–5)** | | | | | | | | |
| Musculoskeletal pain | 3 | 3 | 3 | 3 | 3 | 3 | 1 | 2.71 |
| Neck pain | 3 | 2 | 2 | 2 | 2 | 3 | 1 | 2.14 |
| Shoulder stiffness | 5 | 3 | 3 | 4 | 2 | 3 | 1 | 3.00 |
| Arm pain | 5 | 3 | 3 | 4 | 3 | 3 | 1 | 3.14 |
| Forearm pain | 5 | 3 | 3 | 3 | 3 | 4 | 1 | 3.14 |
| Elbow stiffness | 5 | 2 | 2 | 2 | 2 | 4 | 2 | 2.71 |
| Hand pain | 3 | 3 | 3 | 3 | 4 | 4 | 2 | 3.14 |
| Wrist stiffness | 3 | 4 | 4 | 3 | 3 | 4 | 1 | 3.14 |
| Finger numbness | 1 | 2 | 2 | 1 | 3 | 3 | 2 | 2.00 |
| Back pain | 3 | 1 | 1 | 2 | 3 | 3 | 1 | 2.00 |
| Leg pain | 2 | 2 | 2 | 2 | 3 | 4 | 2 | 2.43 |
| Eye strain | 0 | 2 | 2 | 2 | 3 | 2 | 1 | 1.71 |
| **Total score** | **38** | **30** | **30** | **31** | **34** | **40** | **16** | **31.3**[a] |
| **RA-RIRS, complaints (0–5)** | | | | | | | | |
| Musculoskeletal pain | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0.14 |
| Neck pain | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0.29 |
| Shoulder stiffness | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0.43 |
| Arm pain | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 0.71 |
| Forearm pain | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0.57 |
| Elbow stiffness | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0.29 |
| Hand pain | 2 | 0 | 0 | 0 | 1 | 1 | 1 | 0.71 |
| Wrist stiffness | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0.29 |
| Finger numbness | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0.86 |
| Back pain | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0.14 |
| Leg pain | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0.29 |
| Eye strain | 0 | 1 | 1 | 0 | 2 | 1 | 1 | 0.86 |
| **Total score** | **10** | **5** | **4** | **3** | **6** | **7** | **4** | **5.6**[a] |

[a] $P < 0.01$.

*Source:* [26]. Reproduced with permission of Elsevier.

were protected (0.5 mm lead apron and thyroid shield), and positioned near the operating table with eye, thyroid, extremity, and gonad region TLDs. The anesthesiologist mannequin was 1 m, the surgeon 0.74–0.8 m, and the Avicenna Roboflex console surgeon was 1.74–2.46 m from the fluoroscopy tube.

Retrospectively reviewed medical records revealed 30 seconds' mean cRIRS fluoroscopic screening time. Mean fluoroscopy tube potential and tube current were 66 kV and 4.99 mA, respectively, and were used to irradiate the RANDO phantom for 10 minutes (600 seconds) corresponding to 20 (600/30) RIRS operations, with a mobile multidirectional C-arm fluoroscopy unit.

In this study, for 600 seconds of fluoroscopic guidance time, the patient surface dose was 1.41 mSv (=70.5 μSv per operation), the anesthesiologist's exposure was 0.1 mSv (=5 μSv per operation), the patient-side surgeon was exposed to 0.11 mSv (=5.5 μSv) for left foot and 0.15 mSv (=7.5 μSv) for right foot. All radiation doses were below the 0.1 mSv (=5 μSv per operation) detection limit for the unprotected surgeon at the Avicenna Roboflex master console. In a urology department where 250 annual RIRS procedures take place, the annual mean dose equivalent for the anesthesiologist and patient-side urologist were calculated to be 1.25 and 1.63 mSv respectively. These preliminary results indicated that patient's and medical professional's radiation doses were quite low, but could be safely eliminated for the Avicenna Roboflex console surgeon without needing any lead protection whatsoever [31]. Self evidently, this has a significant beneficial impact on surgeon comfort and endurance.

### Training study [32]

Five experts and novices were compared in classical versus RA-RIRS for complete stone fragmentation time in five cases. There was a longer average time for RA-RIRS versus cRIRS for experts (28.84 vs. 22.04 min) and vice versa for trainees (29.84 vs. 35.72 min), who were >13 minutes slower than experts in cRIRS. Trainees learned and approached expert RA-RIRS proficiency levels after only four trials in the bench model training setting.

### Flexible ureterorenoscope and manipulator arm durability

Preliminary personal communication data (Dr R. Saglam) suggested that Avicenna Roboflex use at the Medicana Hospital, Ankara, Turkey, coupled to a first-generation Karl Storz Flex-XC yielded a scope durability of 42 cases with the first instrument coupled to early prototypes, and 210 RA-RIRS stone cases thereafter with multiple users, before scope electrical failure occurred in each instance. A dedicated team member plus Cidex sterlization techniques may have both contributed to some of this instrument longevity. Moreover, the second instrument was also used to demonstrate the Avicenna Roboflex at all major urological congresses over 3 years. There has only been one instance of MA malfunction due to water seepage into electronics in early trials, resolved by better custom drapes.

## Discussion

Incremental cRIRS technology improvements over two decades have culminated in dual active endoscope deflection capability, dual-channel digital ureterorenoscopes, hybridized semirigid and coaxial flexible instruments [33], and now disposable/limited-use digital and fiber-optic scopes. Laser fiber technology has also improved with adjustable pulse duration and rounder tips to protect scope work channels better during introduction when new, coupled with a wide array of nitinol stone-retrieval accessories with allied techniques (LC clot [34], blue spritz, etc.). These developments have been actively disseminated by pioneering experts through didactic lectures and hands-on courses, under the aegis of all the major national and international urological societies including the Endourology Society, culminating in widespread cRIRS adoption [35]. Early cRIRS champions and experts have recently tackled more complex intrarenal pathologies, particularly renal stones >1.5 cm, as reflected in updated international European and American guidelines. However, cRIRS is not without its challenges, particularly in these complex cases (e.g. larger stone burden or multiple intrarenal and/or ureteral calculi). Ergonomic problems [36–38] (hand elbow, shoulder, neck, back, hips, knees, ankles) are related to wearing protective lead gowns, thyroid shields, and hand and eye protection in some cases, when performing standing or seated cRIRS on stools for long time periods, leading to operator fatigue. Further challenges include respiratory renal excursion, hindered working space, and the need to simultaneously use various foot pedals to control lasers and/or fluoroscopy equipment, while relying on allied team members to activate laser panel settings and between standby and active settings, or for irrigation adjustments and fluid bag changes, and simultaneously dealing with rapidly changing intraoperative circumstances and fleeting stone treatment opportunities which may influence ultimate success or failure. Together, these lead to cumulative operator fatigue amd physical exhaustion, particularly when treating several such challenging cases of over an hour each throughout the day. This has obvious

**Table 57.3** Summary of cRIRS series in the last decade.

| Study | Year | No. of patients | Stone size (cm) | Mean no. of procedures | % Stone-free rate |
|---|---|---|---|---|---|
| Mariani [39] | 2007 | 16 | ≥4 | 2.4 | 88 |
| Riley [40] | 2009 | 22 | 3 | 1.8 | 90.9 |
| Breda [9] | 2009 | 27 | >2 | 1.6 | 85 |
| Bader [41] | 2010 | 24 | 2.975 | 1.7 | 92 |
| Hyams [42] | 2010 | 120 | 2.4 | ? | 98 |
| Aboumarzouk [43] (meta-analysis) | 2012 | 445 | 2.5 | 1.6 | 93.7 |
| Takazawa [44] | 2012 | 20 | 3.1 (2–5) | 1.4 | 90 |
| Cohen [45] | 2013 | 145 | 2.9 | 1.6 | 87 |
| Miernik [46] | 2013 | 38 | 2.71 | 1.1 | 82 |

detrimental knock-on effects to fine motor skills, task performance, and precision, even in expert hands! This may result in premature termination of a planned procedure, double-J stent placement, and the inevitable consequence of staged treatment to render the patient stone free. This was validated by cRIRS treatment outcomes in expert hands this past decade (Table 57.3).

Consequently, an opportunity to implement mechanically controlled devices into cRIRS procedures was presented. Desai et al. first exploited this opportunity with the Sensei-Hansen Robotic Catheter System, a cardiology/vascular system, adapting it for RA-RIRS, testing it in pigs (one renal pelvic perforation) and then in 18 patients [4, 5] (0.5–1.5 cm renal stones). Their four-component device consisted of a master input device, a dual catheter system with an inner flexible steerable component, a remote inner catheter/manipulation system, and an electronic rack containing computer hardware, power supplies, and video distribution units. The robotic flexible catheter system had a 12/14 Fr outer catheter sheath and inner 10/12 Fr catheter guide. A passive optical fiberscope was inserted through the inner catheter guide lumen. Remote catheter system manipulation maneuvered the flexible fiberscope tip, glued in place within the inner guide. The larger outer sheath tip, positioned at the ureteropelvic junction to stabilize the inner navigation guide within the collecting system, allowed passenger fiberscope manipulation within the inner catheter guide. Of 18 patients only three minor complications (transient fever in two and limb paresis in one), three secondary PCNL for stone residual, and 89% 3 month CT excretory urogram stone-free rate were reported. This device has since been discontinued in urology.

The Avicenna Roboflex robotic system was developed to be specifically dedicated to RA-RIRS. It has tackled many of the ergonomic challenges of cRIRS. After a proof-of-concept phase [25] (IDEAL stage 1) and progression from prototype to working design (IDEAL stage 2a), Saglam et al. demonstrated safe, efficacious device deployment, with a short learning curve, and disseminated the technology among selected experienced endourologists with varying cRIRS expertise (IDEAL stage 2b), publishing data from the first seven's early cases (Table 57.1). RA-RIRS performed in a comfortable ergonomically sound seated position remote from the operating table eliminated the drawback of surgeon (±assistant) fatigue from prolonged standing between the patient's legs at the operating table. Additionally, the surgeon doesn't need to wear protective lead items, for the Avicenna Roboflex MCC surgeon seat can be parked at a suitable safe distance from the operating table as our preliminary studies have shown [31]. The cumulative benefits of these ergonomic stress relieving RA-RIRS aspects was subjectively scored by initial users in Saglam et al's *European Urology* publication [26], and reported significant superiority over cRIRS, a finding verified by this author's current personal series of 17 cases.

The robotic MA enhances and directly drives all mechanical FUR functions, providing a further level of external control beyond the inherent endoscope mechanics, but does not eliminate disadvantages inherent to the FUR deflection cable-drum design mechanism, leading to slightly lagged responses in fine up-and-down tip deflection. Custom-made endoscope hand-piece couplers (different for each manufacturer's scope model) can be made, (an advantage) and are attached directly to a specially designed master plate of the robotic MA. The hand-piece deflection lever is moved by computer-controlled micromotors in the coupler, which communicate with the MCC unit via a cable connector. The RA manipulator also enables two-point shaft stabilization, allowing safe bidirectional rotation, plus advancement and retraction of the fixed instrument hand piece. Thus, RA-RIRS can be performed using standard 10–12 or 12–14 Fr variable length UAS, although shorter length/wider lumen is preferred to allow maximum deflection and dust efflux at the lowest pressures. All endoscope movements can be fine-tuned and scaled to adjustable degrees through the MCC. This level of control is not possible manually in a sustained manner in cRIRS. The laser fiber actuator allows fine motorized forwards and backwards movements beyond the endoscope tip without moving the endoscope itself, with automatic repositioning to a baseline neutral position where it cannot damage the endoscope tip. This lends further operator-controlled precision to stone dusting performance, fragmentation, and ablation, by allowing the operator to maintain the optimal distance between fiber tip and target to maximize the photo-acoustic pulsed stone surface ablation without having to adjust the scope tip position every time. Tables 57.4 and 57.5 describe and compare the ergonomic demands of cRIRs to RA-RIRS.

A key goal for introducing surgical master/slave robotic devices is to reduce the cumulative surgical ergonomic stresses of long and arduous cRIRS procedures for complex and large renal stones. A comfortable environment potentially augments an individual surgeon's capabilities, improves quality and throughput, and provides a comfortable learning environment for the less experienced urologist/trainee endourologist. Hand/wrist/other ergonomic problems reported in up to one-third of endourologists were re-iterated by Saglam et al. [26]. Avicenna Roboflex provided a comfortable platform that significantly improved ergonomics after a short learning curve (subjective score 5.6 vs. 31.3, $P < 0.01$). The fatigued surgeon translates to higher complication rates, longer operating times, additional treatment sessions, and frequent repair of delicate expensive FURs.

Carey et al. [47] reported new FUR damage-repair rates of 8.1% (6% unusable) at a single tertiary center after 40–48 uses, mainly due to errant laser firing (36%) and excessive instrument torque (28%). In our own evaluation, cRIRS instrument durability in a tertiary referral center was increased to >100 cases [48] by using the semirigid instrument as the workhorse and having the FUR tip occupied by a laser fiber in full deflection mode for the shortest possible time. However, initial experience reported here by Saglam (personal communication), if verified by others, suggests much greater scope longevity in RA-RIRS compared to cRIRS. The Avicenna Roboflex design, requiring laser fiber insertion only in a straight scope position using a console based memory function, stepwise motorized advancement of the laser fiber, and force-controlled (maximal $1\,\text{N/mm}^2$) deflection of the scope with similar controlled rotation of the supported torque-free shaft outside the UAS, are just some of the features that should contribute to potential FUR longevity (partially offsetting robot costs cumulatively).

Possible Avicenna Roboflex limitations are current lack of tactile feedback (as with all master/slave robotic devices),

**Table 57.4** Ergonomic demands of cRIRS.

| Operative action | Extremity(ies) required | Performed by |
|---|---|---|
| FUR insertion | Fingers of both hands (at glans-access sheath hub, and FUR handpiece) | Surgeon |
| FUR deflection | Hand holding handpiece and thumb deflection lever; fingers of other hand at meatus-access sheath hub to maintain straight shaft for optimal deflection capability | Surgeon |
| FUR rotation | Hand-holding hand piece; fingers of the other hand rotating shaft at meatus | Surgeon |
| Fluoroscopy activation | Hand/foot | Radiology technician or certified surgeon |
| Multifunctional operating table or C-arm movement | Arms/hand, foot, and torso | Radiology technician or certified surgeon |
| Irrigation control | Thumb and hand | Nurse or assistant |
| Syringe (contrast-flush-aspiration) | Thumb and hand | Surgeon |
| Nitinol accessories insertion or activation | Thumb and index finger(s) | Surgeon |
| Laser fiber insertion, advancement, and retraction | Thumb and index finger | Surgeon |
| Laser settings | Index finger | Nurse or assistant |
| Laser ready, standby modes | Index finger | Nurse or assistant |
| Laser activation | Foot | Surgeon |

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**Table 57.5** Comparing control of cRIRS and RA-RIRS.

| Feature | cRIRS | RA-RIRS |
|---|---|---|
| Surgeon's position | Standing between patient legs in lithotomy | Seated comfortably with arm rest at MCC |
| FUR insertion | Manually through UAS | Manually through UAS |
| FUR advancement, rotation | With both hands | MCC joysticks (2) |
| Fine regulation of deflection | Not available, manual attempt | MCC right joystick pin wheel |
| Laser fiber insertion | Manually through working channel | Manually through working channel |
| Laser fiber fine movements in and out | Manually through working channel | MCC touch screen control |
| Laser activation in ready mode | Foot pedal (standing), not fixed to floor by operating table | Red foot-pedal control (sitting), fixed to MCC floor (right) |
| Laser energy/frequency, standby/active mode adjustment | Manually at device | Manually at device |
| Fluoroscopy activation | Hand/foot pedal control, radiographer | White foot-pedal control (sitting), fixed to MCC floor (left) |
| Table or C-arm movement | Manually, anesthetist/radiographer | Manually, anesthetist/radiographer |
| Irrigation control | By irrigant bag height (nurse) and/or surgeon-controlled pump (syringe, hand or foot pump) | MCC touch screen control |
| Nitinol accessories, insertion/activation | Manually at scope work channel | Manually at scope work channel |

*Source:* [26]. Reproduced and adapted with permission of Elsevier.

underpinning the enduring need of a certain degree of surgeon expertise using compensatory visual clues and precisely controlled movements, and spatial awareness of the scope in all three dimensions. This will change in the future as haptic feedback technology evolves, but is not as critical in RA-RIRS as compared for laparocopic surgery, as the FUR coupled to the MA is introduced and advanced up the ureter inside the lumen of a ureteral access sheath. Additionally, there is the issue of the two-dimensional image monitor screen for scope tip navigation, and problems with the continued need to use baskets for stone fragment extraction where dusting or pop-corning is not possible. Although some have debated whether cRIRS should aim at complete stone ablation by dusting, or whether larger fragments should be actively retrieved using a nitinol basket via the UAS, the need for the latter should be minimal except for harder large stones once fragments are sub-5 mm or in high frequency recurrent large stone formers with uncorrected underlying metabolic risk factors, thus avoiding the need for time consuming partial undocking from the MA shaft support feature. Finally, the device cost may become a significant issue, particularly with respect to financial restrictions of healthcare systems in austerity. Following the IDEAL framework, a multicenter multinational prospective randomized controled trial should be planned to provide more specific details about the potential advantages of RA-RIRS versus cRIRS and smaller access PCNL techniques, for medium–large or branched renal stones, using CT-based end points for stone-free rates.

Presently, of over 4000 companies, 150 have a market cap of > US$200 million, with $2 billion worth of mergers and acquisitions, and $1.3 billion equity funding in the robotics sector of the global economy, with Japan leading the way. Most of this investment is dominated by civilian drone technology, with a 122% compound annual growth rate for 3D printing, and 36% industrial robotics growth in China alone between 2008 and 2013.

As surgeons, we need the surgical tools of tomorrow, not as replacements for ourselves, but as a means to enhance our individual abilities in order to be our best selves without fear of fatigue, so as to deliver superior patient outcomes. With this in mind, many have asked if they really need an expensive tool such as a robotic device? The lab data perhaps suggest not, but the answer must surely be … only if it can deliver patient outcomes that are worth the premium price or ultimately lead to other cost savings (shorter operating time, lower operating room support personnel requirement, lower complication rates [intra-and postoperative], less operator fatigue leading to lower retreatment rates, less FUR breakage, shorter operating room times per stone volume unit disintegrated, for a given stone hardness, location, and collecting system configuration, and lower auxiliary procedure rates). Ideally, it should allow us to tackle bigger stones in difficult places in the urinary tract without making painful holes [49] or risk bleeding, improving on current stone-free rates, and still be able to send patients home safely in minimal discomfort the same day without fear of re-admission or retreatment.

New technology is “new” but never born perfect out of engineering development! After birth, it must pass through an evolutionary and clinical refinement process driven by a cadre of key experts collaborating with the engineering brains, by using it over a realistic time period in real-world settings, based on complexity and learning curve issues. During this time, views are often polarized, sometimes perjoratively depending on how it is presented and who the early adopters are. Nevertheless, it generally creates public awareness, which leads to excitement and debate, especially (as seen with the Da Vinci), when marketed directly to patients and providers by organizations with vested interests. Thus at a time of increasing healthcare consumption, bottlenecks, and fiscal constraints, any new technology must ultimately prove its worth rather than being just another example of fulfilling the prophecy of “the emperor’s new clothes” [50]. This means that for all technology, there are price points for affordability and cost-benefit to be considered. To underpin these, there must be a high-quality evidence base. Currently, Avicenna Roboflex RA-RIRS is somewhat limited by two factors: current FUR design and ureteral lumen size for access and fragment removal. So with RA-RIRS we must ask ourselves, will this tool extend what we as expert surgeons can do for our patients today or in the near future? Does it enhance their, our, or our team’s safety? Does it have future development potential and versatility inside of and beyond the urological specialty? And is it future-proofed for modifications that could lead to improved performance for a reasonable time period to make the high initial investment outlay viable? Will most people be able to afford it eventually? Will it allow acquisition of advanced skill sets across a wider spectrum of practitioners, trainees, and novices, and can these be honed to perfection outside the clinical working environment, or is it just another very expensive comfortable chair?

The answers to these questions will vary from unit to unit, and will depend on many factors such as skill sets and referral patterns. For example, you don’t need Avicenna Roboflex if the majority of ureters you deal with will not readily accept a UAS, or the majority of stones you treat are large branched hard renal stones where PCNL may still be arguably superior! However, if one’s goal is to maximize the control a surgeon has over their endourological working environment and potentially increase it in the future, improve ergonomics to reduce fatigue and allow increased quality and throughput other factors notwithstanding, reduce the need for invasive painful percutaneous surgical procedures in an increasingly elderly and obese population dynamic, afflicted by comorbidities and needing blood-thinning medications, in whom stone disease is increasing and has a higher recurrence rate, then RA-RIRS should certainly be a mouth-watering prospect. This is especially true in a training center with a tertiary referral practice of sufficient volume, where young surgeons are increasingly challenged in skills acquisition and transfer by reduced working hours. Together, they may provide a strong argument for expensive technology to be limited to regional centers to begin with.

Moreover, it certainly is a potential asset where endourological precision is key such as in the renal conservative management of upper urinary tract urothelial cancer, where this author has undertaken the first RA-RIRS case to date (see Video 57.1), or complex stone disease with reduced renal function that needs to be preserved to avoid dialysis, or for those at significant risk of bleeding complications (multiple puncture PCNL in high risk patients on blood thinning or antiplatelet medications that cannot safely be discontinued). Moreover, if by simply changing a coupling adaptor, the device becomes a flexible multispecialty tool, it has the potential for real cost-effectiveness and becomes a viable part of the future hospital landscape beyond urology. Our young successors may be much safer (with regards to the long-term consequences of cumulative radiation exposure) and proficient much faster than this endourologist generation [32]. The heavy burden of wearing lead protection for the whole duration of our careers, with long-term impact on our vertebrae and attached musculature will finally be shed.

With surgical robotics, we are not yet at the stage where we have self-learning programmable autonomous systems like the proverbial autopilot that can fully operate aircraft from take off to landing. Will we ever want this in the human body shop? Only time will tell, depending on where processor and biosensor functions along with machine learning, drive us as physicians and surgeons. What is clear is that we are at the beginning of a global social robotic revolution and the future may bring us hybrid machines possessing ambient intelligence, which can bring lasting value to surgical procedure outcomes. Human empathy and creativity may be the last bastion against the rule of artificial intelligence. Quintessentially, human roles in medical care can be enhanced, leaving individuals with more time to care, teach, create, and innovate, by embracing technology and innovatively shaping it to human needs. The future is exciting indeed!

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# SECTION 4

# Shock-Wave Lithotripsy

# 58

# Physics of Shock-wave Lithotripsy

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## Introduction

Since its inception in the early 1980s shock-wave lithotripsy (SWL) has become the treatment of choice for the majority of urinary stones because of its non-invasiveness compared to traditional stone treatments [1–3]. In the early 1990s more than 85% of stone patients in Europe and the United States were treated with SWL [4]. Although this trend has been in decline since then because of the rapid advance in endourological technology and technique, still about 70% of kidney stone patients in 2002 and fewer than 50% in 2005 were managed by SWL [2, 4–6].

A primary factor that has contributed to this gradual decline in the clinical use of SWL is the reduced treatment efficiency, compounded by the increased retreatment rate and higher risk of tissue injury produced by the second- and third-generation lithotripters, compared to the first-generation HM3 lithotripter [7, 8]. Although SWL technology has evolved significantly over the past two decades, there is still debate regarding the physical basis and clinical benefits of technical modifications such as the tight focal width and high peak pressure fields often used in many contemporary lithotripters [9–11]. Better design as well as effective and safe use of shock-wave lithotripters must rely on a clear and fundamental understanding about the physics of this innovative technology.

The physics and acoustical principles of SWL have been reviewed previously [12–14]. This chapter will therefore focus on the most salient features of SWL physics that are relevant to understanding the mechanisms of stone comminution and tissue injury with emphasis on contemporary technologies. The materials in this chapter are condensed in acoustics and physics content from a recent review of the topic by the senior author [15], but otherwise expanded based on the latest studies in order to provide a guideline for better lithotripter design, and effective and safe clinical use of this non-invasive technology for stone management.

## Overview of the clinical goal and physical process in SWL

The overarching goal of SWL is to pulverize kidney stones into gravels for spontaneous discharge in urine without inflicting adverse effects to surrounding tissues. As illustrated in Figure 58.1, disintegration of kidney stones by focused shock waves is a progressive process in which fragments of different size, shape, and distribution in the renal collecting system will be produced that may all influence the clinical outcome. In particular, the rate of stone comminution is not uniform throughout SWL. Stone disintegration accelerates initially within a few hundred shocks, followed by a gradually decelerating process towards the end of treatment. This critical observation suggests that different mechanisms of stone fragmentation may exist during the course of SWL, a unique feature that was not taken into account in the design of the second- and third-generation lithotripters. To succeed in SWL, it is important to gain a fundamental understanding about acoustic waves (Box 58.1), the characteristics of focused shock waves produced by lithotripters (Box 58.2), and the physical basis for the optimal selection of lithotripter parameters and treatment protocol (or strategy) to maximize stone comminution while minimizing tissue injury.

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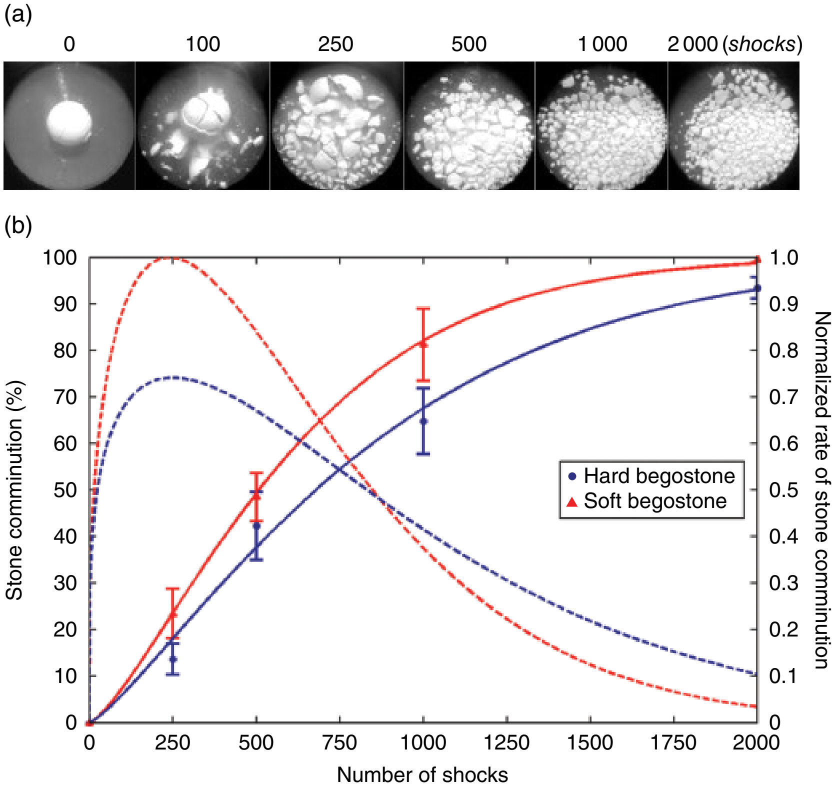

**Figure 58.1** (a) Progressive comminution of a 10 mm spherical artificial stone in a membrane holder. (b) Dose-dependence in stone comminution (solid lines) and normalized rate of stone comminution (dashed lines) produced by a contemporary electromagnetic shock-wave lithotripter. *Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

**Box 58.1 Basics of acoustic waves [12].**

An acoustic (or sound) wave is a form of mechanical vibration that propagates within a fluid (either gas or liquid). The wave locally compresses the fluid particles, i.e., the molecules are forced closer, pushing against each other. Compression in one region is accompanied by rarefaction (or tension) of the fluid particles in the adjacent region due to conservation of mass. This alternating vibration of compression and tension leads to the formation of a "wave" that travels through the fluid. The speed of wave propagation (referred to as the sound speed) is a material property of the medium, which is about 340 m/second in air, and about 1500 m/second in water and most soft tissues of the body. Notably, individual molecules of the medium do not travel with the acoustic wave; rather they just jostle adjacent molecules. Therefore, the medium serves as a carrier for the acoustic wave to propagate. This is an important physical distinction between mechanical waves (e.g., acoustic waves, water waves, elastic waves in solids) and electromagnetic waves (e.g., light waves, radio waves, X-rays). For electromagnetic waves energy is carried by photons, which may be thought of as particles that physically travel through space without the need of a carrier medium. For example, light can travel through a vacuum; in contrast, sound cannot.

## General principles of shock-wave lithotripsy

All clinical lithotripters are constructed using four primary components: (i) shock-wave generator, (ii) focusing device, (iii) coupling medium, and (iv) stone localization system. The original Dornier HM3 lithotripter employed a water tub for coupling to ensure effective transmission of the lithotripter-generated shock wave (LSW) without significant loss of energy at the patient's surface (Figure 58.2a). In contrast, for operation convenience all contemporary lithotripters use dry coupling modalities with a water cushion system (such as the Siemens Lithoskop shown in Figure 58.2b). Three primary types of shock-wave lithotripters have been developed – electrohydraulic (EH), electromagnetic (EM), and piezoelectric (PE) shock sources – with a variety of focusing systems (Figure 58.3). Stone localization in modern lithotripters is performed using isocentric C-arm fluoroscopy with optional inline or offline ultrasound imaging [3]. The combination of the shock-wave generator and the focusing device determines the main characteristics of the lithotripter field.

### Shock-wave generation

In EH lithotripters, a spherically divergent shock wave is generated by a high voltage (12–30 kV) discharge between

### Box 58.2 Basics of lithotripter-generated shock waves.

Several different approaches have been used to model the shock-wave propagation and focusing in a lithotripter [19–21]. Majority of the models use the Euler equations for compressible fluids, in combination with the Tai equation of state for water shown below:

$$p = B\left[\left(\frac{\rho}{\rho_0}\right)^n - 1\right] \tag{1}$$

where $p$ and $\rho$ are the pressure and density of water immediately behind the shock front, $\rho_0$ is the density of water under ambient conditions, $B$ (= 3000 bars) is a characteristic constant, and $n = 7.15$ [22]. It can be shown based on conservation of mass and momentum analysis that the Mach number at the shock front ($M_s = c/c_0$; where $c$ is the speed of the shock front and $c_0$ is the sound speed in water under ambient conditions) is determined by [14]:

$$M_s^2 = \frac{r}{n}\frac{r^n - 1}{r - 1}, \text{ with } r = \frac{\rho}{\rho_0} \tag{2}$$

Considering that positive peak pressure $p+$ in a lithotripter field is usually below 100 MPa, equations (1) and (2) indicate a density ratio below 1.05 and a Mach number less than 1.09 across the shock front of typical lithotripter-generated shock waves (LSWs). As a LSW approaches the lithotripter focus, a Mach stem will be formed, leading to a planar shock front followed by diffracted waves originated from the aperture of the shock-wave source [14, 23].

LSW can be significantly attenuated when propagating through interposing skin and soft tissues to reach the kidney stone. Although the pulse profile of the LSW remains similar, there is about 30% reduction in $p+$ with a concomitant threefold increase in the rise time of the shock front and 44–67% broadening of the focal width from *in vitro* to *in vivo* [24]. Thermal effects in SWL are negligible. In clinical SWL, a pulse repetition frequency (PRF) of ≤ 2 Hz is typically utilized. However, even at a PRF of 100 Hz, the accumulated temperature increase produced by a clinically relevant shock-wave exposure was estimated to be less than 2 °C [25]. Therefore the interaction of LSWs with biological tissues and renal calculi is primarily through nonthermal mechanical effects.

In comparison, electromagnetic (EM) and piezoelectric (PE) lithotripters have a larger dynamic range in pressure output, longer lifetime of the shock source, and more stable output than electrohydraulic (EH) lithotripters. Clinically, EM and EH lithotripters are more commonly used because of their broader focal width in combination with the higher effective acoustic pulse energy produced than PE lithotripters [9, 26]. Low energy output compounded with narrow focal width of the PE lithotripters result in longer treatment time, making them less favorable in high-volume stone clinics [10, 27]. The primary field parameters of different types of lithotripters are summarized in Table 58.1.

the tips of an electrode, which vaporizes and expands supersonically the surrounding fluid. In EM lithotripters, a magnetic field is produced by applying a high voltage (8–20 kV) pulse to a coil in flat, cylindrical, or spherical configuration to inject a strong current into the coil that repels an adjacent thin metallic membrane (in which a counter current is induced) to launch a high-amplitude acoustic wave into the surrounding fluid. In PE lithotripters, a high-voltage (1–10 kV) pulse is applied simultaneously to a mosaic of hundreds to few thousands piezoceramic elements that are mounted on a spherical carrier to generate a strong converging acoustic wave towards a common focus. Shock waves in EM and PE lithotripters are formed by nonlinear wave propagation in the coupling medium or interposing soft tissues between the shock source and the lithotripter focus [13].

## Shock-wave focusing

Different designs of acoustic reflector and lens have been utilized for shock-wave focusing. In EH lithotripters, the spark-generated shock wave (at $F_1$) is focused by a truncated ellipsoidal reflector to the second focus ($F_2$) of the ellipsoid where the kidney stones are aligned under imaging guidance. In majority of EM lithotripters, either an acoustic lens or parabolic reflectors are used (Figure 58.3). In PE lithotripters, self-focusing ensured by the geometrical configuration of the shock-wave source is typically utilized. Self-focusing is also employed in a recently developed EM lithotripter by Eisenmenger et al. [16].

## Lithotripter-generated shock-wave profile and distribution

Representative shock waves measured at the focus of the three different types of lithotripters are shown in Figure 58.4. A fiber-optic probe hydrophone (FOPH) [17] recommended for lithotripter output characterization by the IEC standard is often used for such measurements [18]. All shock waves at the lithotripter focus consist of a leading shock front with a positive peak pressure ($p+$) of 40–70 MPa (1 MPa is about 10 times the atmospheric pressure) and an associated compressive

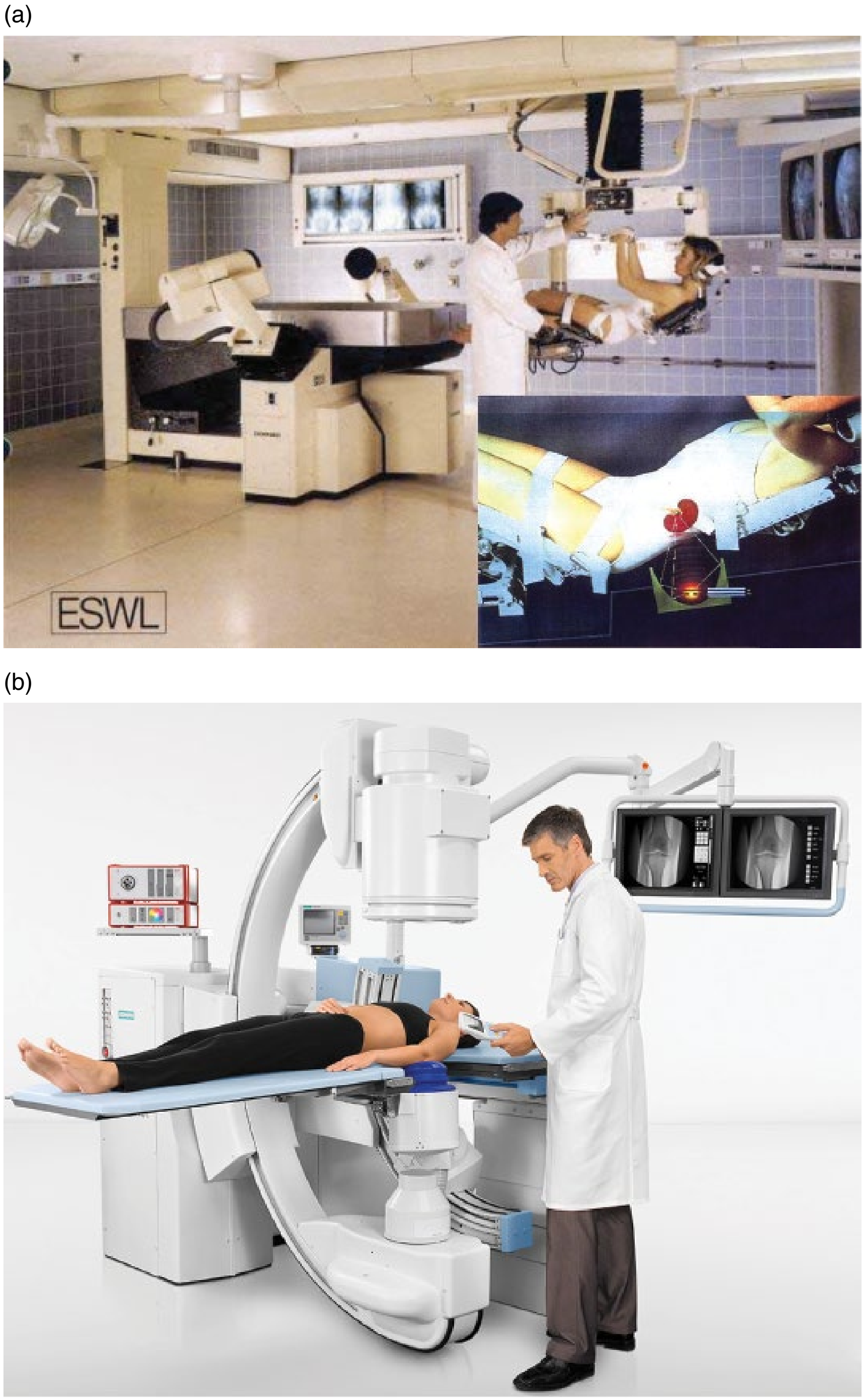

Figure 58.2 Shock-wave lithotripters: (a) first-generation Dornier HM3 and (b) third-generation Siemens Lithoskop. *Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

wave of 1–2 microseconds in duration (1 microsecond = 1 millionth of a second). This fast rise of the compressive wave is referred to as “shock.” After falling to zero there is then a region of tensile wave lasting about 3–5 microseconds in duration with a peak negative pressure ($p-$) about −10 MPa. The entire shock-wave pulse duration varies from 5 to 10 microseconds. Shock waves are broadband acoustic waves with a fundamental frequency in the range of 150–800 kHz (Figure 58.4a inset) [13]. As depicted in Figure 58.4a there is a notable pressure oscillation after the tensile wave produced by EM and PE lithotripters but not in EH lithotripters. In contrary to EH lithotripters in which the rise time of the leading shock front is less than 30 ns the shock-wave rise

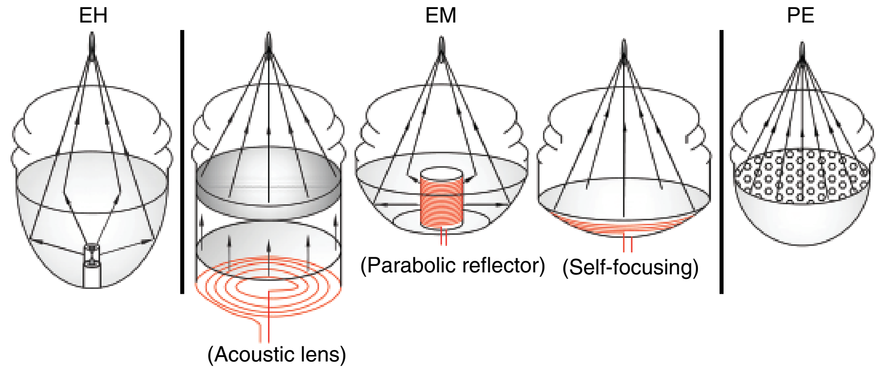

**Figure 58.3** Different types of shock-wave lithotripters. EH, electrohydraulic; EM, electromagnetic; PE, piezoelectric. *Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

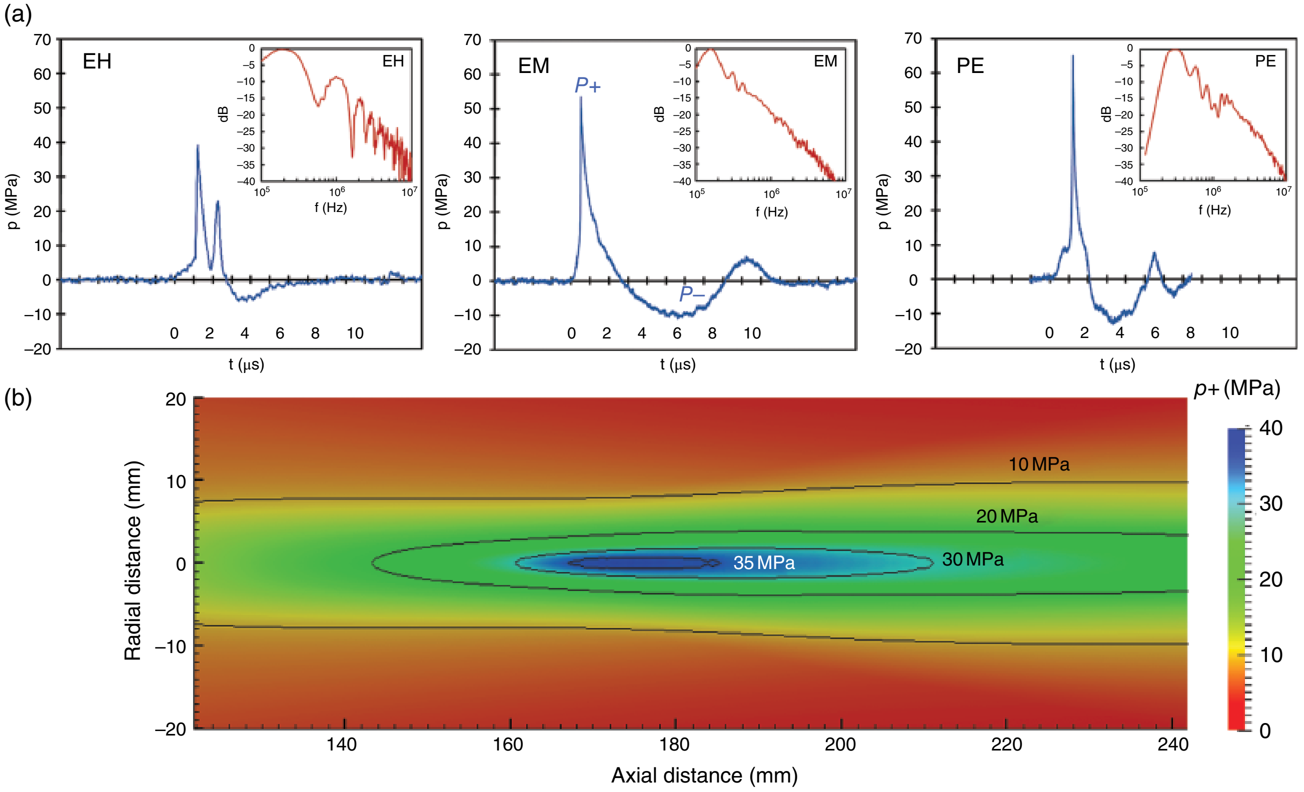

**Figure 58.4** (a) Pressure waveforms produced by different types of lithotripters and (b) model calculated peak pressure distribution in an EM lithotripter. EH, electrohydraulic; EM, electromagnetic; PE, piezoelectric. *Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

time is about 100 ns for EM and PE lithotripters [13]. In general, pressure amplitudes are machine- and output-setting-specific, and the values of $p+$ can vary from 20 to 120 MPa and $p-$ from −4 to −15 MPa (see Table 58.1).

Limited aperture size of the shock source causes the pressure field to be elongated along the central axis of the lithotripter to form a so-called "cigar-shaped" focus (Figure 58.4b). The size of the lithotripter focal region is measured by the −6 dB focal width (i.e., the dimension in which the positive pressure is equal or above half of $p+$) along the longitudinal and transverse axis of the lithotripter, respectively. It should be noted that the focal width is only a measure of the tightness of the pressure concentration in a lithotripter field. In general, the focal width may not be equated to the dimension of the fragmentation zone in a lithotripter field.

## Composition and physical properties of kidney stones

To understand the mechanisms of stone fragmentation some basic features of kidney stones need to be considered. Kidney stones vary substantially in their chemical composition and structure. Stones are about 95%

**Table 58.1** Characteristics of different type of shock-wave lithotripters.

| Lithotripter type | | C (nF) | V (kV) | Focal length (cm) | Aperture angle (°) | $p+$ (MPa), typical/max | $p-$ (MPa) | $t_r$ (ns) | $t+$ (μs) | $t-$ (μs) | Focal width (mm) | $E_{12\text{mm}}$ (mJ) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| EH | | 20–200 | 12–30 | 13–17 | 60–80 | 20/80 | −8 to −10 | <30 ns | 1–2 | 4–6 | 8–17 | 20–70 |
| EM | Acoustic lens | 500–1500 | 8–20 | 15–18 | 50–70 | 50/80 | −5 to −12 | 30–120 | 1–2 | 2–4 | 6–12 | 10–120 |
| | Parabolic reflector | | 8–20 | | 85–90 | 70/120 | −5 to −15 | 50–500 | ≈1 | 2–3 | 4–9 | 20–150 |
| | Self-focusing | | 8–12 | | 30–34 | 20/40 | −4 to −7 | 70–120 | 2–3 | 4–5 | 15–20 | N/A |
| PE | | 300–800 | 1–10 | 10–16 | 70–90 | 80/120 | −9 to −10 | 30–250 | ≈1 | 0.5–1 | 2–6 | N/A |

*Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

aggregated crystalline substances by weight, which are bound by cellular matrix proteins [28, 29]. As depicted in Figure 58.5 the composition of a kidney stone can often change from the core to the shell, as revealed by micro-computed tomography (CT) images [30]. Calcium oxalate monohydrate (COM) or dihydrate (COD) stones represent the most common kidney stones. Other prevalent compositions include calcium hydrogen phosphate dihydrate (or brushite), carbonate-apatite (CA), magnesium ammonium phosphate hexahydrate (MAPH or struvite), uric acid (UA), and cystine. It has been observed that the fragility of kidney stones during SWL varies significantly with composition and structural heterogeneity [31–33].

Table 58.2 summarizes the acoustic and mechanical properties of kidney stones of different compositions, together with their counterpart values in artificial kidney stones that are often used in research to understand the mechanisms of stone fragmentation, and for comparisons of different lithotripters and treatment strategies.

## Mechanisms of stone fragmentation in SWL

Stone fragmentation in SWL is the direct consequence of shock-wave–stone interaction, which is illustrated in Figure 58.6 by high-speed photoelastic and shadowgraph imaging [34]. When a LSW strikes on the stone surface, part of the wave will be reflected back into the water while the other part will be refracted (or transmitted) into the stone. In general, the wave refraction at a fluid/solid boundary will produce two types of stress wave in the solid. One is called the longitudinal (or P) wave, in which the solid particles vibrate in the same direction as the wave propagation. The other is called the transverse (or S) wave, in which the solid particles vibrate perpendicular to the direction of the wave propagation. The acoustical principles of wave reflection and refraction at fluid/solid boundaries are described in Box 58.3. In addition, cavitation – the

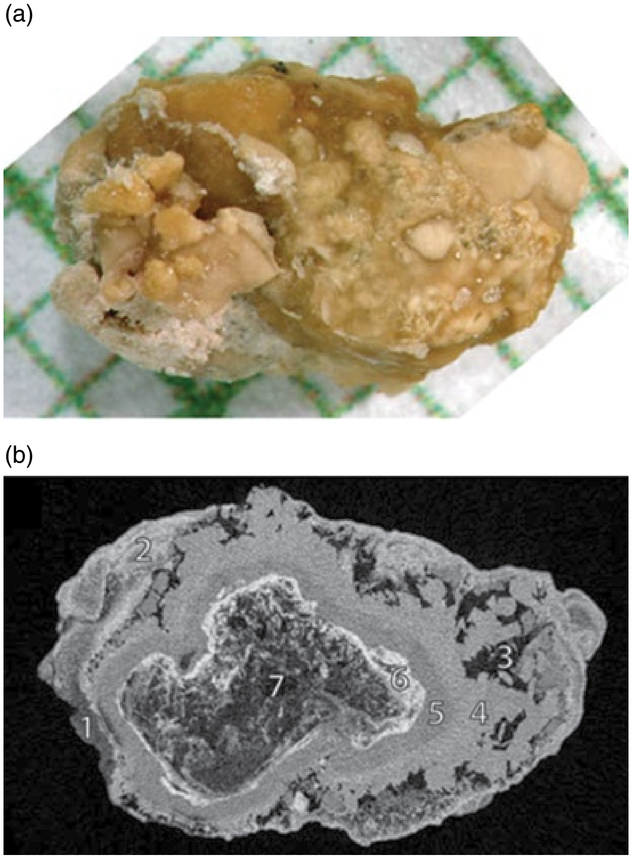

**Figure 58.5** Example of the complexity of mineral regions revealed by micro-computed tomography (CT). (a) Photomicrograph of stone on millimeter grid paper; (b) micro-CT slice through the same stone. Minerals appear to be quite varied, as judged by morphology and X-ray attenuation; e.g., there is a low-attenuation region on the stone exterior (labeled 1) that is distinct from the high-attenuation shell surrounding the stone (2). Beneath that shell are some regions that appear to be void of mineral (3), interspersed among crystalline extensions of an evenly absorbing material (4); inside there is a layer that absorbs X-rays less well (5), which is in turn lined by a highly absorbing mineral (6); finally, the innermost region of the stone (7) is filled with a low-absorbing material that could be subdivided into two or more morphologies. *Source:* from [30] with permission of Springer-Verlag, Berlin, Heidelberg.

**Table 58.2** Acoustic and physical properties of kidney stones of different chemical compositions and artificial stones.

| Stone type | $\rho$ (kg/m$^3$) | $c_P$ (m/s) | $c_S$ (m/s) | $I_P/I_i$ (%) | $I_S/I_i$ (%) | $\theta_P$* (°) | $\theta_S$* (°) | $E$ (GPa) | $G$ (GPa) | $H_V$ (MPa) | $K_{IC}$ (kPa*m$^{1/2}$) | $\sigma_f$ (MPa) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Kidney stones** | | | | | | | | | | | | |
| Cystine | 1624 | 4651 | 2125 | 74 | 90 | 19 | 45 | 20 | 7.3 | 238 | High* | |
| COM | 2038 | 4535 | 2132 | 69 | 86 | 19 | 45 | 25 | 9.3 | 1046 | 136 | 0.1–3.4 |
| Brushite | 2157 | 3932 | 1820 | 71 | 89 | 22 | 56 | 19 | 7.1 | 727 | 119 | |
| UA | 1546 | 3471 | 1464 | 83 | 99 | 26 | N/A | 9.2 | 3.3 | 312 | 90 | |
| CA | 1732 | 2724 | 1313 | 86 | 100 | 33 | N/A | 8.5 | 3.0 | 556 | 57 | |
| MAPH | 1587 | 2798 | 1634 | 87 | 96 | 32 | 67 | 11 | 4.2 | 257 | 56 | |
| **Artificial stones** | | | | | | | | | | | | |
| PoP | 1670 | 2478 | 1471 | 88 | 99 | 37 | N/A | 8.9 | 3.6 | N/A | N/A | 1.4 |
| U30 | 1693 | 3180 | 1880 | 83 | 90 | 28 | 53 | 15 | 6.0 | N/A | N/A | N/A |
| Hard BS | 1995 | 4159 | 2319 | 72 | 83 | 21 | 40 | 27 | 11 | N/A | N/A | 7.1 |
| Soft BS | 1563 | 3148 | 1813 | 85 | 93 | 29 | 56 | 13 | 5.1 | N/A | N/A | 3.2 |

Energy flux density ratio ($I_P/I_i$ and $I_S/I_i$) for the refracted P and S waves in stones are their respective maximum values. COM, calcium oxalate monohydrate; UA, uric acid; CA, carbonate apatite; MAPH, magnesium ammonium phosphate hexahydrate; PoP, plaster of Paris; BS, BegoStone. $\theta_P$*, critical incident of the pressure wave in the fluid that leads to total reflection of the P wave in the solid; $\theta_S$*, critical incident of the pressure wave in the fluid that leads to total reflection of the S wave in the solid. $E$, Young's modulus; $G$, shear modulus; $H_V$, Vicker's hardness; $K_{IC}$, fracture toughness; $\sigma_f$, tensile failure strength of the solid.
*Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

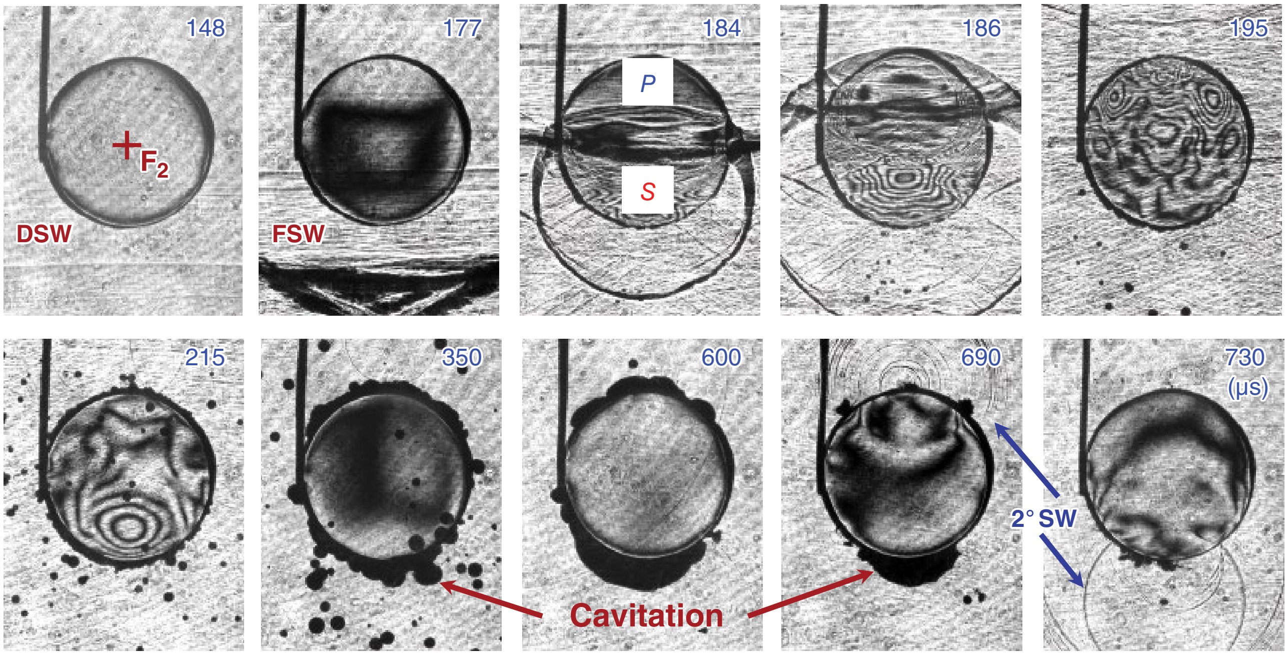

**Figure 58.6** High-speed photoelastic and shadowgraph imaging sequence of shock-wave–stone interaction and cavitation activities produced by an HM3 lithotripter in water around an artificial stone (an epoxy disk of 14 mm in diameter). DSW, direct shock wave; FSW, focused shock wave; SW, shock wave. P and S denote the longitudinal (or P) and transverse (or S) wavefronts in the epoxy sample. Time zero corresponds to the spark discharge. *Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

formation, expansion, and collapse of gas/vapor bubbles in liquids – will be generated by the tensile component of the LSW, which plays an important, yet different, role in stone comminution and in tissue injury.

Figure 58.8a illustrates the partition ratio in energy flux density of an incident LSW into a reflected pressure wave in water and refracted P and S waves in the solid at different incident angles for six types of kidney stones.

**Box 58.3 Acoustics of wave reflection and refraction at fluid/solid boundaries.**

Figure 58.7 illustrates several general scenarios of wave reflection and refraction (or transmission) at fluid/stone boundaries that are relevant to SWL. The directions of the reflected pressure wave ($P_r$) in the fluid, and the transmitted P and S waves into the solid are determined by the Snell's law:

$$\frac{\sin\theta_i}{c_0}=\frac{\sin\theta_r}{c_0}=\frac{\sin\theta_P}{c_P}=\frac{\sin\theta_S}{c_S} \tag{3}$$

where $\theta_i$, $\theta_r$, $\theta_P$, and $\theta_S$ are the incident and reflected angles of the pressure waves in the fluid, and refracted angles of the P and S waves in the solid; $c_0$, $c_P$, *and* $c_S$ are the wave speed in water, and P and S wave speeds in the solid, respectively. The mode conversion from pressure wave in water into P and S waves in the solid is ensured by the boundary conditions (i.e., continuities of displacement and stress [force per unit area] along the surface normal direction of the boundary). In general the reflection coefficient of the potential for the pressure wave in water ($R$), and transmission coefficients of the potentials for the P and S waves ($T_P$ and $T_S$) in the solid depend critically on $\theta_i$ and are given by: [35]

$$R=\frac{Z_P cos^2 2\theta_S+Z_S\sin^2 2\theta_S-Z_o}{Z_P cos^2 2\theta_S+Z_S\sin^2 2\theta_S+Z_o} \tag{4.1}$$

$$T_P=\frac{2\left(\dfrac{\rho_0}{\rho_s}\right)Z_P cos 2\theta_S}{Z_P cos^2 2\theta_S+Z_S\sin^2 2\theta_S+Z_o} \tag{4.2}$$

$$T_S=\frac{-2\left(\dfrac{\rho_0}{\rho_s}\right)Z_S\sin 2\vartheta_S}{Z_P\cos^2 2\vartheta_S+Z_S\sin^2 2\vartheta_S+Z_0} \tag{4.3}$$

where $\rho_s$ is the density of the solid, and the acoustic impedances (i.e., the product of medium density and wave speed) for the oblique incident pressure wave in water ($Z_0$), and refracted P and S waves in the solid ($Z_P$ and $Z_S$) are given by:

$$Z_0=\frac{\rho_0 c_0}{cos\,\theta_0},Z_P=\frac{\rho_s c_P}{cos\,\theta_P},Z_S=\frac{\rho_s c_S}{cos\,\theta_S} \tag{4.4}$$

When $\theta_i$ exceeds the critical value for total refraction of the P wave (i.e., $\theta_P=90°$) in the solid, only an S wave will be produced in the solid until $\theta_i$ reaches the critical incident angle for total refraction of the S wave in the solid. Thereafter, head waves (H) emanating into both the fluid and solid, and surface acoustic waves such as leaky Rayleigh wave and Scholte wave may be produced at the fluid/solid boundary [15].

The ratios of the normal components of the energy flux density (or intensity) of the reflected pressure wave in water ($I_r$), the transmitted P and S waves in the solid ($I_P$ and $I_S$) with respect to the corresponding value of the incident pressure wave in water ($I_i$) can be determined by [35]:

$$\frac{I_r}{I_i}=|R|^2,\frac{I_P}{I_i}=\frac{\rho_s\tan\theta_0}{\rho_0\tan\theta_P}|T_P|^2,\frac{I_S}{I_i}=\frac{\rho_s\tan\theta_0}{\rho_0\tan\theta_S}|T_S|^2,$$
$$\text{with } I_r+I_P+I_S=I_i \tag{4.5}$$

The last equation in (4.5) indicates energy conservation for wave reflection and refraction at a fluid/solid boundary.

The most striking feature is the broad range of incident angles (after the critical incident angle of the P wave is reached) in which strong shear waves are generated in the stone. In particular, soft stones such as MAPH, UA, and CA can more efficiently convert shock-wave energy into shear over a broad range of $\theta_i$ (26–90°) than hard stones such as cystine, COM and brushite in a narrow range of $\theta_i$ (19–56°). In contrast, the generation of P wave is limited in a small range of $\theta_i$ up to 19–33°, with hard stones possessing lower energy transmission efficiency than soft stones. Moreover, it has been shown that the convergence of the shear waves from the stone boundary into the central region, combined with focusing upon S wave reflection from the lateral and posterior surfaces of the stone leads to the generation of the maximum tension inside the stone (Figure 58.8b) [36]. Multiphysics modeling in COMSOL has confirmed this general feature of LSW–stone interaction (Figure 58.8c). Quantitatively, the modeling results have demonstrated that higher maximum tensile stress ($\sigma_T$) is produced in soft stones such as UA ($\sigma_T=193$ MPa) than hard stones such as COM ($\sigma_T=149$ MPa) under the same lithotripsy condition ($p+=46$ MPa). Similarly, the maximum tensile strain ($\varepsilon_T$) is also higher in UA ($\varepsilon_T=280\times10^{-3}$) than COM ($\varepsilon_T=75\times10^{-3}$) because UA has much lower elastic moduli than COM (see Table 58.2). These results are consistent with the clinical observation of stone fragility in SWL [37].

## Basic concepts of fracture mechanics

Two important concepts in fracture mechanics need to be appreciated in order to understand the mechanisms of stone fragmentation in SWL. First, kidney stones, like other brittle materials (which are fragile under tension or shear), have pre-existing flaws (e.g., defeats, voids, interfaces, cracks; see Figure 58.5). Second, when kidney stones are subjected to the dynamic loading produced by

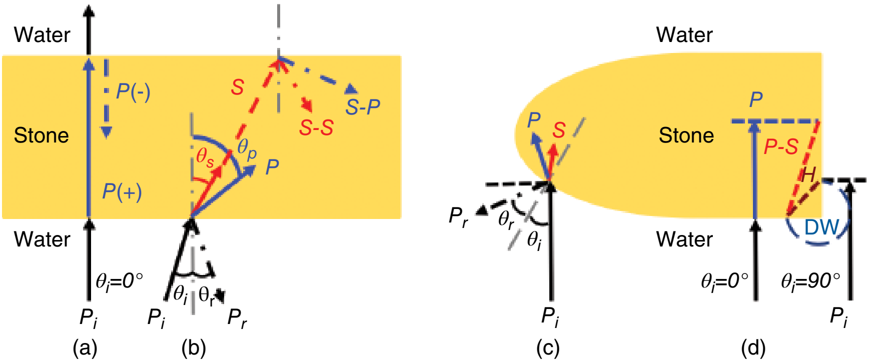

**Figure 58.7** Shock-wave reflection and refraction (transmission) at the fluid/solid boundary. Left: shock-wave incidence on a stone of flat surfaces, (a) zero incident angle ($\theta_i = 0°$) and (b) at an oblique incident angle ($\theta_i > 0°$). Right: shock-wave incidence on a stone with curved surfaces and sharp corners, (c) at an oblique incident angle ($\theta_i > 0°$) on a curved surface and (d) wave diffraction at a sharp corner when the incident angle changes abruptly from $\theta_i = 0°$ to $\theta_i = 90°$, leading to generation of strong shear wave (*P*–*S*) and head wave (*H*) near the lateral boundary of the stone. In water, $P_i$ and $P_r$ denote incident and reflected pressure wave, DW indicates diffracted wave. In stone, *P* indicates longitudinal (or *P*) wave, *S* denotes transverse (or *S* for shear) wave, and *P*–*S*, *S*–*S*, and *S*–*P* indicate different reflected waves (denoted by the second letter) produced by the incident wave (denoted by the first letter) at stone/water boundaries. Lines with arrowheads indicate rays along the wavefront propagation direction, and dashed lines are used to show the locations of different wavefronts in water and stone.

LSW–stone interaction and resultant cavitation bubble collapse (see Figure 58.6), the stresses produced inside the stone will be significantly intensified at the tips of the pre-exsiting microcracks, which are the weak spots inside the material (Figure 58.9a). Consequently, if the stress concentration exceeds a threshold value, measured by the fracture toughness of the stone material [38], there will be a progressive opening and growth of the microcracks. They coalesce to form macrocracks (Figure 58.9b), which eventually leads to fracture under repeated LSW bombardments (Figure 58.9c). This dynamic fatigue process is the fundamental mechanism by which stone fragmentation is produced in SWL [14, 39]. Although the theoretical framework has been well described, significant challenges remain in applying the principle of dynamic fatigue to analyze stone comminution because of the lack of understanding about the specific mechanisms that drive fracture formation in kidney stones during SWL [40, 41].

## Traditional theories of stone fragmentation

Extensive research has been devoted to uncover the mechanisms of stone fragmentation in SWL since the invention of this remarkable technology in the early 1980s. Figure 58.10 shows chronologically the primary mechanisms described previously in the literature, including (i) stress gradient and tensile failure at stone/fluid boundaries [42, 43], (ii) cavitation [44–46], (iii) spalling [34, 47, 48], (iv) dynamic fatigue [14, 39], (v) quasi-static squeezing [49], and (vi) dynamic squeezing [41]. Several of these mechanisms, however, are either descriptive or based on stone fracture observed in the early stage of SWL under special circumstances. For example, spalling damage is often produced in large stones with flat surfaces such as a slab (or in lithotripters with a narrow focal width) at the beginning of SWL when the reflected tensile wave from the leading compressive component is superimposed constructively with the trailing tensile component of an advancing refracted P wave (see Figure 58.7a). Spalling will gradually become less effective as the size of fragments decreases [34] or in stones with curved boundaries [40] or when wave attenuation in the stone material is high [50]. As illustrated in Figure 58.8, the intensity of the P wave will decrease when the incident LSW impinges on a flat stone surface from an oblique angle (Figure 58.7b) or a stone with curved boundaries (Figure 58.7c). Moreover, although the importance of shear waves in stone comminution has been recognized for years [34, 40, 41, 49], the mechanism of shear wave generation was not adequently clarifed. In particular, “dynamic squeezing” has often been described in the literature as the dominant mechanism to create strong shear in stones [3, 41] using an idealized stone geometry (i.e., a cylindrical stone placed on the axis of the lithotripter with its flat surface facing the incident LSW). In contrast, as shown in Figure 58.8, the strong shear waves in kidney stones with smooth or curved surfaces are generated by the mode conversion at the proximal surface of the stone produced by the oblique incidence of the LSW based on the acoustical principles described in Box 58.3.

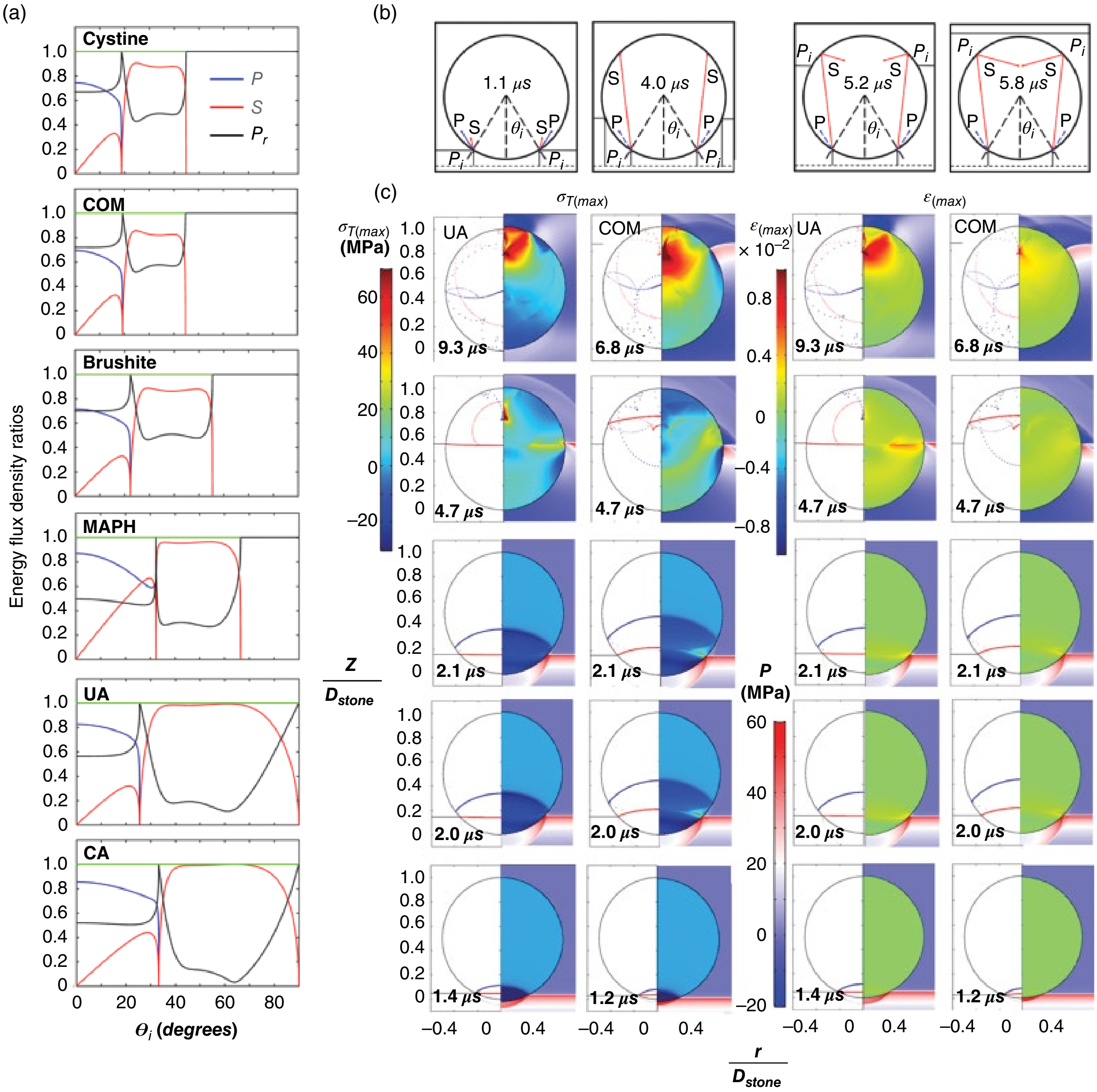

**Figure 58.8** (a) Variations in wave reflection and refraction (transmission) coefficients with incident angle ($\theta_i$) for kidney stones of different compositions; (b) ray tracing showing the generation of P and S waves, and propagation and focusing of *S* wave in a spherical stone; and (c) transient LSW–stone interaction, generation of different stress waves, and the production of maximum tensile stress ($\sigma_{T(max)}$) and maximum tensile strain ($\varepsilon_{T(max)}$) inside COM and UA stones of spherical geometry. Reproduced with permission of Ying Zhang.

## Contemporary theories of stone fragmentation

While the traditional theories of stone fragmentation often focus on mechanims responsible for creating the initial fracture, contemporary theories of stone fragmentation [15, 51] aim at identifying the key lithotripter field parameters and their interactions that govern the overall process of stone comminution to achieve the ultimate goal of SWL. Based on dimensional analysis (a tool used by engineers to identify the key nondimensional [or unitless] parameter of a particular problem, such as the Mach number for describing the compressibility of a fluid), recent studies have demonstrated a clear correlation between stone comminution and the average peak positive pressure ($P_{+(avg)}$), or the local peak positive pressure of the LSW, incident on the stone

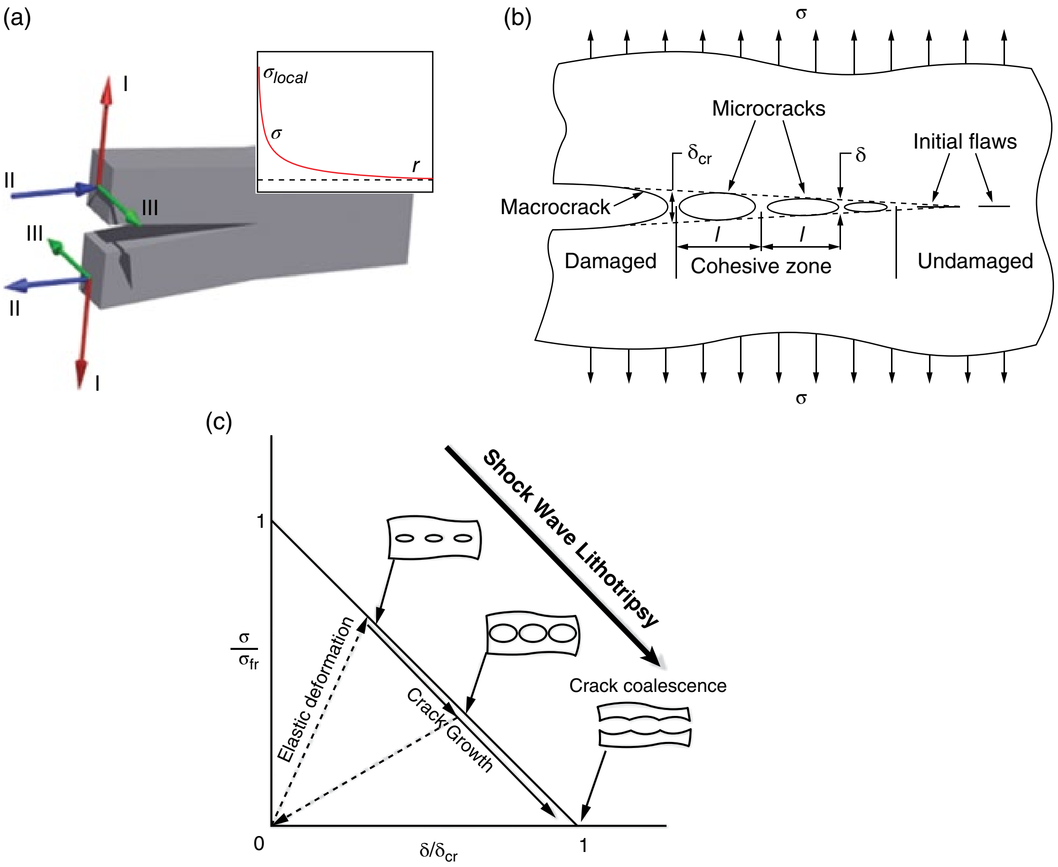

**Figure 58.9** Fundamental fracture mechanics. (a) Stress concentration near a crack tip and three primary modes of brittle fracture: mode I, opening mode due to tensile stress applied normal to the plane of the crack; mode II, sliding mode due to shear stress acting parallel to the plane of the crack and perpendicular to the crack front; and mode III, tearing mode due to shear stress acting parallel to the plane of the crack and parallel to the crack front. (b) Cohesive zone model of dynamic fatigue failure of brittle materials. (c) Progressive microcrack opening, growth, and coalescence in kidney stones during SWL. Symbol σ indicates stress and δ denotes crack tip displacement with subscripts "fr" and "cr" correspond to "fracture" and "critical," respectively. *Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

surface [51]. As shown in Figure 58.11a, this correlation holds true for both hard and soft artificial BegoStone of different geometries and sizes, which cover the broad range of acoustic and mechanical properties measured from kidney stones. More importantly, the results show that there is a distinct threshold of $P_{+(avg)}$ (denoted by $P_f$) for each stone type to initiate fragmentation, independent of the fluid medium around the stone. Hard BegoStone has a higher $P_f$ than soft BegoStone, indicating that material properties of the stone such as the shear modulus ($G$) or Young's modulus ($E$) may also be important in determining the fragmentation outcome. In fact, a new nondimensional parameter, $Z = \frac{P_{+(avg)} - P_f}{G}$, in which $G$ can be replaced by $E$ or $K$ (bulk modulus), has been constructed that unifies all the fragmentation results from both the hard and soft BegoStone samples treated in water [15]. Physically, $Z$ indicates that stone fragmentation in SWL is manifested by the competition between $P_{+(avg)}$ that represents the impact load imposed by the LSW on the stone and $G$ (or $E$) that represents the resistance of the stone materials against shear- (or tension-) induced material deformation.

During SWL, kidney stones are fragmented progressively to smaller and smaller pieces (see Figure 58.1a). It has been shown as the stone (or fragment) size decreases, the $P_{+(avg)}$ threshold will increase [36] (see also Figure 58.11b). This observation has been attributed to the destructive wave interference in stones of small sizes, which will reduce the maximum tensile stress or stress integral that can be built up inside the stone to produce fracture (Figure 58.12a). This finding is consistent with the monotonic decrease in the rate of stone comminution after the initial accelerating phase in stone comminution observed during SWL (see Figure 58.1b). Furthermore, shape and orientation can also profoundly influence the location and magnitude of the maximum tensile stress produced in stones of ellipsoidal geometry with equal

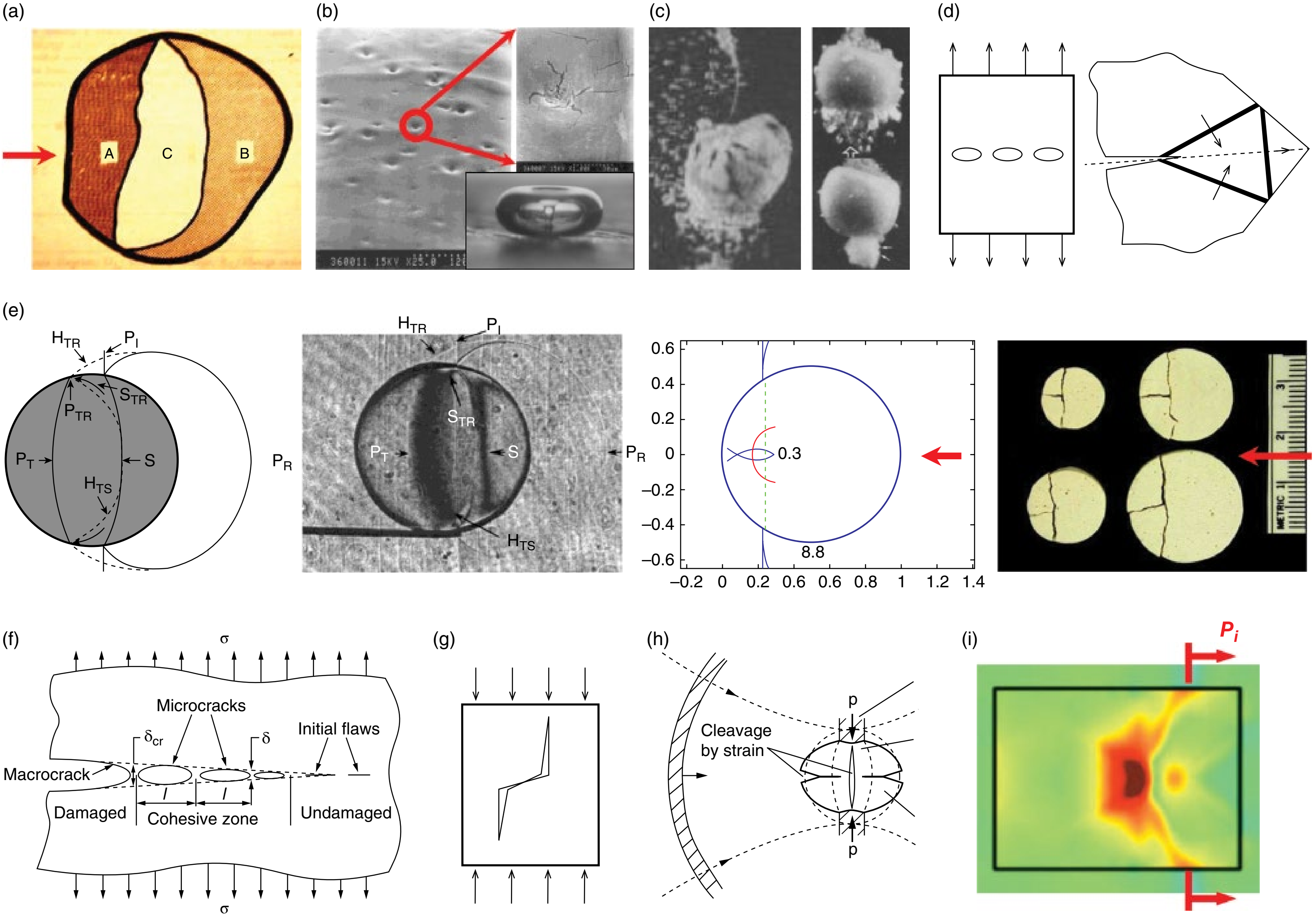
(a)
A
C
B
(b)
(c)
(d)
(e)
H_TR
P_I
S_TR
P_TR
P_T
S
H_TS
P_R
0.6
0.4
0.2
0
−0.2
−0.4
−0.6
0.3
8.8
−0.2
0
0.2
0.6
0.6
0.8
1
1.2
1.4
METRIC
(f)
σ
Microcracks
δ_cr
δ
Initial flaws
Macrocrack
l
l
Damaged
Cohesive zone
Undamaged
σ
(g)
(h)
Cleavage by strain
p
p
(i)
P_i

**Figure 58.10** A chronological list of different proposed mechanisms for stone fragmentation in SWL. (a) Stress gradient and tensile failure at stone/fluid interface, (b, c) cavitation damage, (d, e) spalling and corner fracture due to reflected tensile wave, and shear-enhanced damage, (f) dynamic fatigue, (g) compression-induced tensile failure, (h) quasi-static squeezing, and (i) dynamic squeezing. *Source:* from [15] with permission of Springer-Verlag, Berlin, Heidelberg.

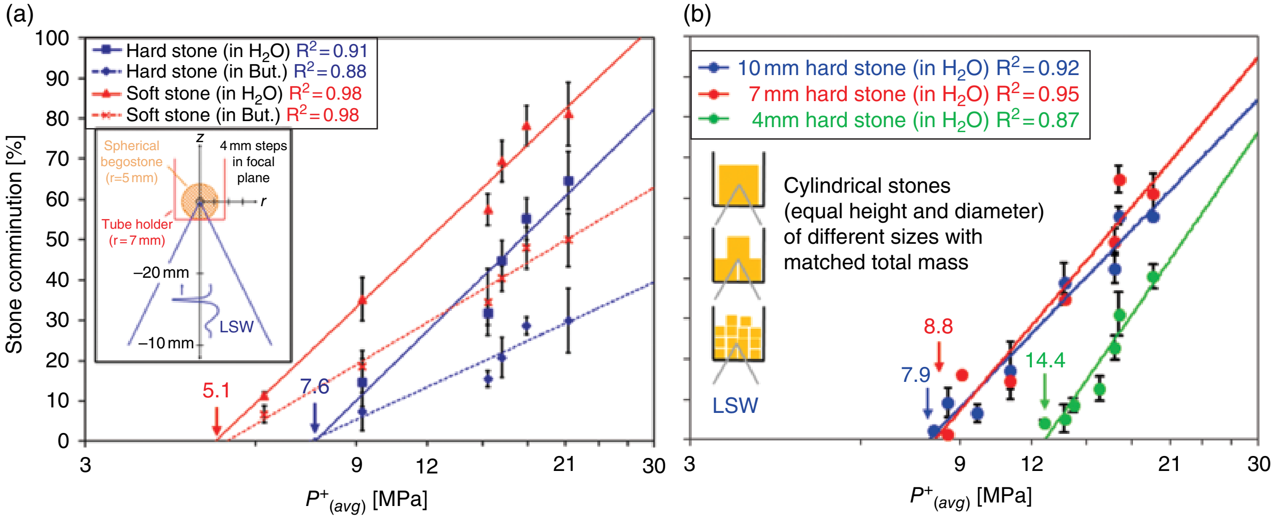

**Figure 58.11** Correlation between stone communication and the average peak pressure $P_{+(avg)}$ incident on the stone. (a): 10 mm spherical hard and soft stones, adapted from [51]. (b): cylindrical hard stones of different sizes with matched total mass, adapted from [36]. The $P_{+(avg)}$ threshold for initiating stone fragmentation is indicated by arrows in different cases. *Source:* from [51] with permission of Elsevier.

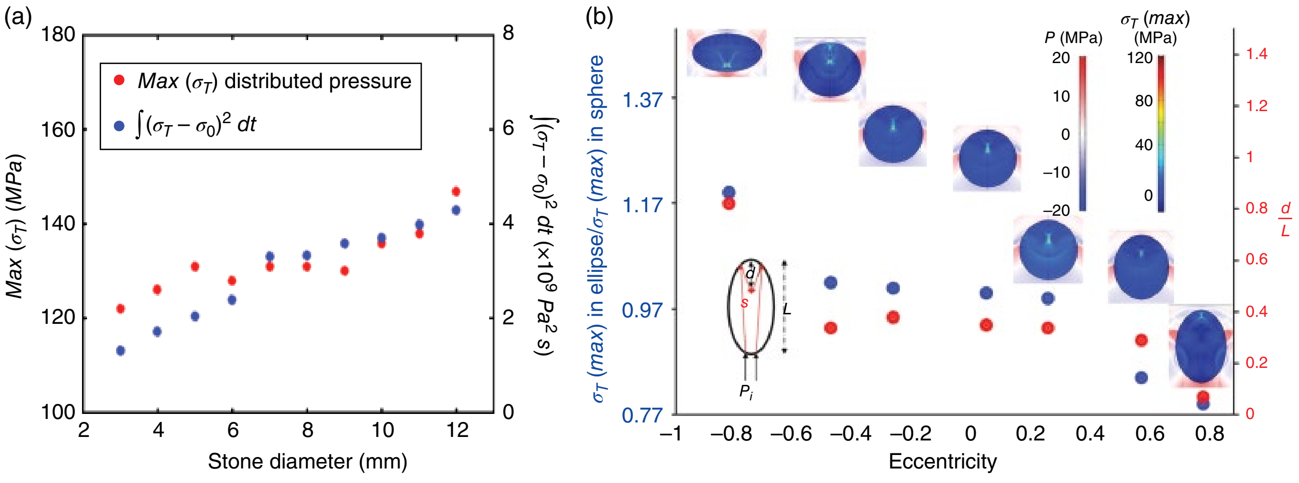

**Figure 58.12** (a) The effect of size on the maximum tensile stress (red) and tensile stress integral (blue) produced inside spherical stones. *Source:* from [36] with permission of Elsevier. (b) The effect of eccentricity on the magnitude and location of the maximum tensile stress produced in stones of ellipsoidal geometry (courtesy of Ying Zhang). In both cases, stones are subjected to the lithotripter field of a Siemens Modularis with a peak pressure of about 45 MPa.

volume but different eccentricities (Figure 58.12b). As eccentricity increases, the "hot" spot corresponding to the region of maximum tensile stress will shift from the anterior to posterior surface of the stone with decreased stress magnitude.

In summary, it is worth noting that the size of the fragmentation zone of a lithotripter is determined by $P_f$ (i.e., the dimensions around a lithotripter focus where the local peak positive pressure is equal or above $P_f$). At a given output setting, the fragmentation zone of a lithotripter will vary for different types of kidney stones (because of their varying elastic stiffness), and will be affected by stone geometry and size (because of their influence on internal wave focusing and interference). In general, the size of the fragmentation zone of a lithotripter will decrease as the treatment progresses unless the output energy is ramped up at the risk of higher propensity for tissue injury.

## Role of cavitation in stone fragmentation

In contrast to stress-wave-induced fracture, cavitation produces primarily surface erosion due to the localized strong secondary shock wave or microjet impact from inertial (symmetric or asymmetric) collapse of bubbles near the stone boundary [52] (see also Figure 58.6). Damage produced by cavitation is largely confined on the surface and does not penetrate deep into the bulk of the stone [53]. Although cavitation activities will intensify as fragmentation progresses [54], it has been shown that stone comminution produced by cavitation alone in SWL is very limited [53]. On the other hand, as shown in Figure 58.11 and other studies, stone comminution produced by stress waves without cavitation will also be significantly reduced [41, 53, 55, 56]. All in all, it has been suggested that both stress waves and cavitation are needed simultaneously in SWL, and they act synergistically to produce effective and successful stone comminution [53].

## A heuristic model of stone comminution in SWL

Recently, a heuristic model that describes the overall progression of stone comminution in SWL has been developed, accounting for the contribution of two important lithotripsy parameters: (i) $P_{+(avg)}$ (controlled by the output kV or energy setting of the lithotripter) and (ii) dose of the shock waves delivered [57]. The model is based on the Weibull theory for brittle fracture [58], incorporating threshold values of $P_{+(avg)}$ and dose that are required to initiate fragmentation. Validated by experimental data obtained both in water and 1,3-butanediol (a viscous medium that suppresses cavitation, but with similar acoustic impedance to water so that LSW transmission and generation of stress waves in the stone are not affected), the model provides physical insight that may directly benefit the design and implementation of safe and effective treatment protocols in SWL. For example, the asymptotic lines in the contour plot of stone comminution in Figure 58.13 suggests that effective treatment can be achieved by using moderate $P_{+(avg)}$ in the range of 15–20 MPa within 2000 shocks. Increasing $P_{+(avg)}$ beyond 20 MPa would not necessarily accelerate stone fragmentation, but may increase the propensity for tissue injury. Similarly, the model also indicates that in the low $P_{+(avg)}$ range of 10–15 MPa prolonged treatment to high doses will only marginally improve stone comminution, at the cost of longer treatment time and, potentially, elevating the risk of tissue injury. The optimal treatment strategy appears to be a progressive ramping of the lithotripter output (and thus $P_{+(avg)}$) that can achieve effective stone comminution with minimal risk of tissue injury, as illustrated by the dashed line in Figure 58.13.

## A unified theory of stone comminution in SWL

Figure 58.14 summarizes the mechanisms and processes of stone comminution in SWL. At the beginning (within a few hundred shocks), multiple mechanisms can be effective in producing fracture because the initial large size and smooth geometry of the stone favor wave focusing and constructive interference of different stress waves produced inside the stone by LSW–stone interaction. Moreover, the pre-existing (or intrinsic) flaws in the stone provide ample weak spots to intensify tensile stress and, as a result, stone fragmentation accelerates. Thereafter, fragments of irregular shapes and smaller sizes are produced, which disrupt the conditions required for internal wave focusing and constructive wave interference. Further, the intrinsic flaw population is gradually depleted, making

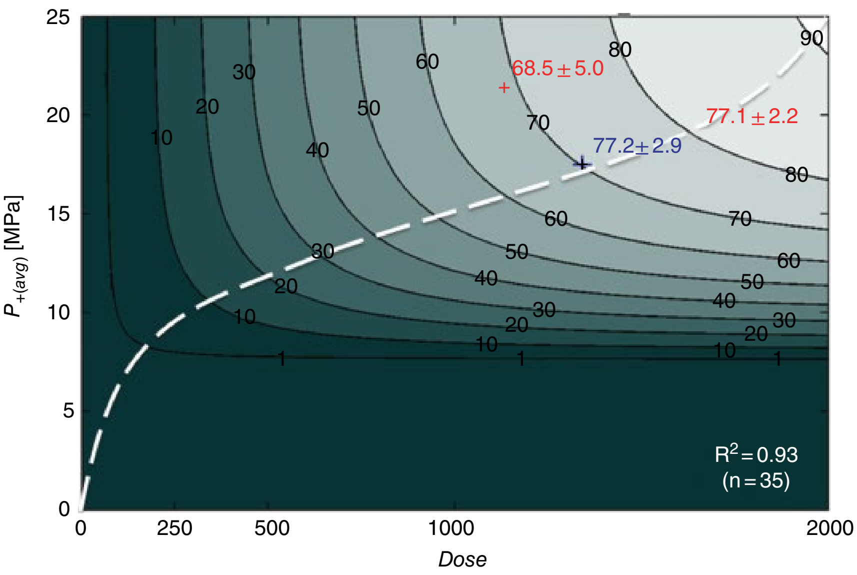

**Figure 58.13** A heuristic model of stone comminution in SWL, adapted from [57]. The contour lines (with numbers) denote the percent of stone comminution as a function of the average positive pressure incident on the stone ($P_{+(avg)}$) and shock-wave number delivered (dose). The dashed line shows an example of the optimal treatment strategy with pressure ramping in SWL. *Source:* from [57] with permission of Acoustic Society of America.

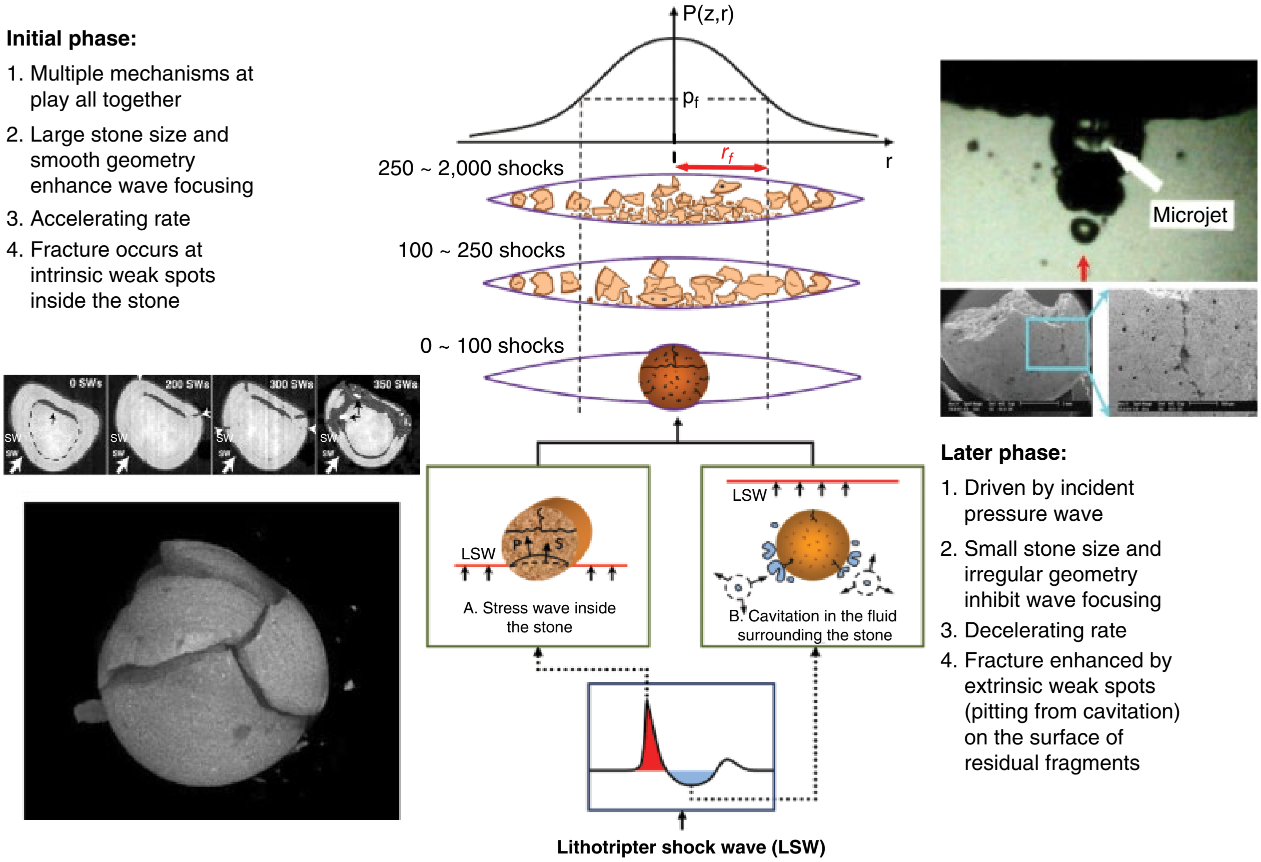
Initial phase:
1. Multiple mechanisms at play all together
2. Large stone size and smooth geometry enhance wave focusing
3. Accelerating rate
4. Fracture occurs at intrinsic weak spots inside the stone
P(z,r)
p_f
r_f
r
250 ~ 2,000 shocks
100 ~ 250 shocks
0 ~ 100 shocks
0 SWs
200 SWs
300 SWs
350 SWs
SW
Microjet
LSW
P
S
A. Stress wave inside the stone
B. Cavitation in the fluid surrounding the stone
Later phase:
1. Driven by incident pressure wave
2. Small stone size and irregular geometry inhibit wave focusing
3. Decelerating rate
4. Fracture enhanced by extrinsic weak spots (pitting from cavitation) on the surface of residual fragments
Lithotripter shock wave (LSW)

**Figure 58.14** Summary of the mechanisms and processes of stone comminution in SWL, adapted from [15]. The radius of effective fragmentation zone in the lithotripter field is denoted by $r_f$. Micro-CT images are adapted from [102] and from images taken by James Williams Jr. *Source:* from [102] with permission of Acoustic Society of America.

it more difficult to initiate fracture from inside the stone. In addition, after the initial fracture spreading of stone fragments away from the lithotripter focus will effectively reduce the $P_{+(avg)}$ incident on the residual fragment population. Altogether, these multiple factors dictate that stone comminution will decelerate as the treatment progresses. Consequently, in the late stage (if not majority) of SWL, the dominant mechanism of stone comminution is likely to be the $P_{+(avg)}$-driven opening of surface (or extrinsic) flaws produced by cavitation damage, through a synergistic interaction between stress waves (including surface acoustic waves) and cavitation-generating surface pitting [15].

## Tissue injury

There is no doubt that LSWs can cause trauma to renal tissues surrounding the stone, and, in a very few severe cases, even resulted in death of the patient [59–61]. A detailed description of the various clinical complications of SWL is given in Chapter 63 of this book. Here we will focus on reviewing the potential physical mechanisms of shock-wave–tissue interaction that may lead to injury.

As mentioned earlier in this chapter, the cigar-shaped focal region of a lithotripter exceeds the average stone size along the propagation direction of the incident shock waves. Therefore, a significant volume of the kidney, including the perirenal tissues, will be exposed to high-energy and high-pressure shock waves. Moreover, the patient's motion (due to respiration or pain-induced movements) will exacerbate the risk of tissue injury because a significant portion of the shock waves (30–40%) may completely miss the target stone and hit the renal tissue solely [62, 63]. As a result, a higher dosage of shock waves will be needed in a single treatment session, which further increases the risk of renal injury [63].

Tissue injury in SWL has been described mainly as vascular lesions in the form of endothelial cell damage and rupture of small blood vessels along the lithotripter beam path throughout the thickness of the kidney [64, 65]. Based on *in vitro* phantom and *in vivo* animal studies, shear stress [66, 67] and cavitation [68–71] have been hypothesized to be the two main physical mechanisms responsible for tissue injury. Shear stress can be generated by the propagation of LSW through inhomogeneous tissue spaces [14, 39, 67] that may cause injury by accumulated shear deformation, especially in the papilla and at high pulse repetition frequency (PRF) [66]. In addition, LSW-generated rapid and large intraluminal bubble expansion and collapse with resultant significant hoop stress imposed on the vessel wall may cause rupture of capillary and small blood vessels [71, 72]. In contrast, damage in large blood vessels or in the interstitial hemorrhage site may be mediated by LSW–bubble interaction with jet formation [73], a scenario that may be responsible for the deep poration of renal parenchyma produced by narrow focal width and high peak-pressure lithotripters [74]. Furthermore it has been demonstrated that injection of contrast agents for imaging prior to SWL can greatly increase the propensity of renal injury and should be avoided [68, 70].

Although the mechanisms of tissue injury have not been completely understood, several risk factors for tissue injury have been identified, including lithotripter output settings such as PRF, output energy and energy flux density, total number of shocks, and patient characteristics such as pre-existing hypertension in older people, pre-treated kidneys, and pediatric patients [59, 69, 75–77].

Tissue injury in SWL increases substantially at high PRF [69]. Compared to the early days of SWL, it has been advocated in recent years that shock waves should be administered at a slower rate [9]. The benefit has been demonstrated in HM3 that even at the highest output setting of 24 kV tissue injury can be significantly diminished when PRF is reduced from 2.0 to 0.5 Hz [78]. Moreover, current clinical treatment protocols often include an initial priming of the kidney with a low dose of shock waves (i.e., ≈500) at low energy levels followed by a few minutes pausing of the treatment, which has been demonstrated by animal experiments in HM3 to exhibit a protective effect probably due to vasoconstriction [79–81]. However, the mechanism of this tissue-protective strategy is not completely clear and needs to be thoroughly investigated using contemporary lithotripters under clinically relevant output settings.

## New technologies in SWL

### Lithotripters with broad focal width and low peak pressure

Motivated by the success of the self-focusing EM lithotripter (XX-ES) [16], there is a resurgence of new clinical lithotripters (e.g., LG-380 and Lithospace) with broad focal width and low peak pressure, which are the acoustic field characteristics exemplified by the original HM3. Comparison studies between broad focal width (18–20 mm)/low peak pressure (12–30 MPa) lithotripters (LG-380 and XX-ES) and a narrow focal width (≈2.6 mm)/high peak pressure (≈90 MPa) lithotripter (SLX) have shown that the former can disintegrate stones more effectively in a large area around the lithotripter focus [82]. The high peak pressure of the SLX, while beneficial for breaking up stones located precisely at the lithotripter focus, is also responsible for producing more tissue injury [83]. Moreover, the narrow focal width/high peak pressure lithotripter field with its inherently large pressure gradient will exert a strong radiation force on the target stone that may cause more fragment dispersion. In contrast, LG-380 and XX-ES with minimal tissue injury produced even at their maximum output settings are considered relatively safe lithotripters [82]. The advantages of a broad focal width/low peak pressure lithotripter in stone fragmentation have also been attributed to other factors, including (i) a more uniform cavitation field, (ii) progressive fragmentation of the stone, (iii) less dispersion of residual fragments, and (iv) higher $P_{+(avg)}$ or local positive pressure at off-axis locations in the lithotripter field [51, 52, 57, 84]. Overall, a lithotripter with broad focal width and low peak pressure will be more effective for treating stones that are less accurately aligned with the lithotripter focus, or when residual fragments are dispersed or significantly translated away from the lithotripter focus due to respiratory motion of the patient [84].

### New acoustic lens design for electromagnetic shock-wave lithotripters

Over the past two decades, EM shock-wave lithotripters have become the technology of choice primarily due to the durability and reproducibility in output pressure and acoustic pulse energy [85]. However, compared to the gold standard HM3, several fundamental drawbacks exist in EM lithotripters: including (i) the relatively narrow focal width, (ii) the non-idealized pressure waveform exemplified by the secondary compressive wave immediately following the tensile wave, and (iii) the significant shift in the locations of $p+$ (i.e., acoustic focus) and peak negative pressure ($p-$) towards the shock source, especially at high output settings [86, 87].

These fundamental drawbacks have been recently addressed through acoustic lens modification of the Modularis lithotripter. By introducing a groove in the outer region of the original lens (Figure 58.15), the second compressive wave can be eliminated while the focal width of the lithotripter is broadened simultaneously via *in situ* pulse superposition [86]. Under the same effective acoustic pulse energy, the new lens design leads to a lower $p+$ on the lithotripter axis, but higher off-axis local peak pressure

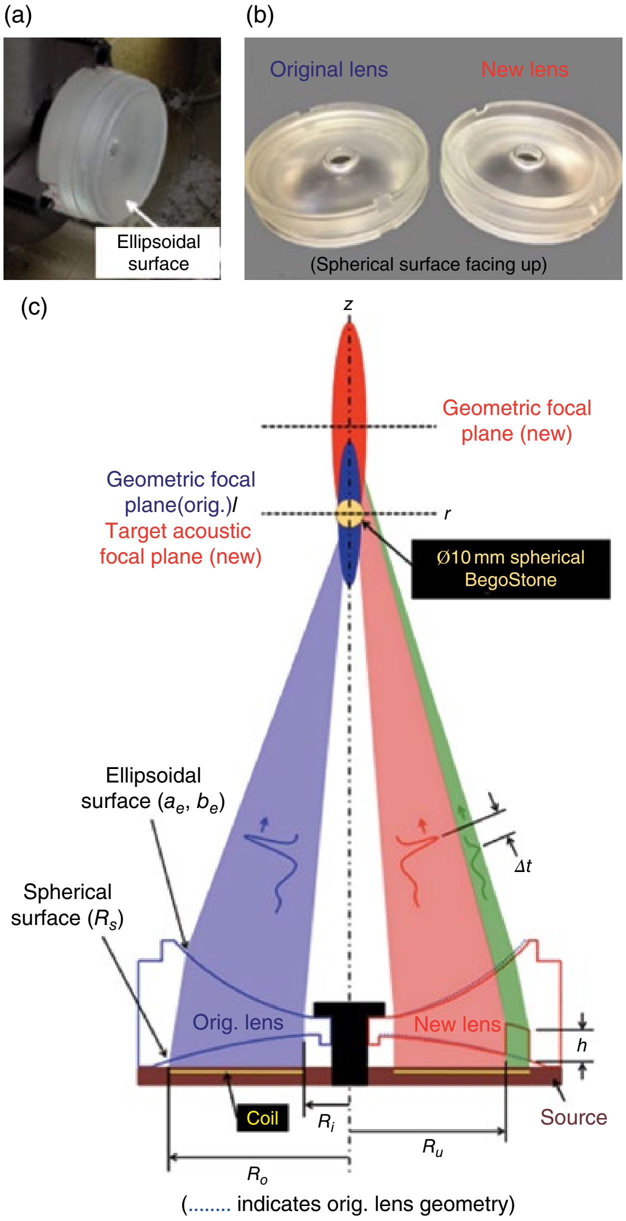
(a)
Ellipsoidal surface
(b)
Original lens
New lens
(Spherical surface facing up)
(c)
z
Geometric focal plane (new)
Geometric focal plane(orig.)/
Target acoustic focal plane (new)
r
Ø10 mm spherical BegoStone
Ellipsoidal surface ($a_e$, $b_e$)
Spherical surface ($R_s$)
Δt
Orig. lens
New lens
h
Coil
$R_i$
Source
$R_u$
$R_o$
(........ indicates orig. lens geometry)

**Figure 58.15** Improvement of contemporary electromagnetic shock-wave lithotripter through lens modification. *Source:* from [87] with permission of PNAS.

with stronger cavitation activity [87]. Moreover, by reshaping the lens geometry the location of the acoustical focus at high energy settings can be aligned closely with the geometric focus of the lithotripter where kidney stones are placed during treatment. Both *in vitro* and *in vivo* studies have demonstrated that the new lens can significantly improve stone comminution with minimal tissue injury under clinically relevant energy settings [87]. Because of the simplicity in the modification, this design upgrade of acoustic lens or reflector can be easily implemented in principle in all clinical EM shock-wave lithotripters.

## Other emerging technologies and techniques in SWL

There are other emerging technologies under investigation that require substantial modifications of the lithotripter system. For example, tandem pulse technology has been extensively evaluated in a hybrid EH-PE shock source with coaxial alignment [88, 89], dual shock-head source aligned either opposite to each other [90], or at an acute angle [91], and a single PE source driven by a dual high-voltage pulse generator [92], all aimed at promoting the contribution of cavitation in stone comminution. Despite proof of principle, challenges exist in the cost-effective integration of the tandem pulse technology in clinical lithotripters and evaluation of its impact on tissue injury.

Treatment monitoring is another area with active research, including stone targeting via spectral Doppler ultrasound [93] and assessment of stone fragmentation via cavitation-produced acoustic emission [94] or acoustic scattering from residual fragments [95]. In most cases, further refinements are needed before clinical applications. It should be noted that there is no current imaging technology that can monitor tissue injury during SWL.

More recently, transcutaneous pulsed focused ultrasound has been demonstrated to displace stones or fragments in the renal collecting system without thermal damage [96]. This technology may be used to facilitate stone clearance following successful SWL. Focused ultrasound has also been used in burst wave lithotripsy to effectively fragment artificial and natural stones fixed on a holder *in vitro* using focal pressure of 6.5 MPa at less than 200 Hz burst repetition rate [97]. Further studies under clinically relevant conditions and *in vivo* experiments to assess potential tissue effects are warranted [97]. Finally, several techniques of cavitation manipulation have been demonstrated *in vitro* for either removing residual bubbles in the coupling medium using a turbulent jetting flow [98] or along the lithotripter beam path [99, 100] and near the stone surface using low-pressure ultrasound bursts [101] for improved treatment efficiency.

## Summary

As a remarkable engineering innovation, SWL truly represents a milestone in the surgical management of urolithiasis. Because of its non-invasiveness and easy of use, SWL still remains as the therapy of choice for a majority of patients with kidney and upper urinary stones. In parallel to the widespread clinical applications, our understanding about the general physical principles

**Box 58.4 Future outlook.**

- Development and integration of novel SWL technologies into contemporary clinical shock-wave lithotripters, including the design of new shock source and focusing device, miniature wet coupling technique, adaptable and steerable beam formation in lithotripter fields, cavitation control and monitoring.
- Development of real time (acoustic) tracking of the stone or large residual fragments to fire shock waves only if the stone is in the focal zone. Development of acoustic techniques to monitor stone comminution process so that the treament can be stopped once the stone is sufficiently fragmented.
- Development of new imaging techniques for real-time monitoring of hemorrhage and hemotama formation in peri- and intra-renal tissues, which will be crucial and necessary for establishing a pressure or energy flux density based threshold for tissue injury in SWL. With this knowledge, we'll be able to better define the lithotripter output parameter space to ensure a safe and effective treatment using high-energy shock waves.
- Development of pulsed focused ultrasound techniques for effective and safe fragmentation of kidney stones with reduced treatment time or clearance of residual fragments from the collecting system following successful SWL.
- Further improvement in the fundamental understanding about the physics of SWL and the mechanisms of stone comminution and tissue injury will help us in rational selection of lithotripter characteristics and output settings to optimize treatment strategy for maximal stone fragmentation with minimal tissue injury and adverse effects.

and process of SWL has improved significantly in the past two decades. The state-of-the-art theories regarding stone fragmentation and tissue injury during SWL are reviewed in this chapter. In the following, we summarize several main points pertinent to current status of SWL together with future overlook outlined in Box 58.4:

- EM and EH technologies for shock-wave generation and associated focusing means are predominantly used in contemporary clinical lithotripters while PE technology is less favored because of limited acoustic energy output. There is a trend of resurgence in broad focal width and low peak pressure lithotripters, exemplified by the original HM3.
- Dry coupling has replaced wet coupling in almost all contemporary lithotripters in favor of user convenience, but at the cost of providing an imperfect coupling interface between the shock source and the patient. Problems may arise in shock-wave transmission if care is not taken in ensuring the quality of the coupling interface.
- The acoustic field of a lithotripter is determined primarily by the design characteristics of the shock source and focusing device. Among clinical lithotripters, the maximum of peak positive pressure of LSWs varies in the range of 20–120 MPa, with the minimum of peak negative pressure in the range of –4 to –12 MPa. The focal width of clinical lithotripters varies from 2 to 20 mm, and is inversely correlated with the aperture angle of the shock source.
- Stone fragmentation in SWL is the consequence of dynamic fatigue produced by stress waves and cavitation generated by lithotripter shock-wave–stone interaction. Stress waves (longitudinal, transverse, and surface acoustic waves) and associated tensile and shear stresses are the primary driving forces to create fracture, initially from the pre-existing (or intrinsic) flaws or weak spots in kidney stones. In contrast, cavitation produces pitting and therefore introducing new weak spots (or extrinsic flaws) on the stone surface, leading to weakened mechanical integrity of the stone. Caviation induced in SWL is not sufficiently strong enough to disintegrate stones. Stress waves and cavitation are both necessary and work synergistically to produce effective and successful stone comminution in SWL. Cavitation damage can be considered as catalysts to enhance the efficiency of stress-wave-driven stone fracture.
- Average peak positive pressure incident on a stone, $P_{+(avg)}$, has been identified as a key lithotripter field parameter that is directly correlated with stone comminution. The threshold of $P_{+(avg)}$ to initiate stone fracture depends on the composition, geometry, and size of the stone. Kidney stones with higher wave speeds, acoustic impedance, and fracture toughness, such as calcium oxalate, brushite, and cystine stones, are more difficult to disintegrate than those with lower corresponding values such as uric acid, carbonate apetite, and struvite stones. A new nondimensional parameter $Z$ has been identified that can be used to gauge the effectiveness of lithotripter field in stone comminution.
- Tissue injury in SWL is related to shear stress and cavitation, yet the exact mechanism has not been completely determined. In SWL, it is crucial to ensure treatment safety before pursuing treatment efficiency. Lowering peak pressure, energy flux density, PRF, and

dose of shock waves delivered in a single treatment have all been demonstrated to lessen the risk of tissue injury during SWL.

- A heuristic model accounting for the effects of both $P_{+(avg)}$ and dose has been developed to assess the overall process of stone comminution in SWL. The model suggests that a progressive ramping of the lithotripter output (and hence $P_{+(avg)}$) will be effective for achieving successful stone comminution with minimal risk of tissue injury.
- New technologies in SWL, such as self-focused EM shock-wave lithotripter and the new acoustic lens for Modularis or other EM shock-wave lithotripters, have been either developed or demonstrated. Other promising technologies and techniques for improving treatment efficacy and safety will continue to emerge. The integration of new technologies into clinical lithotripters will depend critically on the demand by urologists for better and safer lithotripters as well as the desire of medical device manufactuers to bring them to the markert to alleviate millions of kidney stone patients worldwide from their painful conditions.

## Acknowledgments

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# 59

# Lithotripsy Systems

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## Historic perspective

Prior to the introduction of extracorporeal shock-wave lithotripsy (ESWL) and other minimally invasive techniques such as percutaneous nephrolithotomy and ureterorenoscopy, open surgery was the principal treatment modality for urolithiasis. The first extracorporeal shock-wave lithotripsy (ESWL) that was performed on a stone-bearing patient in 1980 therefore thoroughly revolutionized modern stone management. As early as 1963 physicists at Dornier, an aircraft manufacturer in Friedrichshafen, Germany, had investigated the impact of raindrops on flying objects, as these impacts caused shock waves which not only damaged the outer shell of airplanes but also structures within. During these experiments an engineer at Dornier accidentally discovered the effects of these shock waves on biological tissue. At the same time the German Ministry of Defense was also interested in the interaction between shock waves and biological tissue. In 1974 a partnership to conduct research on the application of shock waves in humans was formed between Dornier Development and Research (W. Hepp and G. Hoff), the Department of Urology at the Ludwig-Maximilians Universität in Munich (E. Schmiedt and F. Eisenberger), and the Institute of Surgical Research at the same university (W. Brendel and Ch. Chaussy). Funding was obtained through the German Research and Technology Ministry [1–3].

Early on it was found that shock waves caused no damage when traveling through muscle, fat, or connective tissue, except at transition zones with high acoustic impedance. In the course of this project someone then formed the idea to fragment kidney stones in the human body [1, 2]. After extensive experiments the first lithotriptor for human treatment, the Dornier Human Model 1 or HM1, was built, in 1979.

Patient selection for the first treatments was very strict:

- a radiopaque stone not larger than a cherry pip in the renal pelvis
- unobstructed urological tract
- no urinary tract infection
- no comorbidities.

The first patient was successfully treated using a Dornier HM1 on 7 February 1980 by Christian Chaussy, B. Forssmann, and D. Jocham [4]. The results of the first clinical study on 221 treatments in 206 patients were published in 1982 [5]. In order to promote the new technique as reproducible and safe, the HM1 needed several improvements:

- an improved X-ray system
- an improved patient support
- an improved installation to produce the 1200 liters of degassed water for the waterbath
- an improved shock-wave generator
- an ellipsoid with a treatment depth of 13 cm.

The Dornier HM3 was born.

In 1983 the second lithotripsy center was opened in the Department of Urology (F. Eisenberger) of the Katharinen Hospital in Stuttgart. In March 1984 the first Dornier HM3 in the United States was installed in the Methodist Hospital in Indianapolis (Daniel M. Newman and James E. Lingeman). A study for marketing approval by the US Food and Drug Administration was monitored by Georges Drach [6]. The rest is history.

Originally lithotripters were devices only dedicated to shock-wave lithotripsy (SWL). With modern stone management demanding a judicious combination of endourologic techniques and SWL, there was an evolution toward the construction of multifunctional urologic

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workstations. A modern stone center needs to tailor the most appropriate treatment to both the patient and their stone. A multifunctional workstation where both endourological techniques and ESWL can be performed in great comfort therefore seems an essential tool.

## Components of a lithotripter

The Dornier HM3 lithotripter represented the archetype of the first-generation lithotripter, characterized by a large water bath in which the patient was immersed for optimal shock-wave coupling. Equipped with an electrohydraulic shock-wave source and an ellipsoidal reflector with a small aperture to focus the shock wave, the treatment required general or spinal anesthesia. A bidirectional fluoroscopic imaging system allowed targeting to move the stone into the therapeutic focus F2. Multifunctional or multidisciplinary use was impossible. The results achieved with this device are still considered the basis for comparison in evaluating all new devices.

Second-generation lithotripters utilize an electrohydraulic, electromagnetic, or piezoelectric shock-wave source. Transmission of the shock wave is provided by means of a water cushion or partial water bath. Stone localization is performed with an ultrasonic or fluoroscopic imaging system [7–10]. The anesthesia requirements have been reduced so that SWL can be performed without any medication or only in analgosedation. Multifunctional or multidisciplinary use is limited.

Third-generation lithotripters are also equipped with an electrohydraulic, electromagnetic, or piezoelectric shock-wave source. All systems allow anesthesia-free treatments. Apart from that they use both fluoroscopy and ultrasound, alternately or simultaneously, to target the stones. Finally, all components are integrated into a multifunctional system with a treatment table allowing both SWL and endourologic procedures to be performed on the same device.

### Shock-wave sources

Shock waves are acoustic waves. Acoustic waves are mechanical waves consisting of pressure and density variations which can travel through media in any of its phases: gaseous, liquid, or solid. They are also referred to as pressure waves. Acoustic waves propagate through a medium by alternating decompression and compression of the medium. At the interfaces of the media they pass, absorption, reflection, or refraction of the shock waves can occur [11]. An acoustic wave of very short duration is called an acoustic pulse and a shock wave is a very short acoustic pulse. On the wave front the positive pressure rises in a very short time from the ambient pressure to the maximum pressure. Afterwards a short phase of underpressure follows. While the wave propagates through the medium, it gets continuously steeper until it forms a shock wave. The generated shock wave is characterized by a sudden drop from overpressure to underpressure. The short phase of underpressure generates cavitation in the transmission medium. The bubbles induced by cavitation subsequently collapse violently and create microjets or secondary shock waves. For medical purposes shock waves are generated in water and transmitted into the patient's body using a (partial) water bath or a water cushion for coupling. Water is used as transmission medium due to having comparable acoustical properties to human tissue, leading to impedance matching with low reflection at the contact surface between the water bath or water cushion and the patient.

In the Dornier HM3, the first lithotripter commercially available, shock waves were generated using an electrohydraulic shock-wave source. In second- and third-generation lithotripters any of three principles of shock-wave generation are used: electrohydraulic, electromagnetic, or piezoelectric.

#### Electrohydraulic shock-wave sources

#### *Electrohydraulic shock-wave generation*

Electrohydraulic shock-wave generation is based on an underwater spark discharge. A spark plug with two opposing electrode tips is positioned in the focus F1 of an ellipsoidal reflector. A capacitor of about 100 nF connected to the spark gap is charged to a voltage of 15–30 kV and then abruptly discharged, producing a fast-growing plasma channel between the electrode tips and resulting in rapid vaporization of the surrounding water like a micro-explosion. This releases a spherical shock wave that is reflected by the wall of the ellipsoidal reflector towards the therapeutic focus F2 of the reflector. The intensity of the shock wave can be adjusted by changing the discharge voltage. The treatment depth and focusing are defined by the geometrical parameters of the ellipsoidal reflector. This type of shock wave is still used in lithotripters today, and the shock-wave source of the HM3 is still considered to be the most effective of this type. Electrohydraulic shock waves have the disadvantage, in that the life span of the electrode tips is limited to several thousand shocks. Degradation of the electrode tips causes output variations and instabilities of the focus position, particularly near the end of the electrode's lifetime.

#### *Electroconductive shock-wave generation*

To compensate for the degradation of the electrode tips which causes variations and instabilities of the focal position and energy and limits the life span of the electrode to several thousand shocks, Technomed developed a modified electrohydraulic generator, the Diatron IV, an electroconductive shock-wave generator.

The electroconductive generator is a 100 nF generator connected to an electrode immersed in a highly conductive solution instead of degassed water. Due to a better conduction of electricity this highly conductive solution allows an extremely accurate spark position. This combined with reduced interelectrode distance leads to a reproducible and consistent focal spot. This spark gap technology also allows the generation of a focal zone that varies in size with the power output.

An automatic pressure regulator permanently adapts the voltage input to consistently deliver the requested pressure to compensate the variations due to electrode wear and also controls the total energy delivered to the patient.

### Electromagnetic shock-wave sources

#### *"Flat coil" electromagnetic shock-wave emitter*

The electromagnetic shock-wave emitter (EMSE; Dornier, Siemens) features a flat coil that generates a strong magnetic field when a high current pulse flows through it. This field causes an isolated metallic membrane to be repelled into the surrounding water. This causes the water in the vicinity of the membrane to be compressed and a plane acoustic pulse is released, which is focused into the therapeutic focal area by a lens. The pressure across the membrane surface is essentially constant. During propagation to the focal area the pressure pulse undergoes nonlinear effects, leading to the generation of a shock wave. Specifically, the pulse's rising slope becomes steeper and the pulse duration becomes shorter. Since the electromagnetic shock-wave generation principle does not rely on the dielectric breakdown of a liquid, all the associated threshold effects and arc-forming instabilities are avoided. An EMSE can therefore produce effective pressure pulses over a very wide intensity range with a high degree of reproducibility. This wide dynamic range allows for different shock-wave treatment strategies to be used. The instrument's life time is in the order of 1 million pulses. An EMSE does not show progressive degradation in its output power but it needs to be exchanged on a regular basis when the insulating materials and the metals have reached their endurance limits.

The plane acoustical pulse generated by the EMSE is focused by an acoustic lens. The choice of the diameter of the EMSE and the focal length of the lens define the aperture angle of the system. The wide dynamic range that is available for EMSE systems, together with the wide choice of aperture angles, provides a unique toolbox for the designer, serving the different needs of shock-wave field shaping in lithrotripsy, in orthopaedic shock-wave application, and in other emerging applications. An EMSE is easily incorporated into a multifunctional device. Newer EMSE designs provide treatment results comparable to or even better than the results with the unmodified Dornier HM3.

There is ongoing research to improve the performance of electromagnetic lithotripters through modification of the lens geometry [12].

#### *Storz electromagnetic shock-wave source: cylinder source with parabolic reflector*

The electromagnetic cylinder source was also developed to overcome some drawbacks of the powerful but unstable spark gap technology with a short life span of the eroding electrodes. The cylinder generator is based on a hollow electromagnetic cylinder composed of a cylindrical coil covered by an insulating membrane, which again is covered by an electrically conducting membrane of high strength. An intense pulse current with short rise time generates repelling pulse forces due to electromagnetic induction. When immersed in water the radially expanding membrane generates, primarily, an acoustic cylinder wave which is focused by a special rotational parabolic reflector. The principle works on the same basis as a loudspeaker, but with very intense and short acoustic pulses.

The cylindrical coil/membrane configuration is very stable and delivers more than 1 million pulses without degradation or significant fluctuations of acoustic energy. The parabolic reflector can be designed with large apertures and, accordingly, large aperture angles without technical limitations. Due to the large aperture angle, the acoustic energy can be concentrated to laterally narrow and axially short focal zones with high peak pressure and high energy flux density values. Thus, the fragmentational shock-wave energy is restricted to a relatively small area, reducing tissue lesions in front or behind the target stone. Also, anesthesia requirements and shock-wave load affecting the coupling area at skin level are minimized. Contrary to the electrohydraulic spark gap technology, the energy level of each single shock-wave pulse can be precisely adjusted between very low (painless) and powerful settings, exactly matching the pain tolerance of the patient.

The generator configuration featuring a hollow cylinder provides sufficient space for favourable inline localizations either for fluoroscopic or ultrasonic targeting [13–15].

### Piezoelectric shock-wave sources

Piezoelectric shock-wave generation was developed simultaneously by EDAP and Wolf [16–20]. The conversion of electrical to acoustic energy takes place in ceramic platelets that expand or contract in the surrounding water because of the piezoelectric effect when a pulse of several thousand volts is applied. Several dozen to several thousand platelets are usually mounted on a spherical segment transmitting the shock wave into the center of the sphere through direct focusing. However, compared to other generation principles the intensity of a typical piezoelectric generator is lower and a large converter surface is required to mount the platelets. The diameter of such a shock-wave source is therefore large, providing sharp focusing of the acoustic pulse. The large diameter of the piezoelectric dish makes its incorporation in a multifunctional device more problematic, however. The piezoelectric shock-wave source of the Wolf Piezolith 3000 features a double layer of piezo-ceramic elements, known as Double Layer Piezo-technology.

Each type of shock-wave source produces a shock wave, i.e. an acoustic pulse of which the energy is focused towards and concentrated in the therapeutic focus. In an electrohydraulic lithoptripter the focusing is achieved by a semi-ellipsoid reflector, whereas in an electromagnetic lithotripter shock waves are focused using an acoustic lens (Dornier, Siemens) or a parabolic reflector (Storz). In a piezoelectric system there is no focusing as such. Each ceramic crystal is to be considered as a separate point source that produces its own miniature shock wave. The ceramic crystals are arranged on a dish that directs the point sources towards the therapeutic focus, where the accumulation of the energy of all these separate point sources produces sufficient energy for stone fragmentation: direct-focusing lithotripsy (DFL).

#### Burst-wave lithotripsy

In a recently published experimental *in vitro* study bursts of high-intensity ultrasound are used to disintegrate artificial and real urinary calculi. The conclusion of the *in vitro* study was that *in vitro* burst-wave lithotripsy is feasible. The clinical use of this novel and interesting technique will of course depend on *in vivo* clinical studies proving both efficiency and the exclusion of adverse tissue effects [21, 22].

## Introduction to shock-wave physics

A shock wave is an acoustic pulse characterized by a very fast rise time, a very high overpressure, a very short pulse duration, and a phase of underpressure. The physics of shock waves being very complex [11], a basic understanding of some of the parameters in shock-wave physics is useful (see also Chapter 58 in this volume). Only the more clinically relevant parameters will be discussed here.

### Maximum treatment depth or penetration depth

The maximum treatment depth is the distance between the shock-wave head and the point of highest pressure in front of the shock-wave head. This is the geometrical focus. The shock-wave focus, however, is cigar shaped, with the axial dimension longer than the lateral. This means that there is still energy that may be sufficient to break a stone beyond the geometrical focus. This is referred to as the “blast path.”

In their published specifications some manufacturers may “extend’ their treatment depth by also incorporate the blast path, thus adding half of the focal length to the geometrical focus and “stealing” some distance.

### Clinical relevance of focus size

There is an ongoing debate on the ideal focus size in a lithotripter [21, 22]. The ideal focus would be a spherical volume exactly matching the size of the targeted stone, thus limiting the administration of energy to the stone and avoiding hitting the surrounding tissue, which would lead to adverse tissue effects [21, 22]. This is technically not feasible, however. Today’s lithotripters have a cigar-shaped focus with energy delivered in front, behind (blast path), and adjacent to the target.

A small focus is highly confined and sharp. The higher pressure in a small focus leads to high efficiency in fragmenting hard stones. In order to obtain optimal fragmentation and to avoid adverse tissue effects, precise targeting is essential. In a large focus pressure is lower. Precise targeting is less critical but there is an increased analgesia need and a higher risk of adverse tissue effects.

Sometimes there is a demand for larger focal zones in order to treat larger target volumes even if surrounding tissue may be affected more than technically necessary. To respond to this demand Storz introduced dual-focus technology. The design of the electromagnetic cylinder source offers the possibility to select different focal zones, precise and extended, according to clinical and anatomical conditions. By modification of the electrical excitation of the coil, longer pulses may be genereated which, in turn, stretch the focal zone, both laterally and axially.

The Wolf Piezolith 3000 features a triple focus: F1, small focus with high energy density (ED); F2, intermediate focus with medium to high ED; F3, larger focus with medium ED. Prospective trials would be useful to document the clinical benefits of selectable foci.

### Shock-wave interaction mechanisms

It is generally assumed that a combination of four different mechanisms is involved in the interaction between shock waves and the targeted stone: the Hopkinson effect, cavitation, quasistatic squeezing, and dynamic fatigue [7]. It is also assumed that cavitation and shear forces (the Hopkinson effect) are the main culprits in the origin of adverse tissue effects. Although both shear forces and cavitation are important and necessary in the stone comminution process, avoidance of the negative effects of shear forces and cavitation is considered important in reducing adverse effects due to shock waves.

The idea behind the dual-pulse technique [23, 24] is to "fill" the negative part of the pressure pulse with a positive pressure pulse. In the Direx Duet dual shock-wave sources are used. Fired synchronized or asynchronized they allow an increase in the total pressure and the shock-wave rate. Sheir et al. [23] demonstrated improved stone comminution with a synchronous discharge of a twin pulse. In another study [24] the same group demonstrated higher performance and efficacy with this twin-head, twin-pulse technique. At the same time this technique produced far less parenchymal damage than with the use of a single treatment head. Theoretically this would reduce cavitation and improve disintegration.

In ongoing efforts to engineer better lithotripters several studies have been and are being conducted to control cavitation and reduce its adverse tissue [25–28]. Eisenmenger and colleagues [29–31] advocate the use of a wide focus with lower pressure to enhance quasistatic squeezing, as this would presumably reduce tissue trauma and improve disintegration. This low-pressure, wide-focus technology is incorporated in the electrohydraulic Lithospace from Jena Med Tech GmbH (Jena, Germany) and the electrohydraulic LithoGold LG-380 from MTS (Konstanz, Germany). In a study by Bhojani et al. [32] comparing the electromagnetic Modulith SLX to the LithoGold LG-380 stone-free rates proved modest with both devices using SWL alone. Outcomes with both systems also proved similar. In this study an advantage of the wide-focus, low-pressure principle could not be demonstrated. Further prospective clinical studies to corroborate (or disprove) this concept are eagerly awaited.

## Coupling

Shock waves are acoustic waves that travel through a medium by alternating decompression and compression of the medium. Absorption, reflection, or refraction of the shock waves can occur at interfaces between media with different acoustic impedance. As water has comparable acoustical properties to human tissue, shock waves are generated and transmitted in water. In order to minimize energy loss of the shock wave at the interface between the patient and the shock-wave source, coupling between shock-wave source and patient is extremely important [31].

Total immersion of the patient in a water bath with degassed water where the shock wave is generated (Dornier HM3) is still considered the ideal coupling system. Second- and third-generation lithotripters, however, feature "dry" coupling which consists of a water-filled cushion that is inflated and pressed against the patient. The water cushion is made of elastic PVC or silicone, and is capable of adapting to the body shape of the patient. In order to guarantee good acoustic transmission, the water cushion is coupled to the patient through the application of ultrasound gel as an interface. In this process, both air bubbles in the coupling gel and folds in the water cushion could impair the transmission of acoustic waves. Even tiny air bubbles in this interface can lead to uncontrolled shock-wave attenuation.

In an *in vitro* experiment, Pishchalnikov et al. [33] found a reduction in fragmentation of 20–40% when air bubbles were included that covered an area equal to 2% of the cushion surface. Decoupling the cushion from the test basin and recoupling it led to a drastic increase in air inclusions. This has led to the recommendation that, if one decouples the patient during treatment, one must repeat the coupling procedure, including cleansing the coupling cushion and subsequently reapplying gel. Based on their own stone model, Jain and Shah [34] were able to identify a considerable influence of air inclusions on the erosion capacity of the shock wave.

After experimenting with various techniques for gel application, as a method of choice Neucks et al. [35] recommend applying the gel as a bolus, specifically from a vessel with a large opening. A small vessel opening and manual distribution of the gel lead to increased air pockets and poor disintegration results. Bergsdorf et al. [36] also recommend the selection of a proper coupling gel disc or gel with low viscosity and the accurate removal of air bubbles to improve efficiency in SWL.

In an experiment with an electromagnetic Dornier lithotripter equipped with an inline ultrasound scanner, Bohris [37] demonstrated that 43% more shock waves were needed to fragment model stones when only 8% of the coupling area, visualized with an inline ultrasound scanner, was covered with air bubbles. Li et al. [38] observed that the coupling interface is invisible during treatment and that the real problem is to avoid the entrapment of air bubbles during the coupling process. To monitor the coupling area in real time during stone treatments Bohris et al. [39] installed a video camera in the therapy head of a Dornier Lithotripter SII. In only 10 of 30 treatments could good coupling with an air ratio of less than 5% be obtained and in eight treatments the air ratio was higher than 20%.

In a prospective clinical study using opical coupling control (see Figure 59.6 below) in a Dornier Gemini Tailly and Tailly-Cusse [40] achieved comparable effectiveness quotients (EQ) with a reduction in shock-wave numbers of 25.4% for renal and 25.5% for ureteral stones leading to a corresponding 25% reduction in treatment time. Energy levels could be reduced with 23.1% for renal and 22.5% for ureteral stones. In this study a video camera incorporated in the therapy head of a Dornier Gemini lithotripter allowed visual monitoring of the coupling area. Air bubbles that inevitably were trapped in this coupling area could easily be removed by gently swiping a hand between the patient and the water cushion, thus consistently achieving perfectly bubble-free coupling.

## Imaging systems

Adequate imaging is vital to the success of ESWL:

- localization and targeting of the stone
- surveillance of treatment progress
- identification of fragmentation.

Imaging modalities available on a lithotripter will to a great extent also define treatment strategies.

Early lithotriptors were equipped either with ultrasound or fluoroscopy. In order to meet all the challenges in modern integrated stone management present day lithotriptors ideally should be equipped with both imaging modalities, to be used either independently and alternately or simultaneously. Inline use of both modalities is essential.

Fluoroscopy allows targeting of radiopaque stones at all levels of the urinary tract. Direct targeting of radiolucent stones is impossible, however. Also smaller renal stones may prove more difficult to locate than with ultrasound. Further drawbacks are the absence of real-time imaging and the exposure to radiation. With ultrasound it is generally impossible to locate stones in most parts of the ureter. On the other hand ultrasound allows direct visualization of radiolucent stones and offers easier targeting of smaller renal stones. A major advantage, however, is the real-time imaging which provides better monitoring of the fragmentation process in the absence of exposure to radiation.

Inline scanners are positioned along the shock-wave propagation path and offer easier targeting of very proximal and very distal ureteral stones and easier dissociation between multiple stones. Image quality usually is poorer than with a lateral outline or free-hand scanner, however, and rib shadows may hide stones from view.

Outline scanners (free-hand or mounted on a lateral isocentric arms) offer far better image quality and allow the selection of the most appropriate window to avoid rib shadows. Usually the appraisal of fragmentation is superior to an inline scanner. Proximal ureteral stones may be more difficult to find and targeting and positioning of prevesical stones is more cumbersome.

To enhance targeting precision several manufacturers offer autopositioning and/or tracking systems: Dornier, EDAP TMS, Jena Med Tech, Storz, and Wolf. Machines where both ultrasound and X-ray are integrated offer the most versatile imaging and targeting possibilities. Ideally these machines offer simultaneous online use of both ultrasound and X-ray. Targeting versatility is further improved by the possibility to couple the therapy head to the patient both under and above the treatment table.

Improved imaging and improved targeting will have a positive effect on the EQ.

## Lithotripter design

### Dedicated or multifunctional machine?

In the years following its introduction ESWL was the privilege of high-volume stone centers. This was mainly due to the high capital, running, and maintenance costs of the first lithotripters. Only “dedicated” to extracorporeal lithotripsy these machines could only be operated in large centers with a high volume of stone patients. The construction of less expensive second- and third-generation lithotripters with lower capital cost and lower running and maintenance costs made extracorporeal lithotripsy available in more and more centers, leading to a reduction of the number of patients treated per stone center.

Stone therapy guidelines from international expert boards consider SWL in most types of stones as the first choice of treatment. However, in some indications endourologic procedures give equivalent or better results than SWL. Modern lithotripters are supposed to support urologists in any of these modalities. Consequently, in the past two decades lithotripters have undergone a transition from pure shock-wave-generating devices to multifunctional urologic workstations.

One of the key components of such urologic workstations is the patient table. An increasing number of obese patients demands high-load-capacity tables with maximum accessibility in order to be able to approach the patient from all sides. For fluoroscopic imaging both in SWL and endourologic procedures the tabletop needs to be radiotransparent. Modern tabletops are therefore made of carbon fiber.

Imaging modalities in a multifunctional workstation need to support the wide range of therapeutic options in urology. Large image intensifiers up to 40 cm ideally offer a large field of view of nearly the entire urinary tract. Full digitization of the X-ray imaging chain provides excellent image quality at low radiation doses. In the newer devices flat-panel detectors (FPDs) replace the traditional image intensifiers. Increasing awareness of radiation safety and dose reduction make ultrasound stone localization an ideal tool for stone targeting and accurate therapy monitoring. Last but not least, a high-performance shock-wave source, which ideally can be coupled to the patient in an over- and undertable position, completes the design of a multifunctional lithotripter.

## Integrated or modular?

Multifunctional machines can have a modular design, where all components are independent and connected according to need, or an integrated design, where all components are integrated in the machine and ideally adapted to their function. A third design, the "hybrid," offers integration of imaging and/or therapy head in a common console with an independent treatment table.

### Modular design

In a lithotripter with a modular design (Figure 59.1) the different components, shock-wave source, imaging components, and treatment table are separate modules to be connected to perform ESWL or endourological procedures. As the imaging components, both a fluoroscopic C-arm and an ultrasound machine are usually available on site; investment cost is thus lower and limited to the shock-wave module. The imaging components can also be used for other purposes both in urology and other departments. Modular systems have no need for a dedicated lithotripsy room and are easily transported from one center to another.

Due to the *ad hoc* combination of different modules the footprint is larger and the floor is cluttered with an array of machinery. In endourologic procedures this footprint is still enlarged by the addition of an electrosurgical unit, light sources, and monitors, etc. The uro-table is less urologist-friendly with limited accessibility. Overall handling is more complicated and less user-friendly.

### Integrated design

In an integrated design the different components are fully integrated in one stand alone system (Figures 59.2–59.4). These systems have a small footprint compared to the modular and hybrid designs. They are usually high-end devices ideal for centers with a sufficient volume of patients for SWL and endourology. Due to the optimal integration and synchronization of their high-end components to a synergistic system these machines offer maximal versatility in targeting and positioning for SWL. Uro-table function usually is excellent and offers great comfort in the performance of endourologic procedures. Ideally the patient table is entirely radiotransparent, accessible over 360°, and capable of bearing obese patients. The high investment cost and the fixed installation in a dedicated endourology/ESWL room may prohibit its acquisition in centers with limited patient loads.

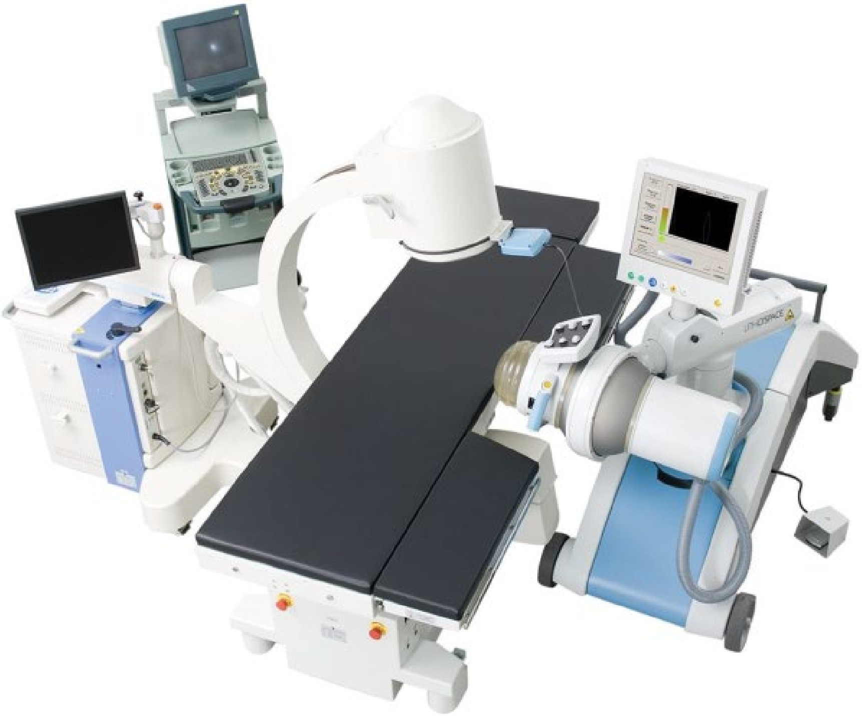

**Figure 59.1** Modular design: Jena Med Tech Lithospace. Reproduced with permission of Jena Med Tech GmbH.

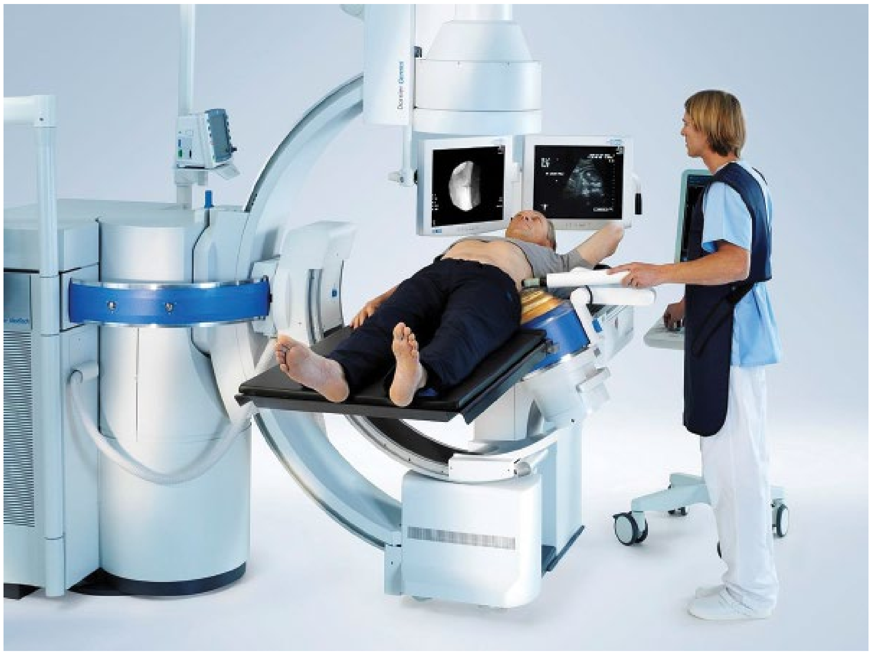

**Figure 59.2** Integrated design: Dornier Gemini. Reproduced with permission of Dornier MedTech GmbH.

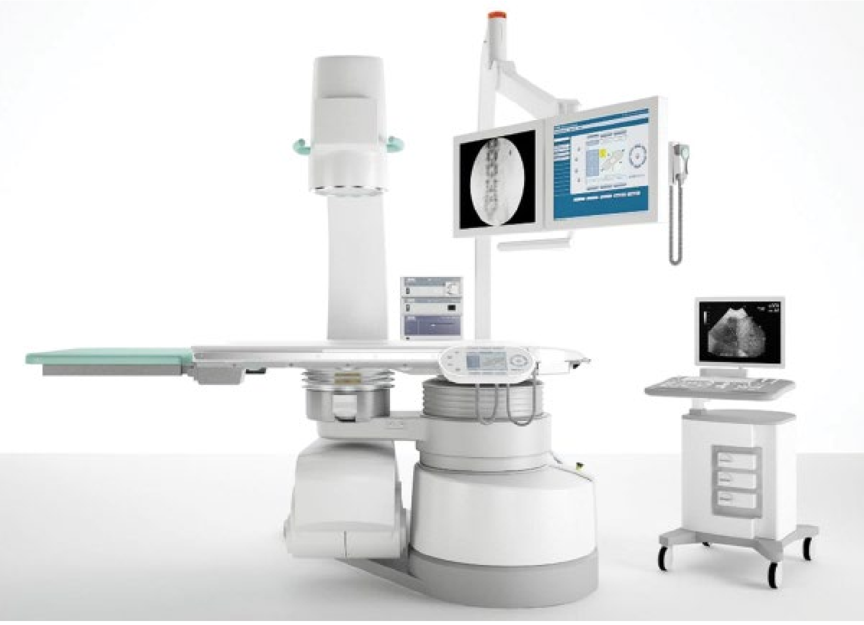

**Figure 59.3** Integrated design: Storz Modulith SLX-F2. Reproduced with permission of Storz Medical AG.

**Hybrid design**

In these machines imaging (fluoroscopy and/or ultrasound) and shock-wave source are mounted on a combined console (Figure 59.5). The patient treatment table is a stand-alone component to be added to the system for SWL or endourological procedures. Both investment cost and footprint are medium, i.e. between that of a machine with integrated design and a device with modular design. These systems are easily transportable and do not need a dedicated room. Some of the components (imaging, patient table) are suited for multifunctional and multidisciplinary usage. Uro-table function usually is adequate and overall handling is in between the modular and the integrated design.

## Performance of lithotripters

To measure the performance of a lithotripter, formulae have been devised that take into account stone-free rate, retreatment rate, and auxiliary procedure rate. The

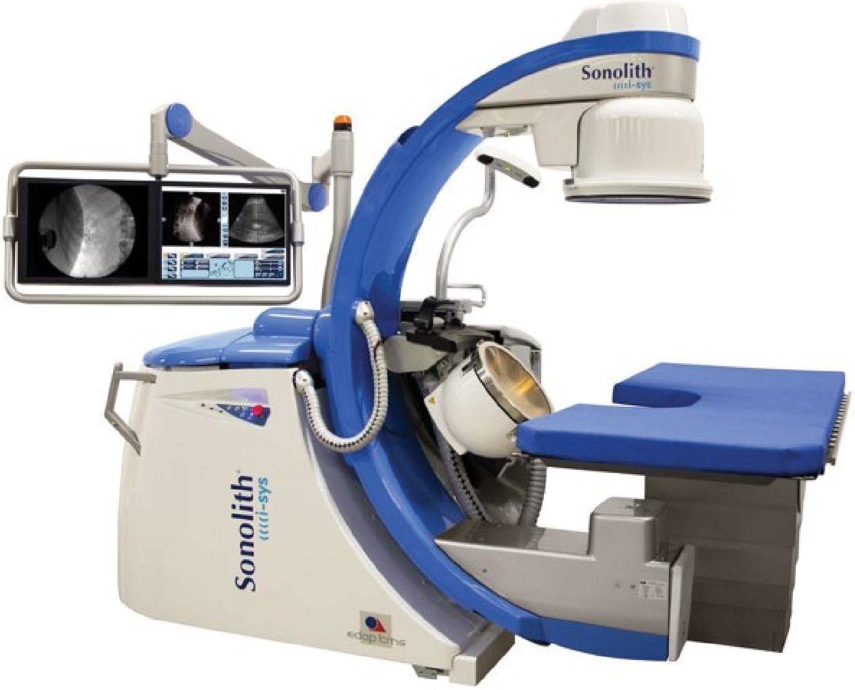

**Figure 59.4** Integrated design: EDAP TMS Sonolith i-Sys. Reproduced with permission of EDAP-TMS France.

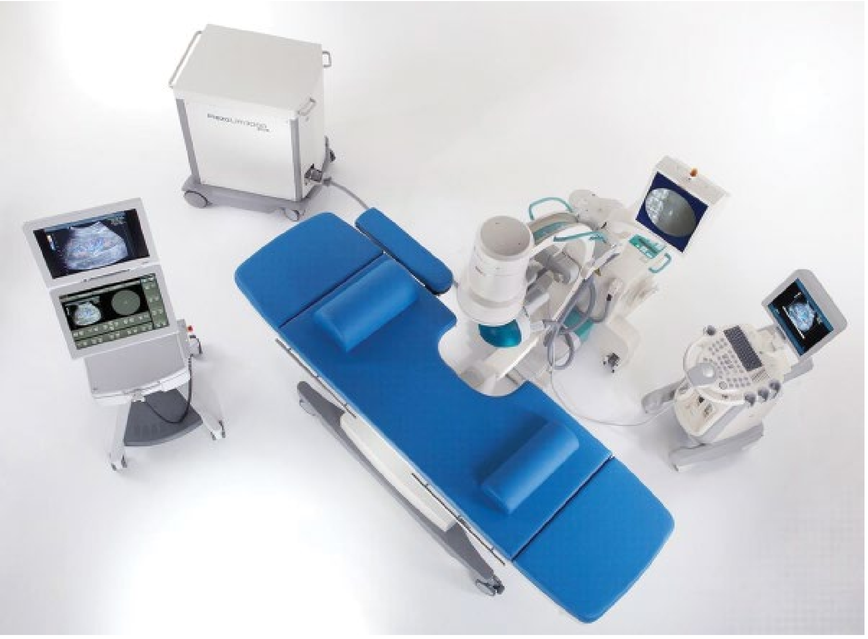

**Figure 59.5** Hybrid design: Wolf Piezolith 3000 plus. Reproduced with permission of Richard Wolf GmbH.

original effectiveness quotient ($EQ_A$) was defined by Denstedt, Clayman and Preminger [7, 41]:

$$EQ_A = \frac{\%\,\text{Stone} - \text{free patients}}{100\% + \%\,\text{retreatment} + \%\,\text{auxiliary procedures post–ESWL}} \times 100$$

The “extended EQ” or $EQ_B$ [10] and the “modified EG” or $EQ_{mod}$ [10] were defined in order to fine tune the performance estimations.

$$EQ_B = \frac{\%\,\text{Stone–free patients}}{100\% + \%\,\text{retreatment} + \%\,\text{auxiliary procedures pre–and post–ESWL}} \times 100$$

Modified EQ :

$$EQ_{mod} = \frac{\%\,\text{Stone–free patients} - \%\,\text{curative auxiliary procedures}}{100\% + \%\,\text{re–ESWL} + \%\,\text{pre–ESWL auxiliary procedures} \ + \%\,\text{post–ESWL auxiliary procedures}} \times 100$$

Although these formulae represent a mathematic tool to quantify and compare the performance of lithotripters, they only quantify stone-free rate, auxiliary procedure rate, and retreatment rate. A number of other factors are not readily quantifiable, but do play an important role in the final outcome of stone management by SWL: shock-wave source, stone burden, stone impaction, imaging modality and quality, targeting, analgesia regimen, shock-wave coupling, shock-wave release frequency, treatment strategy, and last but not least experience of the operator.

Treatment strategies and experience and skill of the operator have long been underestimated in the performance of SWL. Operator skill and experience unquestionably are key factors in success in SWL, however. Although newer electromagnetic machines perform at least equally good or even better than the HM3 the unmodified Dornier HM3 is still considered the gold standard in SWL. Results with newer lithotripters are, often erroneously, claimed to be poorer than with the original HM3 and many urologists therefore tend to shift to endourologic techniques in several indications.

Factors in the poorer results with modern lithotripters without a doubt are:

- Complexity of shock-wave administration is generally underestimated, especially by new users: lack of background and training in SWL is often the cause of poorer results with modern machines.
- HM3 users were extensively trained prior to certification.
- Newer machines are too often misjudged as “plug-and-play” with little attention paid to proper training of new users.

In order to improve results and reduce complication rate all (new) users of shock-wave machines should be certified on the basis of:

- a theoretical understanding of the basic physics of shock waves
- an extensive training in imaging, positioning and targeting, coupling, and treatment strategies
- a comprehensive understanding of shock-wave complications and the ways to avoid complications and improve results.

Although lithotripter manufacturers are directing extensive research towards improvements in focal geometry and energy to improve stone disintegration and at the same time reduce collateral damage to the surrounding tissue, together with urology training centers they should also invest in proper training of lithotripter users.

These coordinated efforts could and should lead to a renaissance of SWL as a valuable treatment of choice for urolithiasis at all levels of the urinary tract.

## The ideal lithotripter

An “ideal” lithotripter would have to have a high-performance shock-wave source producing a spherical focus exactly matching the size of the targeted stone and with the following energy requirements:

- moderate positive peak pressure, $p+$
- sufficient disintegration power (effective energy, $E_{12mm}$) to disintegrate hard stones and to compensate for shock-wave attenuation (obesity)
- minimal cavitation effects and hence minimal risk of adverse tissue effects.

Apart from producing a shock wave with the ideal focus, this high-performance shock-wave source would also have to meet the following requirements: prolonged lifetime without degradation or significant fluctuations of acoustic energy, wide range of energy settings, and adequate treatment depth (minimum 150 mm) to accommodate the ever-increasing proportion of obese patients, easily incorporated in a multifunctional device.

These requirements would almost automatically exclude conventional electrohydraulic sources: the lifetime of the electrodes is limited and the degradation of the electrode tips leads to output variations and instabilities of focal point and energy.

Coupling of the therapy head containing the shock-wave source is an important issue. The water cushion needs to be made of a material that easily adapts to the body curves and that causes minimal absorption, reflection, or refraction of the travelling shock wave.

Ideally the therapy head should incorporate a video camara for optical coupling control

(Figure 59.6). Optical coupling control results in a reduction of the total energy needed to fragment a stone. At the same time this theoretically could result in less shock-wave-induced adverse tissue effects.

Apart from that, the possibility to couple the treatment head to the patient both in an above- and an undertable position (Figure 59.7) is a very important asset, specifically in the *in situ* treatment of ureteral stones and especially in obese patients.

Accurate targeting is key to success in SWL and depends on excellent image quality, both fluoroscopic and ultrasonic. In endourologic procedures image quality is equally important.

A large image intensifier (up to 40 cm) offers a large view of nearly the entire urinary tract without the need to move the patient table. Orbital isocentric movements of the X-ray C-arm may prove useful in targeting in SWL. Full digitization of the X-ray imaging chain guarantees excellent image quality at low radiation dose. Digitization also allows easy and efficient storage of the images in the patient's records (DICOM capability). In newer lithotripters FPDs replace the traditional image intensifiers.

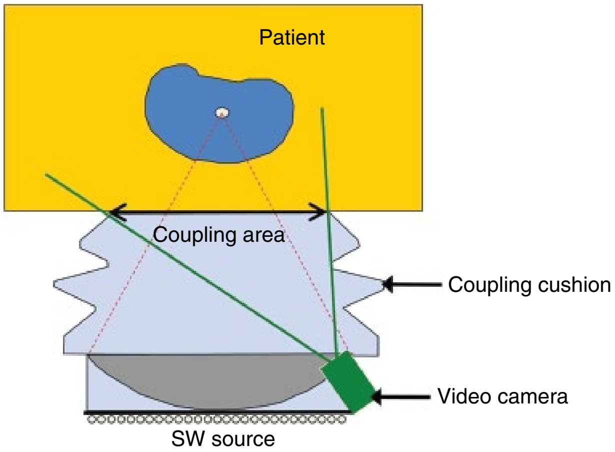

**Figure 59.6** Optical coupling control. SW, shock wave. Reproduced with permission of Dornier MedTech GmbH.

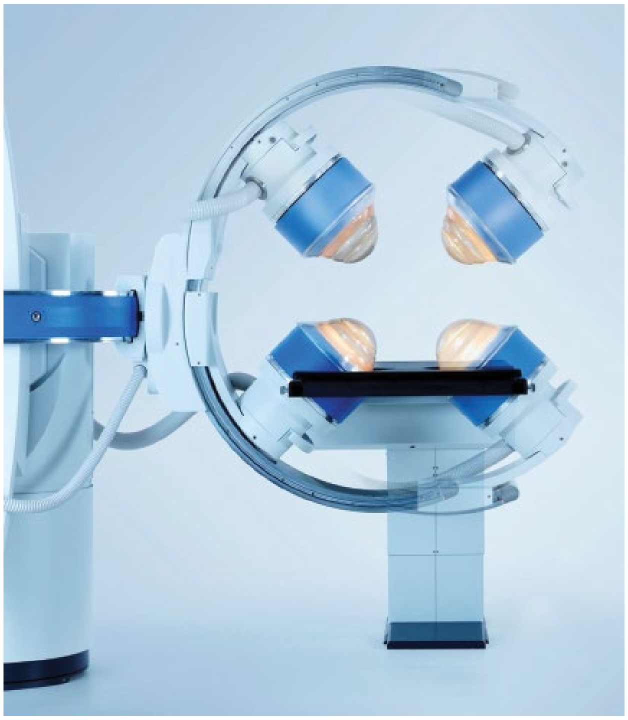

**Figure 59.7** Bilateral over- and undertable position of the therapy head (Dornier Gemini). Reproduced with permission of Dornier MedTech GmbH.

Increasing awareness of radiation safety and dose reduction and the excellent image quality of modern ultrasound machines make ultrasound an ideal tool for stone targeting and real-time monitoring of the entire treatment. An ideal lithotripter thus should be equipped with excellent imaging, both fluoroscopic and ultrasonic, preferably to be used online and simultaneously.

Another key component of a modern multifunctional lithotripter is the patient table. An ever-increasing number of obese and even morbidly obese patients demand a table with a high load capacity. To allow good imaging the tabletop needs to be radio-transparent. Finally, in endourologic procedures such as percutaneous nephrolithotomy and nephrostomy tube placement, maximum accessibility (ideally 360°) of the table from all sides is extremely important.

Good imaging and a careful urologist may provide accurate targeting, but respiratory movements continuously swing the targeted stone in and out of focus. A hit-and-miss system, that would keep track of the stone during respiratory movements and would only release a shock wave when the stone is exactly in the focus, would improve outcomes and at

the same time reduce collateral damage to the surrounding tissue. It would of course also slow down treatment. According to newer insights, however,

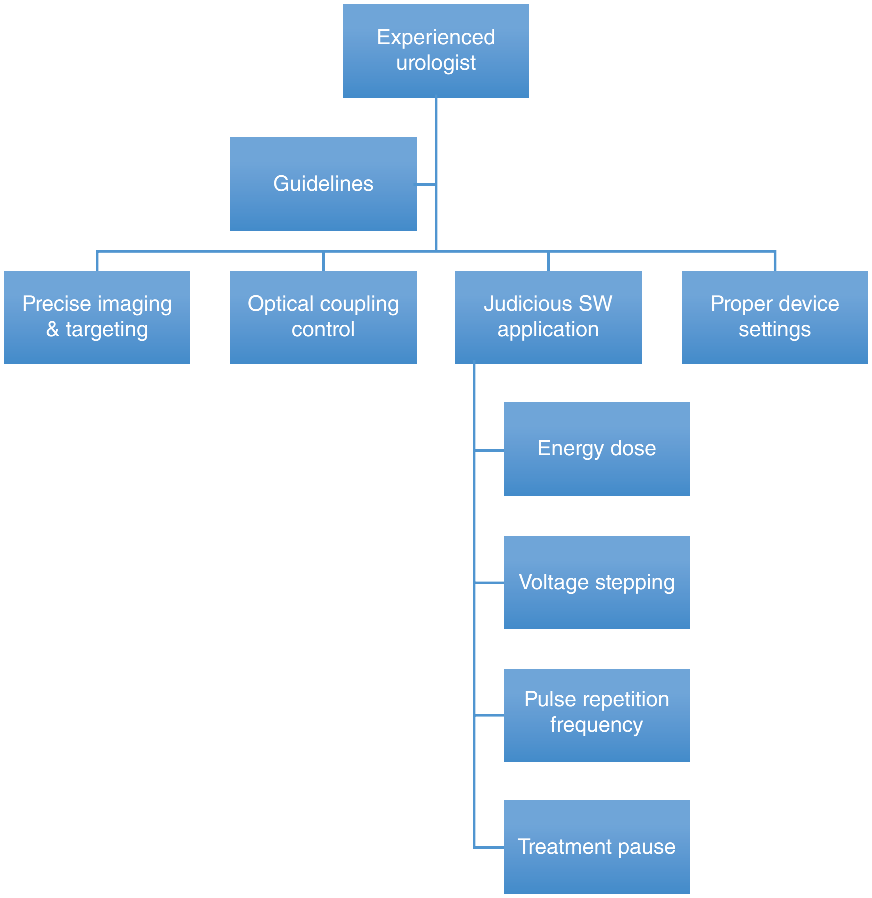

**Figure 59.8** Elements of "good lithotripsy." SW, shock wave.

slowing down treatments not only improves treatment efficiency [42, 43], but also reduces overall treatment cost [44].

Finally, this sophisticated piece of equipment should only be operated by an interested and experienced urologist, who has a basic understanding of the physics of shock waves [11, 31] and who is closely involved in all treatment modalities (SWL, percutaneous nephrolithotomy, ureterorenoscopy, robot-assisted retrograde intrarenal surgery) of modern stone management.

A department of urology looking for the ideal lithotripter should also invest in good clinical practice and "good lithotripsy" (Figure 59.8). The actual choice of the ideal lithotripter for any given stone center will depend on the specific requirements of a specific setting. A multifunctional workstation for SWL and endourologic procedures is the best choice for centers with an adequate patient load in both treatment modalities. An integrated or hybrid design makes economic sense in very active stone centers. In centers with a modest patient load a modular system may probably be the better choice. Our own stone center functions 5 days a week with a patient load of approximately 3000 treatments per year (500 ESWL and 2500 endourologic procedures). We try to solve any acute stone problem within 24 hours of admission, preferably on an outpatient basis. The centerpiece of this "integrated endourology concept" is a high-end multifunctional lithotripter with integrated design.

## Summary

The number of manufacturers and machines currently on the market prohibits an attempt to provide a complete overview of all systems available at present. Also, companies and machines come and go. Therefore this overview (see Tables 59.1–59.5) was limited to those traditional companies that were and still are very much involved in the development of and continued research in SWL. An exception to this rule was made for lithotripters designed with a philosophy derived from the theories of Eisenmeyer [29, 30]: wide focus, low focal pressure (Tables 59.6 and 59.7). Through their product managers most of these companies were very forthcoming in providing information, technical details, and illustrations for this chapter.

See accompanying Video 59.1.

**Table 59.1** Overview of Dornier Gemini, Compact Delta II, and Compact Sigma.

| | Dornier Gemini | Dornier Compact Delta II | Dornier Compact Sigma |
|---|---|---|---|
| Shock-wave generation | | | |
| Source | Electromagnetic (EMSE) flat coil with acoustic lens | Electromagnetic (EMSE) flat coil with acoustic lens | Electromagnetic (EMSE) flat coil with acoustic lens |
| Aperture (mm) | 220 | 140 | 140 |
| Aperture (degrees) | 66 | 50 | 50 |
| Max. treatment depth (mm) | 170 | 150 | 150 |
| Focus (max values) | | | |
| Focus size (−6 dB) (mm) | 5.9 × 89 | 8 × 105 | 8 × 105 |
| Peak pressure (MPa) | 77 | 51 | 51 |
| Energy density ($mJ/mm^2$) | 1.6 | 0.88 | 0.88 |
| Coupling | Water cushion/OptiCouple | Water cushion/OptiCouple | Water cushion |
| Imaging | | | |
| Fluoroscopy | Integrated<br>C-C and orbital movements | Integrated C-arm | Add-on C-arm |
| Ultrasound | Integrated<br>Lateral isocentric | Integrated<br>Lateral isocentric | Integrated<br>Lateral isocentric |
| Overall design | Integrated | Hybrid | Modular |
| Multifunctional use | +++ | With Relax + table | With Relax + table |
| Special features | Patient table:<br>• Load capacity = 250 kg<br>• 360° accessibility<br>• Radio-transparent carbon fibre top<br>Dual imaging: simultaneous online use of X-ray and ultrasound<br>OptiCouple: Optical coupling Control<br>Satellite arms for flat screens, light source, camera controller<br>Bilateral shock-wave coupling over- and undertable<br>UIMS: Urology Information Management System<br>40 cm image intensifier or FPD/Dicom capability<br>Autopositioning in X-ray mode | Tri-mode imaging capability (with FarSight)<br>FarSight Imaging capability with purpose designed transducer<br>Simultaneous on-line use of X-ray and ultrasound<br>Optional patient data management: UIMS<br>Optional Dicom capability<br>Over- and under- table treatment<br>Multidisciplinary use of Relax + table | |

**Table 59.2** Overview of Siemens Modularis Variostar.

| | **Siemens Modularis Variostar** |
|---|---|
| Shock-wave generation | |
| Source | Electromagnetic (EMSE) flat coil with acoustic lens |
| Aperture (mm) | 125 |
| Aperture (degrees) | 48 |
| Max. treatment depth (mm) | 140 |
| Focus | |
| Focus size (−6 dB) (mm) | 12.5 × 145 |
| Peak pressure (MPa) | 59 |
| Energy density (mJ/mm$^2$) | 0.13–1.14 |
| Coupling | Water cushion |
| Imaging | Add-on |
| Fluoroscopy | Add-on |
| Ultrasound | |
| Overall design | Modular |
| Multifunctional use | Yes |
| Special features | No |
| Autopositioning | |

**Table 59.3** Overview of Storz lithotripters.

| | **Storz Modulith SLX-F2 >>connect<<** | **STORZ Modulith SLK >>inline<<** |
|---|---|---|
| Shock-wave generation | | |
| Source | Electromagnetic<br>Cylinder source with parabolic reflector | Electromagnetic<br>Cylinder source with parabolic reflector |
| Aperture (mm) | 300 | 178 |
| Aperture (degrees) | 80 | 61 |
| Max. treatment depth (mm) | 180 | 150 |
| Focus | | |
| Focus size (−6 dB) (mm) | Precise: 6 × 28<br>Extended: 9 × 50 (optional) | 6.3 × 62<br>6.4–95 |
| Peak pressure (MPa) | Precise: 5–150<br>Extended: 5–90 | |
| Energy density (mJ/mm$^2$) | Precise: 0.42–3.65<br>Extended: 0.42–2.4 | 0.04–1.8 |
| Coupling | Water cushion | Water cushion |
| Imaging | | |
| Fluoroscopy | Integrated | Modular (different C-arcs can be used) |
| Radiography (digital) | Integrated | |
| Ultrasound | Inline (optional) | Inline (optional) |
| Overall design | Integrated<br>Modular: MODULITH SLX-F2 with add-on C-arm (optional) | Modular with integrated patient table |
| Multifunctional use | Yes | Yes |
| Special features | 43 cm dynamic flat panel X-ray detector<br>X-ray collimator with light beam localizer<br>Dynamic videorouting of connected video sources<br>Local and remote control operation<br>StorM-Touch: centralized control platform for lithotripsy and KARL STORZ endoscopic equipment<br>Automatic stone postioning (optional)<br>StorM-Base: comprehensive patient database<br>Network Integration via DICOM functionality (optional) | Local and remote control operation<br>Therapy source with inline imaging in over- and undertable positions<br>StorM-Base: comprehensive patient database |

**Table 59.4** Overview of EDAP TMS lithotripters.

| | Technomed Sonolith i-Sys | Technomed Sonolith i-Move |
|---|---|---|
| Shock-wave generation | | |
| Source | Electroconductive (ECL) | Electroconductive (ECL) |
| Aperture (mm) | 291 | 251 |
| Aperture (degrees) | 80 | 77 |
| Max. treatment depth (mm) | 210 | 180 |
| Focus | | |
| Focus size (−6 dB) (mm) | 3.2 × 2.6 × 22.4 | 3.5 × 2.6 × 35 |
| Peak pressure (MPa) | 129 | 144 |
| Energy density (mJ/mm$^2$) | 1.27 | 1.36 |
| Coupling | Water cushion | Water cushion |
| Imaging | | |
| Fluoroscopy | Integrated | Add-on C-arm |
| Ultrasound | Freeline | Freeline |
| Overall design | Integrated | Modular |
| Multifunctional use | Yes | Yes |
| Special features | | |
| Automatic pressure regulator | Yes | Yes |
| Autopositioning: “Stone Locking System” | Yes | No |
| “Visio-Track” | Yes | Yes |
| Fully robotized and motorized isocentric movements of X-ray, C-arm, ultrasound and shock-wave generator | Yes | No |
| Dual X-ray and ultrasound display | Yes | Yes |
| Touchscreen interface | Yes | Yes |
| Simultaneous imaging (X-ray/ultrasound) and shock-wave release | Yes | Yes |

**Table 59.5** Overview of Wolf Piezolith 3000 lithotripters.

| | Wolf Piezolith 3000 | Wolf Piezolith 3000plus |
|---|---|---|
| Shock-wave generation | | |
| Source | Piezoelectric | Piezoelectric |
| Aperture (mm) | 270 | 270 |
| Aperture (degrees) | 74 | 74 |
| Max. treatment depth (mm) | 165 | 165 |
| Focus | Triple focus | Triple focus |
| Focus size (−6 dB) (mm) | 3 × 16, 5 × 24, 8 × 28 | 3 × 16, 5 × 24, 8 × 28 |
| Peak pressure (MPa) | 6–126 | 6–126 |
| Energy density (mJ/mm$^2$) | 0.03–1.67 | 0.03–1.67 |
| Coupling | Water cushion | Water cushion |
| Imaging | | |
| Fluoroscopy | Add-on C-arm | Add-on C-arm |
| Ultrasound | Inline | Inline |
| Overall design | Modular | Modular |
| Multifunctional use | Yes | Yes |
| Special features | | |
| Autopositioning | No | Yes |
| Source | Long-lasting therapy source | Long-lasting therapy source |
| Triple focus | >5 000 000 shocks | >5 000 000 shocks |
| | Triple focus: three adjustable focus sizes | Triple focus: three adjustable focus sizes |

**Table 59.6** Overview of Jena Med Tech Lithospace lithotripter.

| | **Jena MedTech Lithospace** | | |
|---|---|---|---|
| Shock-wave generation | | | |
| Source | Electrohydraulic | | |
| Aperture (mm) | 178 | | |
| Aperture (degrees) | 45.6 (210 mm) | 58.3 (160 mm) | 96.1 (80 mm) |
| Max. treatment depth (mm) | 180 (16 kV) | 205 (22 kV) | 220 (26 kV) |
| Focus | 16 kV | 22 kV | 26 kV |
| Focus size (−6 dB) (mm) | 10 × 64 | 12 × 125 | 20 × 160 |
| Peak pressure (MPa) | 3.6–26.1 | 4.1–35.2 | 5.0–37.9 |
| Energy density (mJ/mm$^2$) | 0.14 | 0.27 | 0.40 |
| Coupling | Water cushion | | |
| Imaging | Add-on C-arm | | |
| Fluoroscopy | Add-on ultrasound machine | | |
| Ultrasound | | | |
| Overall design | Modular | | |
| Multifunctional use | Add-on urotable | | |
| Special features | Flexibility and maneuvrability of shock-wave head: under- and overtable<br>Autonomous contact-free targeting system for all X-ray and ultrasound localization devices<br>Stone localization and treatment volume superimposed in real time on the display<br>Multi-use electrode: RevoTrode for 15 000 shock waves | | |

**Table 59.7** Overview of LithoGold LG-380 lithotripter (MTS Medical UG).

| | **LithoGold LG-380** |
|---|---|
| Shock-wave generation | |
| Source | Electrohydraulic |
| Aperture | N/A |
| Max. treatment depth (mm) | 165 |
| Focus | 20 × 101 |
| Focus size (−6 dB) (mm) | 24.6 – 36.9 |
| Peak pressure (MPa) | 0.1 – 0.37 |
| Energy density (mJ/mm$^2$) | |
| Coupling | Water cushion |
| Imaging | |
| Fluoroscopy | Add-on C-arm |
| Ultrasound | Lateral isocentric |
| Overall design | Modular |
| Multifunctional use | Add-on urotable |

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# 60

# Shock-wave Lithotripsy of Renal Calculi

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## Introduction

Once Chaussy and colleagues introduced extracorporeal shock-wave lithotripsy (SWL) in 1980, SWL spread to other institutions by 1984 and subsequent series confirmed success rates upwards of 90% using the Dornier HM3 lithotripter [1, 2]. Over the ensuing two decades, SWL became the most common procedure for urinary stone disease; by 2005, SWL accounted for 52% of all stone treatments in the United States [3]. Modern lithotripters have eliminated the water bath as a coupling agent, improving accessibility and patient comfort. SWL success rates now range from 48 to 65% but with greater need for auxiliary procedures than before [4, 5]. In this chapter, we present factors and techniques that allow safe and effective treatment of renal stones using SWL.

## Preoperative evaluation

A thorough history and physical examination is crucial for proper patient selection. Urine analysis is necessary for all patients and, if the concern arises for urinary tract infection, urine culture must be obtained [6, 7]. Optional laboratory studies include pregnancy testing when appropriate and coagulation studies for patients with history of coagulopathy. Regarding preoperative imaging, historically, renal ultrasound and plain abdominal radiography (i.e. kidney–ureter–bladder, KUB) were used to confirm stone presence, and intravenous pyelogram (IVP) was used to predict SWL success. However, with computerized tomography (CT) now universally available, noncontrast CT is the preferred imaging of choice [6–8]. Though not absolutely necessary, CT has the advantage of allowing the urologist to assess for factors predictive of SWL success, which will be discussed later in this chapter.

## Absolute contraindications

Box 60.1 lists types of patients in whom SWL is contraindicated. These conditions are described below.

### Pregnancy

SWL is prohibited in pregnant women [8]. Though a small series reported on six females treated safely early during pregnancy [9], animal experiments in mice have shown deleterious effects of shock waves on the mouse fetus, affecting viability [10].

### Anticoagulants or uncorrected bleeding diathesis

Patients in whom anticoagulant/antiplatelet agents cannot be held or reversed, and in whom coagulopathy cannot be controlled, should not be treated with SWL. Expert opinion concludes that bleeding diathesis should be controlled for 24 hours before and 48 hours postprocedure [8]. Renal hematomas are reported to occur in 1% of patients *without* coagulopathy after SWL [11]. The literature on SWL in individuals with iatrogenic and/or pathological bleeding diathesis is sparse, retrospective, and nonstandardized, however [12]. Continuation of aspirin during SWL has been reported but with mixed results [12]. A fourfold increase in the risk of postoperative hematoma was reported in one study when antiplatelet agents (aspirin/nonsteroidal anti-inflammatory drugs) were continued during SWL: these patients were managed conservatively [11]. SWL in patients taking clopidogrel has been associated with cases of nephrectomy and death [13, 14]. Other reports looking at all causes of bleeding diathesis including pathologic conditions

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

**Box 60.1 Absolute contraindications to SWL.**

Pregnancy
Uncontrolled bleeding diathesis
Uncontrolled hypertension
Untreated infection
Significant skeletal malformations or severe obesity
Arterial aneurysms in close proximity to target stone

such as hemophilia, von Willibrand disease, etc., suggested hematology consultation and consideration of SWL only if the coagulopathy can be corrected [15].

### Uncontrolled hypertension

Uncontrolled hypertension has been associated with an increased risk of renal hematoma after SWL and should be controlled prior to treatment [8]. The incidence is as high as 4.3% in this group [16]. Intraoperative hypertension (defined as blood pressure >140/90 mmHg) is also a significant risk factor for hematoma formation with a threefold increase in risk [11].

### Arterial aneurysms in close proximity to the targeted stone

Aortic or renal artery aneurysms near the renal stone are listed as contraindications to SWL [8]. Aortic aneurysm rupture is described after SWL in five case reports [17]. Calcified plaque within the aneurysm may be fragmented by shock waves leading to rupture. These case reports are in contrast to *in vitro* studies showing SWL does not significantly damage human calcified aneurysm tissue [18]. Some authors concede that SWL can be performed in the setting of arterial aneurysms provided that the patient is monitored [17].

### Severe skeletal malformations or obesity

Certain skeletal malformations may prevent positioning of the patient on the lithotripter table [8]. Severe obesity may pose a similar issue and can also make visualization of the stone difficult under fluoroscopy or ultrasound.

### Anatomical or functional obstruction of the urinary tract

Any patient with anatomic or functional ureteropelvic junction or ureteral obstruction distal to the stone should not undergo SWL [6–8]. These abnormalities may delay or impede clearance of residual fragments and lead to significantly lower stone-free rates [19].

### Untreated cystitis, pyelonephritis, or bacteriuria

Patients with untreated cystitis, pyelonephritis, or bacteriuria are at risk of worsening infection and/or urosepsis during SWL. These patients should undergo proper antibiotic treatment first [6, 7].

## Stone characteristics

Early experience demonstrated that stone composition influences SWL success. Dretler first described "stone fragility": stones of various compositions have differing susceptibility to shock waves [20]. Subsequently, Dretler described stone breakability or "stone durility" [21]. Cystine, brushite, and calcium oxalate monohydrate stones are the least fragile (i.e. most durile) while uric acid stones are the most fragile [22]. This can be seen *in vitro* (Figure 60.1); however, the standard deviation of shocks required for each stone type is large, indicating variability in fragility within stones of the same composition [23]. Because of this variability, stone composition is less important in predicting SWL success than other factors such as Hounsfield density, which will be discussed later in this chapter. Secondary mineral composition, spatial arrangement of various mineral components, and variations in layer structures of different mineral components also affect stone fragility [23].

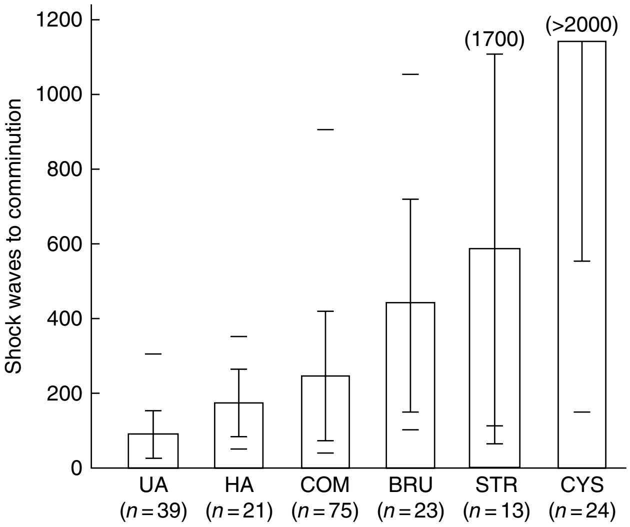


**Figure 60.1** Shock waves to comminution for various types of human kidney stones *in vitro*. Bars show mean value, error bars show standard deviation, and short horizontal lines show range of values. UA, uric acid; HA, hydroxyapatite; COM, calcium oxalate monohydrate; BRU, brushite; STR, struvite; CYS, cystine; *n*, number of stones of each type. *Source:* [23]. Reproduced with permission of Elsevier.

## Imaging characteristics

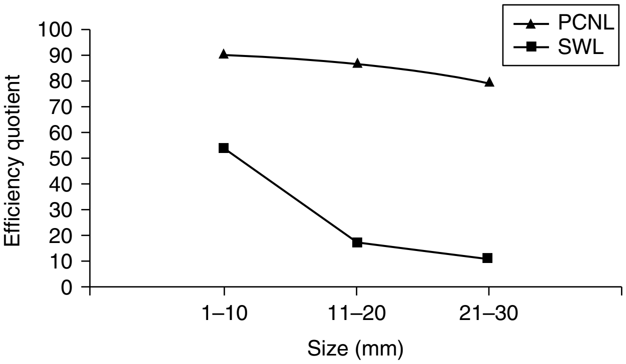
Multiple factors obtained from preoperative imaging are useful for patient selection. While stone size and location can be gathered from plain abdominal radiography or renal ultrasound, Hounsfield density, pelvicalyceal anatomy, and skin-to-stone distance are only available with CT imaging.

### Stone size and location

Stone size and location are the most influential factors in determining the management of renal stones. SWL stone-free rates at 3 months are quoted to be 86–89% for renal pelvis, 71–83% for upper calyx, 73–84% for middle calyx, and 37–68% lower calyx stones across several generations of lithotripters [24]. A critical review of SWL outcomes for lower pole stones first published in 1994 reported stone-free rates of 60% after one treatment. When broken down by stone size, stone-free rates for stones <1, 1–2, and >2 cm were 74, 56, and 33%, respectively [25]. The general consensus is that individuals with stones >2 cm in the upper and middle calyces and >1 cm in the lower calyx should not be offered SWL as first-line therapy [6, 7]. Subsequent studies of newer generation lithotripters have demonstrated lower success rates than initial studies; 3 month stone-free rates for the second-generation Dornier MFL5000 for lower pole stones were 56% [26], and overall stone-free rates for the third-generation Siemens Lithostar Plus were decreased by 40% when compared to the earlier Dornier HM3 [4]. Finally, the fourth-generation Storz Modulith (SLX-F2) lithotripter was found to have equivalent stone-free rates for solitary renal stones compared to the HM3 but required significantly more shocks to achieve this [27].

Incomplete fragmentation can lead to steinstrasse, which is a column of stone fragments that lodge within the ureter causing obstruction after SWL [28, 29]. The word *steinstrasse* is German for “stone street” which refers to the radiographic appearance of this condition. Steinstrasse occurs when the lithotripter fragments the stone into pieces that are not easily passed spontaneously [28]. Size and location are two independent risk factors for this to occur [28, 29]. SWL performed on renal stones is 2.7 times more likely to cause steinstrasse than ureteral stones [28]. Incidence rates for steinstrasse after SWL for renal stones <1, 1–2, and >2 cm were 4.4, 15.7, and 24.3%, respectively. This study also found renal pelvis stones to be a significant predictor of steinstrasse compared with calyceal stones [29].

To date, five randomized controlled trials (RCTs) have evaluated SWL versus other endourological procedures [24]. The two highest quality, RCTs evaluated lower pole stones [30, 31]. The first multicenter study evaluated the efficacy of SWL versus percutaneous nephrolithotomy (PCNL). Of note, multiple generations of lithotripters were used across the institutions. Stone-free rates were significantly higher with PCNL for every stone size (<1, 1–2, and >2 cm), and for stones >1 cm only 21% of patients became stone-free with SWL. Retreatment and auxiliary procedure rates were significantly lower for PCNL. SWL had an acceptable 50% efficiency quotient for stones <1 cm versus an efficiency quotient of less than 20% for stones >1 cm (Figure 60.2). The authors concluded that as stone size increases beyond 1 cm, the likelihood of becoming stone-free with SWL decreases significantly and that SWL is suitable only for lower pole stones <1 cm [30]. A follow-up multicenter trial randomized 67 patients with lower pole stones <1 cm to either ureteroscopy or SWL. There was no significant difference in 3 month stone-free rates or the need for secondary procedures between the groups, supporting SWL as an acceptable first-line therapy for lower pole stones <1 cm in size [31].



$$\text{EQ} = \frac{\%\ \text{Stone free}}{100 + \%\ \text{retreatment} + \%\ \text{auxiliary procedures}} \times 100$$

**Figure 60.2** Efficiency quotients for SWL and PCNL for lower pole calculi stratified by stone size. *Source:* [30]. Reproduced with permission of Elsevier.

### Lower pole pelvicalyceal anatomy

Sampaio and Aragao described an angle between the lower pole infundibulum and renal pelvis <90°, diameter of the lower pole infundibulum <4 mm, and multiple lower pole calyces as risk factors for poor stone clearance after SWL [32]. Subsequent studies have described less acute infundibulopelvic angle, shorter infundibular length, and increased infundibular width of the lower pole as being associated with increased likelihood of stone clearance. Elbhanasy and colleagues correlated stone clearance after SWL in patients with lower pole stones using preoperative IVP, identifying fixed landmarks that allowed for reproducible measurements [33].

Lower pole infundibular length, width, and infundibulopelvic angle were defined very precisely as illustrated in Figures 60.3–60.5, respectively. Their study found that an infundibulopelvic angle >90°, infundibular length <3 cm, and infundibular width >5 mm were all significant predictors of stone-free status [33]. Subsequent studies have yielded equivocal results. In the two most commonly cited RCTs evaluating SWL versus ureteroscopy or PCNL in lower pole stones, neither infundibulopelvic angle, infundibular length, nor infundibular width were found to be statistically significant predictors of SWL success [30, 31].

## Hounsfield density

Chaussy and Fuchs originally compared a stone's radiodensity to that of the spine and hypothesized that if the stone was less dense than the spine, the stone should fragment more easily [34]. Today, Hounsfield units (HU) measured using CT can be used to determine a stone's radiodensity. These values should be obtained using bone windows, in a dimension with the widest stone diameter and in a manner so as to include the largest cross-sectional area of stone without including adjacent tissue [35]. Numerous studies have shown a stone's Hounsfield density value to be predictive of SWL success. The higher the CT attenuation value, the more

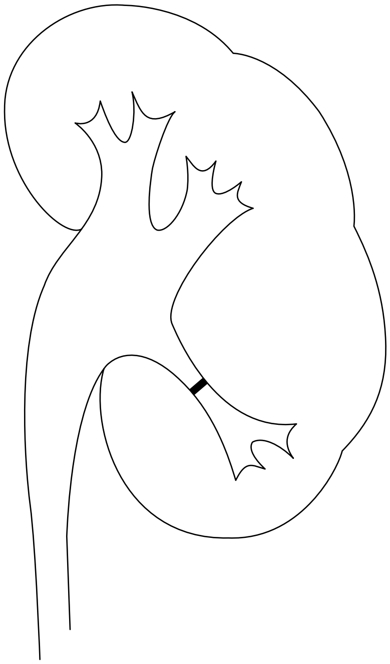


**Figure 60.4** Lower pole infundibular width is measured at the narrowest point along the infundibular axis. *Source:* [33]. Reproduced with permission of Elsevier.

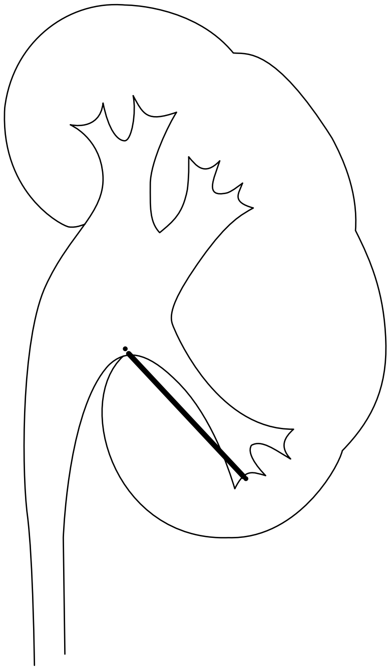


**Figure 60.3** Lower pole infundibular length is measured between the most distal point at the bottom of the infundibulum to a midpoint at the lower lip of the renal pelvis. *Source:* [33]. Reproduced with permission of Elsevier.

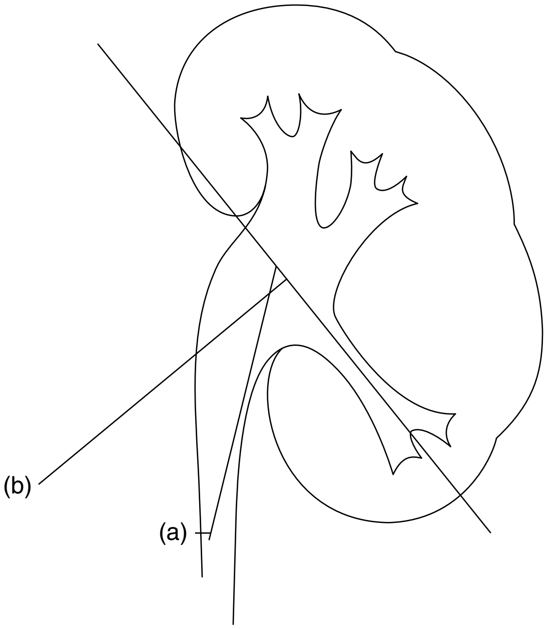


**Figure 60.5** Lower pole infundibulopelvic angle is defined as the angle between two axes: the ureteropelvic axis created by connecting the central point of the renal pelvis opposite the margins of the superior and inferior renal sinuses to the central point of the ureter opposite the lower pole (angle a), and the central axis of the lower pole infundibulum (angle b). *Source:* [33]. Reproduced with permission of Elsevier.

likely SWL will fail. SWL should not be considered when CT attenuation values are greater than 900–1000 HU [6, 7]. Joseph and colleagues studied Hounsfield density in patients undergoing SWL for renal stones <2 cm in size. SWL required a greater number of shock waves as Hounsfield density increased and failed more often in patients specifically when the Hounsfield density of the stone was >1000 HU [36]. Other groups identified a cutoff of 900 HU [35, 37]. One particularly striking study found CT attenuation values <970 HU correlating with a 96% success rate while 62% of patients above that threshold failed treatment [38]. It is important to note that CT attenuation values may be falsely low for smaller stones and are more accurate for larger stones [35]. Likewise, low-dose versus standard dose CT with various collimation widths will also affect CT attenuation values [39].

### Skin-to-stone distance

Skin-to-stone distance (SSD) – i.e. the distance between the stone and the skin – was originally described by Pareek and colleagues [40]. SSD was measured by averaging the distance between the center of the stone and the skin at 0, 45, and 90° from a horizontal line drawn through the stone on axial CT images (Figure 60.6). They found a mean SSD of 8.12 ± 1.74 cm in those patients who became stone-free versus 11.53 ± 1.89 cm in those patients with residual stone ($P < 0.01$) [40]. SSD was a more accurate predictor of SWL success than body mass index in their study. An SSD cutoff of 10 cm is associated with the optimal sensitivity and specificity [40].

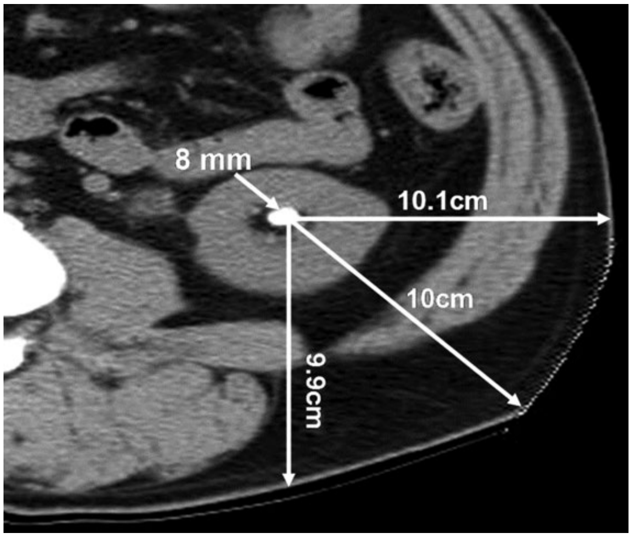


**Figure 60.6** SSD is measured by averaging the distance between the center of the targeted stone and the skin at 0, 45, and 90° from a horizontal line drawn through the stone on axial cuts of a CT. *Source:* [40]. Reproduced with permission of Elsevier.

### Predictive models of shock-wave lithotripsy success

The first SWL mathematical model was created by Vakalopoulos in 2009 after retrospectively reviewing 1997 renal and ureteral stones treated by SWL [41]. The equation $P = 1/1 + e^{-z}$ was used to predict SWL success where $Z$ varies based on the location of the stone. This coefficient for renal stones equals the equation below with the variables determined from Table 60.1:

$$\begin{aligned} Z = 0.95 + 0.24X_1 + 0.77X_2 + 1.18X_3 - 0.61X_4 \\ - 0.72X_5 - 10X_6 + 0.75X_7 + 0.12X_8 + 0.98X_9 \\ + \text{location coefficient}X_{10} \end{aligned}$$

Their model was predictive 85.3% of the time for patients with renal stones in their cohort. Of note, the presence of a stent was not a significant predictor of SWL success. In addition, only 10% of patients had a preoperative CT [41].

**Table 60.1** Variables to be used in the mathematical model for prediction of SWL outcome for urinary stones by Vakalopoulos. Reproduced with permission of Mary Ann Liebert, Inc.

| Variable | Value | Description |
|---|---|---|
| $X_1$ Sex | 0 | Female |
| | 1 | Male |
| $X_2$ Age | 0 | ≤40 and ≥61 years |
| | 1 | 41–60 years |
| $X_3$ Body mass index | 0 | ≤20.0 and ≥28.1 kg/m$^2$ |
| | 1 | 20.1–28.0 kg/m$^2$ |
| $X_4$ Stone size | 0 | ≤10 mm |
| | 1 | >10 mm |
| $X_5$ Stone volume | 0 | <0.5 cm$^3$ |
| | 1 | >0.5 cm$^3$ |
| $X_6$ Stone density | 0 | ≤Bone density |
| | 1 | >Bone density |
| $X_7$ Number of stones | 0 | Multiple stones |
| | 1 | Simple stone |
| $X_8$ Double-J catheter | 0 | No |
| | 1 | Yes |
| $X_9$ UPJ diameter | 0 | <5 mm |
| | 1 | ≥5 mm |
| $X_{10}$ Stone location | 1 | Renal pelvis |
| | 2 | UPJ |
| | 3 | Upper calix |
| | 4 | Middle calix |
| | 5 | Lower calix |

UPJ, ureteropelvic junction.

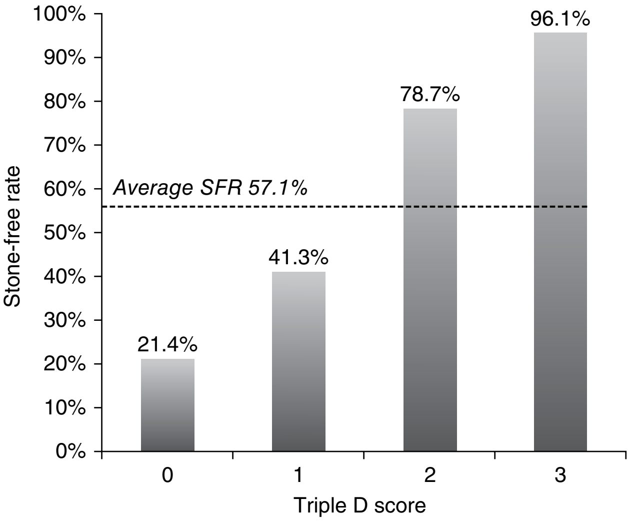


**Figure 60.7** Stone-free rate (SFR) according to Triple D score. 57.1% of patients were stone-free on KUB/renal ultrasound obtained after 4–6 weeks overall. *Source:* [42]. Reproduced with permission of Mary Ann Liebert, Inc.

More recently, the Triple D score was created using factors identifiable on CT for renal or ureteral stones >4 mm in size [42]. SSD (distance), stone attenuation (density), and ellipsoid stone volume (ESV) (dimensions) were found to be significant predictors of single treatment success. To determine the Triple D score, a point is added when ESV is <150 μl, stone attenuation is <600 HU, or SSD is <12 cm [42]. Patients in the study with all three favorable characteristics had a 96.1% single treatment stone-free rate (Figure 60.7).

## Preoperative considerations

### Antibiotic prophylaxis

A recent meta-analysis included 1364 patients with sterile preoperative urine from nine RCTs to examine the effect of antibiotics on post-SWL rates of urinary tract infection. There were no significant differences in symptoms, rate of fever, rate of positive urine culture, and incidence of urinary tract infections (symptoms + urine culture) if prophylactic antibiotics were given. Culture proven urinary tract infection rates after SWL ranged from 0 to 14% of patients across the included studies [43]. Antibiotic guidelines between the European Association of Urology and American Urological Association are now similar and recommend that in the absence of urinary tract infections or other risk factors (external catheters, suspected infected stones, etc.) with documented sterile urine, antibiotic prophylaxis prior to SWL is not indicated [6–8]. When prophylaxis is necessary, antibiotic selection should be based on previous urine or stone cultures and local antibiograms.

### Routine preoperative stenting

Routine preoperative stenting was historically practiced by many urologists to facilitate passage of stone fragments and prevent ureteral obstruction after SWL. However, modern data suggest otherwise. When data from multiple RCTs was pooled in a meta-analysis of 453 patients, the total stone-free rate in those who were stented preoperatively was 78.1 versus 83% in the stentless group ($P = 0.27$). The presence of a stent also does not prevent renal colic, steinstrasse, or additional procedures [44]. Current guidelines no longer recommend routine preoperative stenting; however, prior guidelines (i.e. European Association of Urology 2010 guidelines) recommended stenting prior to SWL of large stones (i.e. >2 cm) [6–8].

## Shock-wave lithotripsy technique

### Shock-wave number and rate

In an effort to maximize stone fragmentation and minimize trauma to the kidney and surrounding structures, variations in the administration of shock waves have been methodologically studied. There are no conclusive data to recommend an optimum number of shock waves [8]; however, most surgeons apply 2000–3000 shock waves [45]. The association between slower shock-wave rate and improved stone fragmentation was described in an *in vitro* study in 1989 after applying 3000 shock waves from a piezoelectric generator to explanted human kidney stones at frequencies ranging from 75 to 600 shocks/minute. Stones treated at the lower rates of 75 and 150 shocks/minute achieved better fragmentation [46]. This effect is thought to be from the interaction of cavitation bubbles: at slower shock-wave rates, a greater proportion of cavitation bubbles will contact the stone, resulting in fragmentation. At faster shock-wave rates, cavitation bubbles may interact with one another as opposed to the stone surface [47]. The negative pressure phase of a shock wave specifically becomes dampened at a faster rate (Figure 60.8); this phase is responsible for the tensile stress induced on a stone. The positive pressure phase of the shock wave is not affected by a faster rate [48].

RCTs have shown that optimal SWL frequency is 60–90 shocks/minute. Three month stone-free rates were found to be significantly better when SWL was performed at 60 versus 120 shocks/minute [49]. Subsequently, a rate of 90 shocks/minute was shown to have significantly better

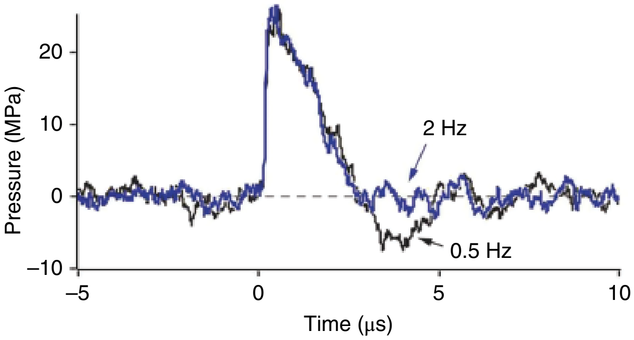


**Figure 60.8** Pressure wave generated from shock waves applied at 0.5 Hz (30 shocks/minute) and 2 Hz (120 shocks/minute) *in vitro* to stones placed in a basket in the focal zone of a laboratory lithotripter modeled from a Dornier HM3. The positive pressure phase is the same but the negative pressure phase is dampened when shock waves are applied at 2 Hz (120 shocks/minute). *Source:* [48]. Reproduced with permission of Mary Ann Liebert, Inc.

outcomes than 120 shocks/minute [50]. A recent meta-analysis of nine RCTs with a total of 1572 patients confirmed that frequencies of 60 and 90 shocks/minute yielded equivalent success rates and both were significantly better than 120 shocks/minute [51]. An additional meta-analysis noted that the benefits of a slower shock-wave rate are most notable for stones >10 mm [51]. While slower shock-wave rates were associated with decreased renal injury in porcine models of SWL [52, 53], no differences in complications due to shock-wave rate were observed in human trials [51].

## Pretreatment

Pretreatment is the application of low-energy shock waves to the targeted renal stone in order to "prime the kidney" and reduce renal injury. Initial studies were done *in vivo* using porcine kidneys and the Dornier HM3 [54]. Willis demonstrated that when 2000 shock waves at 24 kV were applied to one pole of the kidney, the hemorrhagic lesion caused by 24 kV shock waves applied to the opposite pole immediately afterwards was smaller (Figure 60.9) [55]. A subsequent study evaluated 500 shock waves applied at 12 kV followed by standard SWL treatment on the same pole; this correlated with a 20-fold reduction in the size of the resultant hemorrhagic lesion when compared with no pretreatment [55]. More recently, 300 shock waves applied at 12 kV was also proven to significantly reduce the hemorrhagic lesion size [56]. While the exact mechanism is unknown, Doppler ultrasonography has shown that pretreatment is associated with renal vasoconstriction [57].

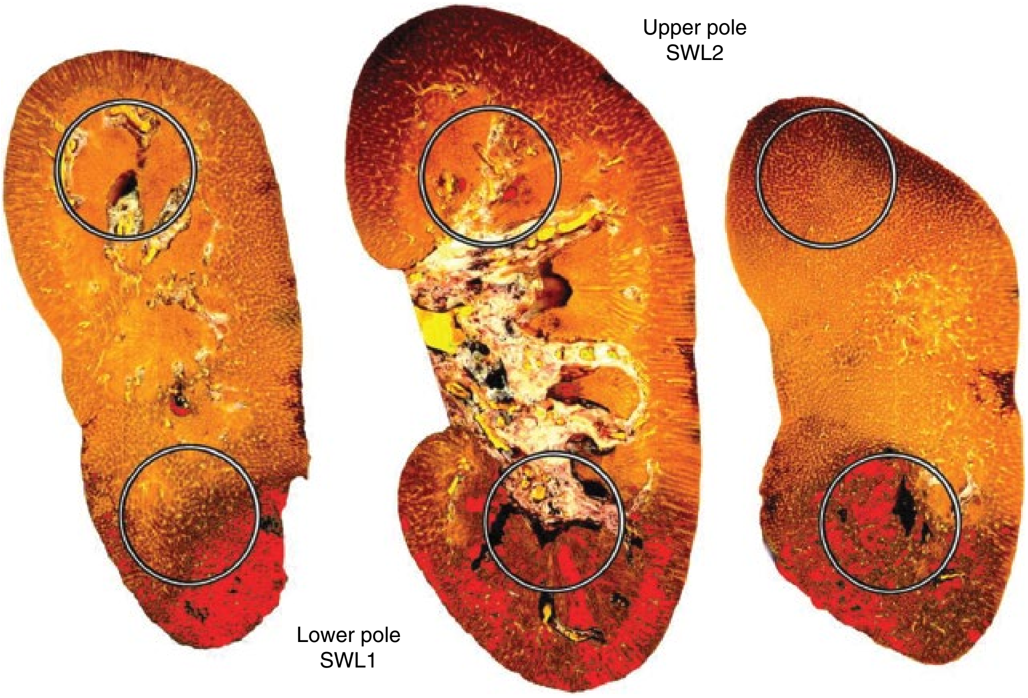


**Figure 60.9** Coronal sections of porcine kidney after the lower pole was first treated with 2000 shock waves at 24 kV followed by the same clinical dose applied to the upper pole. Circles denote the focal zone. Hemorrhagic lesions appear in red. There is significantly less hemorrhage in the second focal zone after the shock waves were applied to the first focal zone. Reproduced with permission of the American Society of Nephrology.

### Pretreatment time and pause

For the initial pretreatment studies, Willis needed a 3–4 minute gap between pretreatment and full-dose shock waves in order to retarget: this lead the authors to hypothesize that a pause during SWL may also reduce renal damage [53]. A pause was subsequently incorporated into all of their experiments. One protocol included pigs treated with 2000 shock waves continuously at 24 kV versus treatment with 100 shocks at 24 kV followed by a 3 minute pause and then an additional 2000 shocks at 24 kV, demonstrating that the 3 minute pause was associated with decreased hemorrhagic lesion size caused by SWL [53]. Further studies have noted that perhaps the greatest influence on reducing trauma is the cumulative time of low dose treatment plus pause. For example, 100 low-dose shock waves followed by a 10 second pause did not confer protection from injury whereas 500 low-dose shock waves followed by a 10 second pause showed a protective effect. It was theorized that the time it takes to administer 500 shock waves, or around 4 minutes, allows adequate time to sensitize the renal vasculature leading to stronger vasoconstriction during subsequent full-dose shock-wave treatment [58].

### Voltage escalation

Escalating shock-wave voltage improves stone comminution in a porcine model with the Dornier HM3 when compared with delivering all shock waves at the highest voltage dose [59]. Escalating the energy level is also thought to “prime” the stone for further fragmentation at higher energy levels [60]. Voltage escalation protocols for SWL have been evaluated in two RCTs in humans. The first trial looked at stepwise voltage increments from 11–13 kV every 500 shock waves versus 13 kV for 3000 shock waves using a Dornier Compact Delta machine. The stepwise escalation group had a 96% stone-free rate at 8 weeks versus 72% in the constant voltage group [61]. In a second double-blind RCT, shock waves were either delivered starting at 14–15 kV followed by immediate escalation every 10 shocks to 23 kV for a total of 3000 shock waves or 15 kV for 1000 shock waves followed by delayed escalation by 1 kV every 10 shocks to 23 kV for a total of 3000 shock waves using a Philips LithoTron machine. Single treatment success at 3 months was 72.5% in the immediate escalation group versus 54.5% in the delayed escalation group ($P = 0.021$) [60]. It is important to consider that in the delayed escalation group, approximately half of the shock waves delivered were at low energy. While many agree that voltage escalation will improve stone fragmentation, escalation must be done promptly enough to deliver a reasonable amount of shock waves to the stone at higher voltage.

### Cardiac arrhythmia, pacemakers, and implantable cardiac defibrillators

Shock waves can affect cardiac rhythm and alter pacemaker and implantable cardiac defibrillator function such that the application of shock waves may have to be adjusted. Arrhythmias were noted especially with first-generation lithotripters (up to 80% of procedures) and persist to a lesser degree with newer-generation machines [62, 63]. It is important to note that cardiac arrhythmias during SWL occur almost exclusively with treatment of renal stones and may be more likely to happen during treatment of the right kidney [64, 65]. To prevent arrhythmias most lithotripters can be switched to a “gated” mode in which a shock wave is initiated during the R wave of the electrocardiogram. Maximal heart effects will then occur during the heart’s refractory period [62]. If premature contractions are noted, pausing treatment long enough to resume normal heart rhythm may solve the problem; if not, then gating is recommended [64]. More recently, rotating the patient 15–20° away from the supine position was described as another maneuver to resolve an arrhythmia without having to gate shock-wave delivery [65].

Today, SWL is considered safe in individuals with these devices [8] and most manufacturers of pacemakers and implantable cardiac defibrillators have recommendations for lithotripsy [66]. Preoperative cardiology consultation may be of benefit for patients with implantable devices or history of arrhythmia.

## Adjunct therapy after shock-wave lithotripsy

### Percussion, diuresis, and inversion therapy

Several investigators have described adjunct techniques to improve stone clearance after SWL, especially for lower pole stones. The kidney lies in an oblique axis such that the upper pole is posterior to the lower pole. Inversion >30° below the horizontal plane allows optimal positioning of the collecting system for fragment expulsion from the lower pole [67, 68]. Diuretics and high volume fluid intake have also been tried in an effort to augment urine production and flush fragments out [69]. Lastly, percussion theoretically employs repetitive mechanical pressure on the flank to vibrate the renal system and discharge fragments in the augmented urine flow [67, 68]. One RCT of SWL for lower pole stones <2 cm in diameter tested a median of four sessions of diuresis, inversion, and percussion performed 1–2 weeks after each SWL plus additional sessions in those with persistent stone at

1 month following the last SWL. This involved drinking 500 ml of water 30 minutes prior to inversion in a prone Trendelenburg position at 45° and continuous manual mechanical percussion over the flank for 10 minutes [67]. Another RCT was limited to lower pole fragments <4 mm in diameter 3 months after SWL and involved 20 mg of furosemide followed by inversion to >60° and flank percussion using a mechanical chest percussor for 10 minutes. This was done weekly for 3 weeks or until stone-free [68]. Both trials demonstrated significantly improved stone-free rates using these adjunct techniques. Based on this evidence, the European Association of Urology recommends consideration of inversion, diuresis, and percussion for well-disintegrated lower pole stones [8].

### Medical therapy after shock-wave lithotripsy

Medications to augment the passage of fragments including α-adrenergic antagonists, calcium channel blockers, corticosteroids, and smooth muscle relaxants have been studied in over 20 RCTs [70, 71]. Pooled data have shown nearly twofold increases in stone-free rates as well as reductions in expulsion time, steinstrasse, and renal colic, with tamsulosin being the most-studied pharmacotherapy [6, 7, 71]. Therefore, use of these medications is endorsed by various guideline panels [6–8]. More recently, *Phyllanthus niruri*, a Brazilian plant remedy which prevents calcium oxalate crystal growth, was shown to improve stone-free rates after SWL of lower pole stones when compared with placebo in a RCT (93.7 vs. 70.8%, $P = 0.05$) and with no side effects reported [72].

Small residual fragments after SWL raise concern as a nidus for recurrent stone formation. In a RCT evaluating potassium citrate therapy after SWL for lower pole renal stones, individuals who were stone-free and prescribed potassium citrate had zero stone recurrences in the following 12 months. In those with residual stone fragments, a 44.5% reduction in stone recurrence was observed in patients prescribed potassium citrate versus 12.5% in those who were not [73].

## Patients with anatomic anomalies or varations

Outcomes of SWL in patients with anatomic variations are described here and in Table 60.2. These findings are from retrospective studies due to a lack of RCTs with such patients. It is important to note that 88% of the cases in these series required auxiliary procedures and/or retreatment including ureteral stenting or catheterization which was argued may augment the success rate in these patients [19].

### Horseshoe kidney

Horseshoe kidney is associated with anterior displacement of the renal pelvis and high insertion of the ureter which may impede stone clearance after SWL. Perhaps based on these anatomic factors, one of the largest reports of SWL for stones in horseshoe kidneys reported a 9.1% 3 month stone-free rate and 72.7% auxiliary treatment rate. In this study, upper calyceal location and increased body mass index were associated with poorer stone clearance [74]. To combat some of these issues, patients can be placed prone, reducing SSD and potentially improving urinary drainage [75].

**Table 60.2** Outcome of SWL based on anatomic anomaly or variation [19].

| | SWL outcome (%) | | |
|---|---|---|---|
| **Anomaly/variation** | **Stone-free** | **>90% clearance** | **Residual stone** |
| UPJ obstruction | 51 | 11 | 38 |
| Horseshoe kidney | 49 | 11 | 40 |
| Malrotation | 44 | 29 | 27 |
| Ectopic kidney | 77 | 10 | 13 |
| Calyceal diverticula | – | 45 | 55 |
| Duplicated ureter | 55 | 16 | 29 |
| Non-obstructive megaureter | 40 | 27 | 33 |
| Medullary sponge kidney | 6 | 12 | 82 |

UPJ, ureteropelvic junction.

### Ureteropelvic junction obstruction, megaureter, duplicated ureter with hydronephrosis

If SWL is to be attempted in patients with ureteral abnormalities, renal scintigraphy should be considered to rule out clinically significant obstruction. Three month stone-free rates for these anatomical variations in those without obstruction range from 40–55% [19].

### Malrotated kidney and ectopic kidney

Malrotated and/or ectopic kidneys may have impaired urinary drainage due to vascular compression of the ureter or ectopic location [76]. In the absence of obstruction, 3 month stone-free rates are reported to be 44% for malrotated kidneys and 77% for ectopic kidneys (mean pretreatment stone size 21 mm) [19].

### Calyceal diverticula

SWL stone-free rates for treatment of diverticular stones ranges from 0–25% [77]. A few reports suggest SWL may be useful for stones <1 cm in size only if there is a radiographically confirmed, short and patent diverticular neck which could allow fragment passage [77]. One study reported fluoroscopic evidence of stone fragmentation in 87% of patients but 3 month stone-free rates of only 21%. Of note, despite low stone-free rates, a majority of patients in this study (61%) reported resolution of pain and/or recurrent infection at 2 years mean follow-up [78].

### Urinary diversion

The incidence of renal stones in patients with colon conduits is 3–4% and with ileal conduits is 10–20% [79, 80]. Postulated mechanisms include metabolic acidosis/hypocitraturia due to urinary diversion, hyperoxaluria, chronic urinary tract dilation/reflux, and chronic or recurrent bacteriuria [81]. SWL is an attractive option in the absence of downstream ureteral obstruction as retrograde ureteroscopy may be challenging in these patients [81]. SWL monotherapy was found to have an 81.5% success rate in a small study with 27 patients with renal stones and urinary diversion. Two sessions were needed in 29.6% of patients, while 14.8% needed three sessions and 7.4% of patients developed obstruction from stone fragments requiring additional, more invasive procedures [82].

## Pediatric shock-wave lithotripsy

SWL has been used in the pediatric population since the 1980s and is widely considered safe [83, 84]. Stone-free rates after the treatment of renal stones in children are generally higher than in adults and range from 80 to 85% [6, 7, 84, 85]. The absolute contraindications are similar to adults. In contrast to adults, SWL for stones >2 cm in size, including staghorn calculi, can be effective and is acceptable in children [6, 7]. Stone-free rates for such stones range from 73.3 to 83.3% with many requiring only one or two treatments despite stone size being well above 2 cm [86–88]. For larger and staghorn stones in children, preoperative stent or nephrostomy decreases SWL complications [6, 7, 86]. Although there is no official recommendation, low energy levels and fewer shocks should be used in children [45].

## Follow-up after shock-wave lithotripsy and managing failure

There is no consensus on follow-up imaging after SWL. Obtaining plain abdominal radiography (i.e. KUB) 1–4 weeks after SWL is reasonable to evaluate success. Stone fragments less than or equal to 4–5 mm can be observed if asymptomatic but may lead to future colic events or serve as a nidus for stone recurrence [8, 89]. In one study evaluating the long-term outcome of stone fragments less than or equal to 4 mm after SWL, 21.4% of residual fragments led to stone recurrence and retreatment in the 5 years of follow-up [90]. Presence of fragments greater than or equal to 4 mm that persist 3 months after SWL were a significant independent predictor of clinically significant events in another study [89].

Repeat SWL can be considered based on initial treatment success or failure. There is no consensus on the timing between repeat sessions of SWL for renal stones; however, European Association of Urology guidelines approve of within 1 day for ureteral stones [8]. When repeat SWL was compared to surveillance in a RCT on persistent renal stone fragments after initial SWL, 3 month follow-up showed significant decrease in residual debris in those who were retreated [91]. Many studies evaluating SWL outcomes document SWL failure as being after three sessions [36, 39, 92]. In a RCT on SWL versus PCNL, renal scarring was assessed using $^{99m}$Tc-labeled dimercaptosuccinic acid (DMSA) scintigraphy; 16% of the patients in the SWL group had scarring, all of whom had three SWL sessions and only one of which became stone-free [92]. Studies have also demonstrated decreasing success rates (i.e. diminishing returns) with each successive SWL treatment for both renal and ureteral stones [41, 93]. American Urological Association guidelines recommend offering endoscopic therapy as the next treatment option in those who fail a single SWL [6, 7].

## Conclusions

In 2017, SWL has a clear role in the surgical management of renal stones and remains the least invasive treatment option. The decision for SWL versus other treatments is affected by many variables outlined in this chapter. Future directions may be aimed at improving SWL success rates on newer-generation machines as well as novel techniques to overcome barriers to stone fragmentation.

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# Shock-wave Lithotripsy of Ureteral Calculi

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## Introduction

Over the past decade, the number of patients with upper urinary tract calculi undergoing shock-wave lithotripsy (SWL) has decreased across the globe [1, 2]. This trend is a reflection of a number of factors including improvements and widespread availability of flexible ureteroscopes and intracorporeal lithotripsy devices, as well as the perception that SWL efficacy with the newest generation of lithotripters is less than with the endourological alternatives. Despite the expanding role in particular for flexible ureteroscopy in the management of upper ureteral calculi, SWL remains a popular therapeutic option for patients [3–5].

Contemporary experience highlights the importance of proper patient selection in achieving successful outcomes with SWL. Technique and the employment of adjunctive measures have also been shown to promote stone fragmentation and stone clearance. In this chapter, the current indications, clinical outcomes, and techniques to enhance efficacy of SWL in the management of ureteral stones are reviewed.

## Current indications for shock-wave lithotripsy of ureteral stones

Current clinical practice guidelines have emphasized the importance of proper patient selection when considering SWL for an individual patient with a ureteral stone. Stone factors such as size, location, multiplicity, radiopacity, composition (if known), as well as patient factors including body habitus, patient body mass index (BMI), and collecting system anatomy may be useful clues predicting success. Surrogate markers can also be used to help determine whether SWL is worth considering for an individual patient. Hounsfield unit (HU) measurements on computed tomography (CT) scanning can reflect stone hardness and the likelihood of successful fragmentation, which maybe especially useful if stone composition is unknown. Skin-to-stone distance (SSD) determined by CT scan provides additional information on the potential impact of patient body habitus on treatment success.

The 2016 American Urological Association (AUA)/ Endourological Society surgical management of stone guideline emphasized the usefulness of CT in optimizing individual patient treatment while remaining cognizant of radiation exposure risk [6]. CT has the highest accuracy in determining stone size and location and can provide HU and SSD information.

Stone burden and individual stone size have well-known effects on SWL outcomes of renal stones. In a multivariate analysis, renal stones <15 mm in size were associated with a 1.94 times greater chance of clearance post-SWL than stones larger [7]. As for renal calculi, different cutoffs, ranging from 8 to 12 mm, have been suggested for ureteral calculi [8–10]. Every research group evaluating the influence of variables on success after SWL retained stone size or a surrogate thereof such as stone diameter or surface area as an independent predictor of success [11–17]. Overall, stones larger than 1 cm are considered to have a lower success rate with SWL.

Obesity and diabetes have been widely recognized as important risk factors for urinary stone disease with an increasing influence on prevalence [18]. The effect of patient BMI was first highlighted by Pareek et al. who demonstrated that failure of SWL for renal and proximal ureteral stones was associated with an average BMI of 30.8 $kg/m^2$ [19]. The effect of SSD as a surrogate for BMI has been clearly demonstrated in a number of studies.

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For ureteral stones, however, the literature does not unanimously report a negative impact of a higher SSD [20–22]. Initially, Wiesenthal et al. reported a SSD <11 cm to be a significant predictor of success for renal and ureteral calculi [20]. In a multivariate analysis on the same population, however, evaluating renal and ureteral calculi separately and using SSD as a continuous variable, SSD was no longer a predictor of success for ureteral calculi [12]. Although initially, a 10 cm cutoff for SSD was proposed above which SWL was less successful [19], more recent reports demonstrate a cutoff of 11–12 cm [20, 22, 23]. Whether this is a reflection of the specific geometry of different lithotripters used is unclear. Needless to say, an understanding of the specifications of one's particular lithotripter is important when considering factors that might affect treatment efficacy.

Stone composition has a well-documented impact on SWL efficacy. Ringdén and Tiselius described stone hardness as a stone's resistance to shock-wave therapy, based on the results of SWL of 114 stones treated *in vivo* [24]. Uric acid/urate, struvite mixed-infection stones, and calcium oxalate dihydrate stones are most responsive to SWL, followed by, in order of increasing hardness, hydroxyapatite, carbonate apatite, calcium oxalate monohydrate, brushite, and cystine stones [24]. This was similarly identified by Parks and colleagues [25]. Among patients with suspected or known cystine or uric acid stones, SWL is typically not the preferred modality, as they are often poorly visualized on fluoroscopy, making stone targeting problematic. Even if ultrasound targeting is available on the lithotripsy machine, identifying a ureteral stone can be challenging. Cystine stones are typically resistant to SWL fragmentation due to their organic nature. The AUA/Endourology Society guideline based on expert opinion recommends ureteroscopy as the first-line therapy for patients with ureteral stones and these specific stone compositions requiring treatment [6]. Cystine and calcium oxalate monohydrate stones, in addition to being hard, also tend to break into relatively large pieces that may be difficult to clear from the collecting system [26, 27]. For those patients with the more difficult to fragment stone compositions, SWL should be reserved only for small volume stone burdens [28]. Matrix calculi although relatively soft being composed of predominantly organic matter, also respond poorly to SWL fragmentation efforts [29].

When stone composition is not known, noncontrast CT imaging with measurement of the stone HU value can be a useful proxy. A number of studies have evaluated different HU cutpoints ranging from greater than 750 to 1000 as predictors of SWL failure for ureteral stones [19–22, 30, 31]. In summarizing the current literature, McClain et al. suggest using a liberal estimate of 1000 HU [32], with higher values associated with lower stone fragmentation rates. It is important to realize that most of these papers included both renal and ureteral stones and that these cutoffs may therefore not be completely applicable to ureteral stones.

Williams et al. demonstrated that with an increasing collimation width, an increasing underestimation of the HU has to be taken into account due to the volume averaging effect of CT imaging [33]. As most stone protocol CTs apply a 5 mm collimation width, the HU measurements of small stones are most likely an underestimation of the actual stone density [34]. This may explain why the calculated cutoff HU for SWL success is lower than the generally applied 1000 HU in datasets including a large proportion of ureteral stones.

Results in the literature are conflicting on whether hydronephrosis has a negative effect on outcomes of SWL for ureteral calculi [13, 16, 35–37]. Recent research indicates that approximately 89% of patients with symptomatic ureteral stones have at least a mild degree of hydronephrosis [38]. The only variable directly correlated with the degree of hydronephrosis was stone size [38]. The degree of obstruction did not appear to have any influence on success rates of SWL for solitary distal ureteral stones in a report by Demirbas et al. [35]. In a cohort of nearly 700 ureteral stones treated by SWL, obstruction appeared to have a negative effect on success, but did not reach statistical significance in a multivariate analysis (odd ratio 1.93, 95% confidence interval [CI] 0.99–3.77, $P = 0.053$) [16]. Although Seitz and associates identified a success rate of 86.7% for nonobstructing and a 70.5% success rate for obstructing proximal ureteral stones, similarly they could not demonstrate this difference to be statistically significant [36]. El-Assmy et al. came to the same conclusion, but did identify patients with hydronephrosis to need more SWL sessions to reach stone-free status and to evacuate fragments after SWL [37]. In an effort to develop a clinical nomogram to predict outcomes after SWL, Kim and colleagues identified hydronephrosis as an independent predictor of failure in a cohort of over 3000 patients [13]. Ureteral wall thickness may be a surrogate for impaction and hydronephrosis and has been demonstrated to decrease success rates of SWL for proximal ureteral calculi [39].

Many variables have been shown to influence stone fragmentation and clearance of fragments after SWL. Although anatomic abnormalities of the urinary tract may not directly influence fragmentation, they may hinder clearance of fragments [40].

Contraindications to SWL of ureteral stones are similar to those for renal stones. Pregnancy remains an absolute contraindication due to the uncertain effects on the fetus [41]. Untreated urinary tract infection (UTI), unrelieved urinary tract obstruction, uncorrected bleeding diatheses, and adjacent arterial aneurysm are other well-described contraindications [42–44].

## Outcomes

### Proximal, mid, and distal ureteral locations

Several large series identify the difference in success rates of SWL for ureteral calculi in different locations: 70–97% for proximal stones, 58–97.8% for mid-ureteral stones, and 54–97.9% for distal ureteral calculi (Table 61.1) [9, 11, 16, 17, 45–47].

Contemporary series of SWL and ureteroscopy for patients with ureteral calculi describe reasonably high stone-free rates (SFR) with both modalities. The ability to achieve a stone-free state with a single procedure was assessed in the 2007 European Association of Urology (EAU)/AUA Guideline for the management of ureteral calculi [48]. For stones in the proximal, middle, and distal ureter the number of ureteroscopy procedures necessary to achieve stone clearance was 1.01, 1.00, and 1.00 respectively. For SWL, the review documented 1.34, 1.29, and 1.26 procedures required for proximal, middle, and distal stones respectively. The 2016 AUA/Endourology Society guideline panel's meta-analysis identified superior SFR overall for ureteroscopy over SWL for stones regardless of size and location (90% for ureteroscopy vs. 72% for SWL) [6]. A subanalysis of upper ureteral stones >10 mm in size determined that SFR was comparable (74% for SWL vs. 79% for ureteroscopy). For mid and distal ureteral stones >10 mm, the evidence favored ureteroscopy over SWL (82.5 vs. 67% and 92 vs. 71% respectively). The greater disparity in SFR for mid and distal ureteral stones between ureteroscopy and SWL lead the AUA/Endourology Society guideline panel to give a strong recommendation in favor of ureteroscopy as the first-line therapy for patients with stones in these specific locations. The updated 2016 EAU guideline recommendations are slightly different and suggest SWL as first-choice for proximal stones <10 mm and no preference of SWL or ureteroscopy for distal stones <10 mm [49].

### Pediatric stones

The 2016 AUA/Endourological Society guideline on urinary stone management reported the results of a meta-analysis indicating SWL and ureteroscopy have similar efficacy for stones of varying size in pediatric patients. Pooled success rates were 87 and 95% respectively for stones <10 mm and 73 and 78% for stones >10 mm [6]. These results are confirmed in a large retrospective cohort of pediatric stones, including 1345 ureteral calculi [50]. Although patients needed fewer auxiliary treatments after ureteroscopy (13.6 vs. 18.8%), the authors reported a higher readmission and emergency room visit rates when compared to patients treated with SWL (7.9 vs. 4.9%) [50].

### Treatment safety

SWL continues to demonstrate lower treatment related morbidity compared to ureteroscopy with a Cochrane review noting a significantly lower complication rate for SWL (relative risk 0.54, 95% CI 0.33–0.88, $P = 0.01$) [51]. The 2016 AUA/Endourology guideline found no differences in the rates of UTI, sepsis, ureteral stricture,

**Table 61.1** Studies reporting on outcomes of shock-wave lithotripsy for ureteral calculi in different parts of the ureter.

| Study | *n* | Ureteropelvic junction | Proximal | Mid | Distal | Ureterovesical junction | Total |
|---|---|---|---|---|---|---|---|
| Pace 2000 [46] | 1593 | | 755/1071 (70%) | 232/340 (68%) | 99/182 (54%) | | 1086/1593 (68%) |
| Delakas 2003 [16] | 688 | | 262/316 (82.9%) | 59/78 (75.6%) | 181/294 (61.5%) | | 502/688 (73.0%) |
| Gomha 2004 [17] | 984 | 110/127 (86.6%) | 466/481 (96.9%) | 40/42 (95.2%) | 302/334 (90.4%) | | 918/984 (93.3%) |
| Kanao 2006 [11] | 292 (ureteral only) | | 147/186 (79.0%) | 25/33 (75.8%) | 56/73 (76.7%) | | 228/292 (78.1%) |
| Tiselius 2008 [47] | 580 | | 244/254 (96.1%) | 88/90 (97.8%) | 231/236 (97.9%) | | 563/580 (97.1%) |
| Sfoungaristos 2012 [45] | 156 | 12/15 (80%) | 32/45 (71.1%) | 25/43 (58.1%) | 37/39 (94.9%) | 14/14 (100%) | 120/156 (76.9%) |
| Demirbas 2012 [9] | 2836 | | 742/871 (85.1%) | 262/312 (83.9%) | 1462/1653 (88.4%) | | 2466/2836 (87%) |
| **Total** | **7129** | **122/142 (85.9%)** | **2648/3224 (82.1%)** | **731/938 (77.9%)** | **2368/2811 (84.2%)** | **14/14 (100%)** | **5883/7129 (82.5%)** |

or avulsion between SWL and ureteroscopy; ureteral perforation occurred more commonly during ureteroscopy [6].

Based on a systematic review evaluating the use of antiplatelet/anticoagulation therapy during SWL of renal and ureteral stones, Schnabel and colleagues highlight that bleeding risk of SWL for patients on acetylsalicylic acid has to be weighed against the risk of a cardiovascular event with discontinuation [52]. Whether SWL of ureteral stones is less likely to be associated with bleeding complications for patients who remain on acetylsalicylic acid is unknown. In patients with uncorrected bleeding diatheses or who are unable to discontinue anticoagulation/antiplatelet agents, SWL should still be considered potentially hazardous due to bleeding risks. Ureteroscopy is the recommended treatment modality in these patients [6].

According to the 2016 AUA/Endourological Society guidelines, SWL does not require pretreatment antimicrobial prophylaxis in the absence of a UTI [6].

As demonstrated by a meta-analysis, antibiotic prophylaxis prior to SWL in low-risk patients does not confer a lower risk of post-SWL UTI [53]. The EAU guidelines suggest that in patients with a higher risk of bacterial burden due to presence of an indwelling catheter, stent, nephrostomy tube, or infectious stones, prophylactic antibiotics may be warranted [49].

The safety of SWL for ureteral calculi in children is well established with multiple reports of low complication rates [54–56].

Polat and colleagues demonstrated almost half of the patients >65 years treated with SWL for ureteral or renal calculi to have at least one medical comorbidity [57]. They observed a low major complication ratio (2.1% steinstrasse, 1.2% hematomas, and 0.4% pyelonephritis), concluding SWL to be safe in the elderly population [57].

Theoretical concerns exist about the effects of SWL on the reproductive organs. Among females, the ovaries may be located in the blast path during treatment of distal ureteral calculi, whereas in males, the vas deferens, seminal vesicles, and prostate may be affected. Although *in vitro* studies suggest spermatozoa are vulnerable to shock-wave energy, animal studies could not uniformly corroborate these results [58]. Results from clinical trials indicate that there may be a transient decrease in sperm motility and sperm count which resolves by 3 months after the treatment [58].

Although concerns about ovarian effects exist, a decrease in fertility has not been demonstrated in female human subjects who underwent SWL for distal ureteral calculi [59, 60]. SWL for distal ureteral stones should be considered a safe treatment not influencing fertility in patients of reproductive age in either sex.

## Strategies to enhance efficacy

In addition to optimal patient selection for SWL, there are many technical factors that can influence treatment success. It is important to emphasize that technical factors should be optimized at the first SWL attempt. Pace et al. demonstrated that repeat SWL treatments for ureteral calculi unresponsive after the first attempt procure only a limited increase in SFR [46]. The cumulative SFR increased from 68 to 76% with one additional treatment and to 77% with a third treatment [46].

### Imaging guidance

Correct targeting is imperative for achieving SWL success. Although ultrasound guidance can be used for SWL treatment of renal stones, this imaging modality is more challenging for ureteral stones. Fluoroscopic guidance is more commonly employed. For faintly radiopaque or radiolucent stones, a bolus of intravenous contrast can be administered or retrograde ureteropyelogram performed, allowing targeting of the filling defect [61].

### Patient positioning

In an *in vitro* SWL study, Olvera-Posada et al. demonstrated that the interposition of bony structures in the shock-wave path had a detrimental effect on shock-wave efficacy [62]. As ureteral stones can overlie the transverse process of lumbar vertebrae, this should be taken into account during patient positioning.

In order to avoid interposition of bony structures in the shock-wave path, Hara and colleagues demonstrated that rotating the patient toward the therapy head increased the success rate significantly for mid- and distal ureteral calculi (from 83.9 to 95% and from 89.1 to 98.0% respectively) and a significant decrease in number of SWL sessions for proximal stones [63].

Kose and Demirbas reported higher fragmentation rates with a modified prone position for distal ureteral stones where the obliquely oriented therapy head is positioned on the opposite side of the stone compared to a conventional prone approach (97.5 vs. 89.9% respectively, $P = 0.015$) [64]. Distal stones can also be targeted in a supine position with the shock-wave energy directed through the greater sciatic foramen or supine with the therapy head positioned in an over-patient position (Figure 61.1). The main drawback of a supine approach is the interposition of bony structures, whereas in a prone position bowel gas may attenuate the shock waves and the SSD distance may be higher. A meta-analysis demonstrated a success rate of 89.6% for the supine position

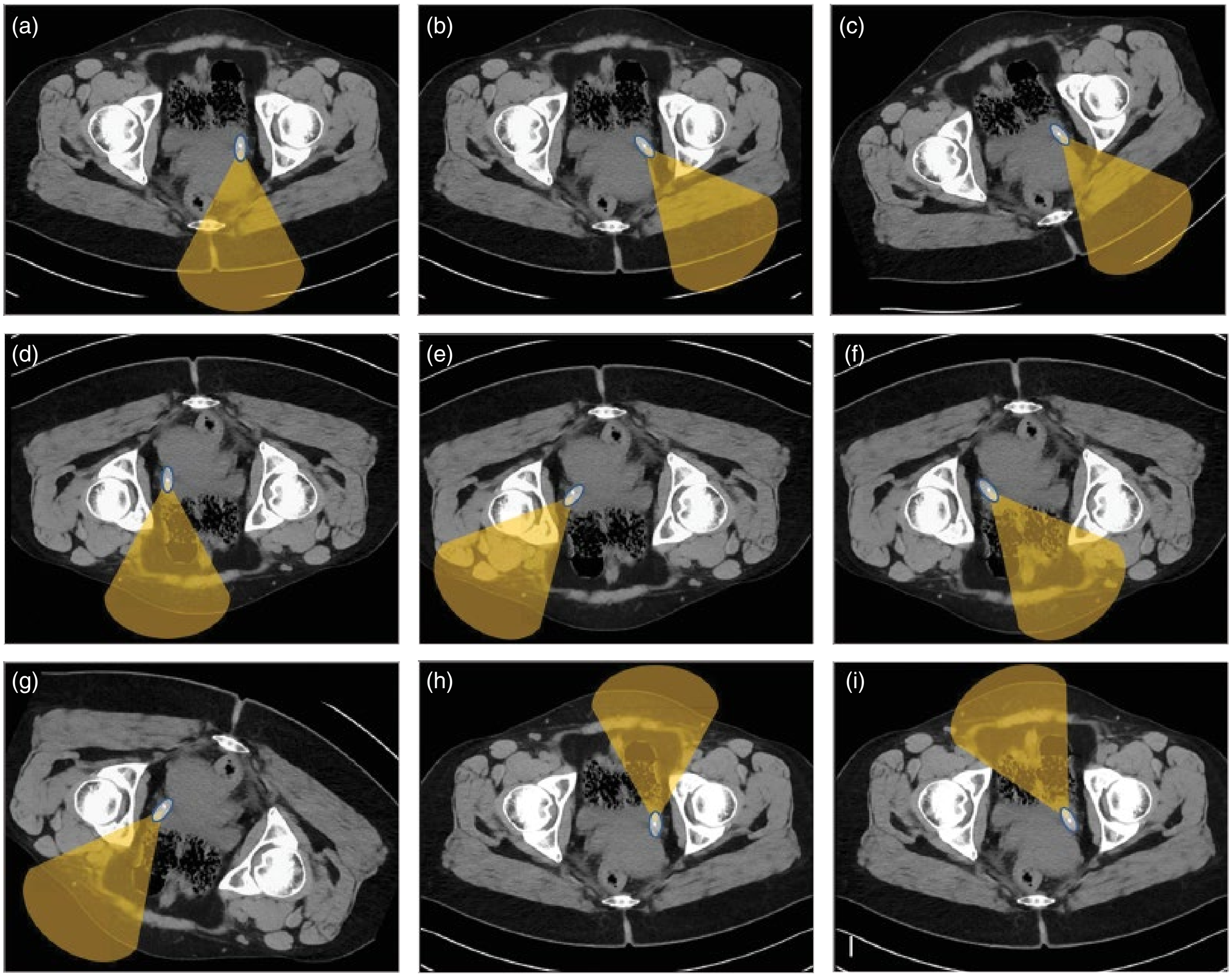

**Figure 61.1** Different possible positions for targeting a distal ureteral stone. (a) Supine vertical therapy head, (b) supine oblique therapy head, (c) modified supine, oblique therapy head, (d) prone, vertical therapy head, (e) prone, oblique therapy head, from ipsilateral side, (f) prone, oblique therapy head from contralateral side, (g) modified prone, oblique therapy head from ipsilateral side, (h) supine, over-patient vertical therapy head, and (i) prone, over-patient oblique therapy head, from contralateral side. *Source:* EDAP-TMS France. Reproduced with permission of EDAP-TMS France.

versus 72.7% for the prone position [65]. Phipps et al. achieved a higher success rate with patients in a supine position using a transgluteal shock-wave path but cautioned that success is operator-dependent and having the sciatic nerve in the blast path may be painful for the patient [66].

## Respiratory motion

Recent data suggests that ureteral stones are considerably less influenced by respiratory motion than renal stones, with renal stones moving over a range of 7.7 ± 2.9 mm and ureteral stones over a range of 3.6 ± 2.1 mm [67]. Abdominal compression belts or plates are therefore of limited benefit for treatment of ureteral calculi.

## Coupling

*In vitro* and clinical research has demonstrated that air bubbles caught in the coupling gel of the therapy head have a detrimental effect on SWL efficacy [68, 69]. Tailly et al. demonstrated that a camera incorporated in the therapy head can help evaluate the coupling area, creating awareness of the presence of air bubbles and prompting manual removal [70].

## Diuresis

Azm and Higazy were the first to report a beneficial effect of forced diuresis on SWL outcomes especially for distal ureteric stones [71]. Whereas Zomorrodi and colleagues achieved similar results [72], Tiselius and colleagues demonstrated no difference in SWL success with or without forced diuresis, but suggest diuresis is still worthwhile post-SWL [73, 74].

### Medical expulsive therapy

Medical expulsive therapy (MET) as the initial management option for ureteral calculi is controversial as a recent large randomized controlled trial (RCT) contradicted a previously published meta-analysis [75, 76]. Skolarikos and colleagues performed a systematic review on the use of MET after SWL to improve clearance of fragments and pooled the results of 26 trials [77]. Their results endorse the use of MET, mainly alpha-blockers, to improve clearance rate and clearance time after SWL [77]. Eryildirim and associates additionally reported that MET post-SWL for ureteral calculi could increase patients' quality of life [78].

### Stenting

According to the most recent AUA/Endourological Society stone guidelines, routine stenting should not be performed in patients undergoing SWL [79]. This recommendation is based on a meta-analysis published in 2011 that included eight studies and 876 patients [80]. Although no difference was noted for success rate after SWL, the review did show a benefit of reducing the steinstrasse rate with stenting [80]. This result was largely influenced by one study including 400 patients with renal stones measuring 1.5–3.5 cm [81]. Several studies have even shown a significantly reduced treatment success after SWL for ureteral stones in stented patients [16, 45, 46, 82].

### Treatment timing

Pooling data from seven studies, Picozzi et al. performed a meta-analysis on the differences between emergent and delayed SWL for ureteric stones [83]. Out of the three included RCTs, only Tombal et al. demonstrated that immediate SWL significantly improved SFR for proximal ureteral stones as determined at 48 hours after treatment [84–86]. A shorter hospital stay as well as the need for fewer auxiliary procedures are some of the reported benefits of emergent SWL [85, 86]. Although underpowered, a recent RCT corroborated these findings with a success rate of 93.8% for immediate versus 80% for delayed SWL [87]. The pathophysiology accountable for this phenomenon is hypothesized to be a lack of edema in the early stages of ureteric colic, which may allow an expansion chamber to form, enhancing fragmentation [83, 88].

## Treatment protocol

### Voltage ramping

Zhou et al. demonstrated that a stepwise increase of voltage procures the best comminution results in *in vitro* and animal experiments [89, 90]. This phenomenon was verified in a clinical RCT including 50 patients with upper tract urinary calculi up to 2 cm, including 20 ureteral calculi [91]. The only RCT on voltage ramping for ureteral calculi did not demonstrate an advantage over fixed voltage SWL [92].

During SWL treatment of proximal ureteral calculi, renal parenchyma may be in the blast path of the shock wave. As several authors have reported voltage ramping to decrease the chance of renal hematoma, this should be taken into account when treating stones in this location [82, 93]. When SWL is not performed under general anesthesia or conscious sedation, Berwin et al. suggested that voltage ramping is additionally of importance for pain tolerance during the treatment [94]. When treating a ureteral stone under general or conscious sedation, without having any renal parenchyma in the blast path, voltage ramping seems to be of minimal benefit.

### Pretreatment and pause

There is extensive *in vitro* and *in vivo* research experience endorsing a low-voltage pretreatment to improve stone fragmentation and decrease damage to renal parenchyma [95–98]. The most recent report would indicate that 300 shocks at low voltage without a pause has the best renoprotective effect while improving fragmentation [98]. Although clinical data is lacking for ureteral stones, pretreatment can be taken into account when renal parenchyma is in the blast path when treating upper ureteral calculi.

### Shock-wave rate

The superiority of a slower shock-wave rate on treatment efficacy has been demonstrated both *in vitro* and *in vivo*. Greenstein and Matzkin initially identified a 1 Hz shock-wave rate to be most efficient for stone comminution in an *in vitro* setting [99]. Paterson et al. corroborated these results in an *in vivo* porcine model, demonstrating that a 0.5 Hz shock-wave rate produced better stone comminution than a frequency of 2 Hz [100]. Utilizing the same *in vivo* model, Connors and colleagues later demonstrated that a shock-wave rate of 1 Hz had a smaller negative effect on glomerular filtration rate(GFR) and renal plasma flow when compared to a 2 Hz regimen, without applying a pretreatment, treatment pause, or voltage ramping [101].

A meta-analysis including 2144 patients from 13 RCTs demonstrated slower shock-wave rates of 1–1.5 Hz to have a superior success rate as compared to 2 Hz, without a significant difference in complication rate [102]. Pooled data analysis, however, could only identify this beneficial effect for stones larger than 10 mm, whereas the shock-wave rate did not seem to influence the success rate for smaller stones [102]. Although this meta-analysis included treatment of 738 ureteral stones from seven studies, of which 339 were treated at a low shock-wave rate, 247 at a intermediate shock-wave rate, and 152 at a high shock-wave rate, a subgroup analysis was not performed [103]. Several groups have focused on differences in shock-wave rate effect on ureteral stones alone [104–106]. Whereas Honey and colleagues demonstrated the benefit of a slow shock-wave rate for proximal ureteral stones, Anglada-Curado et al. have shown a slow shock-wave rate to be superior in a cohort of distal ureteral stones. In contrast to the results of these two trials, Nguyen et al. found a shock-wave rate of 1.5 Hz to result in a higher success rate when compared to 1 Hz [104]. It should be noted that most stones included in this study were smaller than 10 mm in diameter and that analysis could not demonstrate a difference in effect for distal stones [104]. See Box 61.1.

**Box 61.1 Shock-wave lithotripsy of ureteral stones: treatment protocol suggestions.**

- For stones >10 mm, use a shock-wave rate of 60–90 shocks/minute (1–1.5 Hz)
- Low-voltage pretreatment with approximately 300 shocks for proximal ureteral stones (especially if renal parenchyma is in the blast path of the shock wave)
- A treatment pause has no proven benefit
- In treatment of mid-ureteral to distal stones under conscious sedation or general anesthesia, voltage ramping may be omitted.

## Summary

Claims that SWL no longer has a role in the management of upper urinary tract calculi are unfounded. Urologists should be selective when choosing SWL, but in the properly identified patient with a ureteral stone, SWL remains a beneficial therapeutic option with low morbidity and high patient acceptance.

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# 62

# Complications of Shock-wave Lithotripsy

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In comparison with percutaneous nephrolithotomy and ureteroscopy, data on extracorporeal shock-wave lithotripsy (ESWL) show that fewer complications occur for this procedure [1, 2]. To make differentiation easier, this chapter is divided into three parts: side effects, complications (which need medical intervention), and long-term effects. Other complications (cardiovascular and gastrointestinal) are rare.

## Side effects

Shock-wave lithotripsy (SWL) arguably has been the safest available surgical modality for stone removal in the decades since its introduction into clinical use in the 1980s. As with other stone removal modalities there are side effects, which cannot be counted as complications and are therefore listed separately.

### Hematuria

Hematuria following SWL is one of the most common findings and usually resolves within a few hours. The effect in vessels can be differentiated by measuring α2-macroglobulin enhancement found immediately after and 1 day following SWL [3–5]. Changes in specific hemostatic biomarkers in venous blood samples, at least during the first 4 hours post-SWL, underline this side effect [6].

### Detoriation of renal function

Several blood and urine markers can indicate possible renal injury shortly after SWL. Glomerular filtration rate, β2-microglobulin measures in serum and urine, as well as serum creatinine measures after SWL treatment suggest that ESWL does not have any long-term effect on the glomerular filtration rate; however, it leads to transient proximal tubular dysfunction for up to 7–9 days. Early retreatment, at least with piezoelectric sources, does not enhance several marker measures, in particular proteinuria. [5, 7]. Transient proteinuria, however, might last for up to 3 months until a return to baseline [8].

In an animal model it has been shown that small kidneys tend to show more tissue damage when exposed to SWL [9]. Looking at the smaller kidneys of children treated with SWL by analyzing urinary enzyme levels, the regeneration time of tubular function in children appears to be longer than for adults (14 versus 7 days) [10].

### Renal colic (manageable conservatively)

The probability of suffering from renal colic during fragments passing down the ureter appears to be about 2–4% [11]. However, it does depend in several predisposing factors, such as stone size. Most of these events can be managed by oral medication and should be counted as expected side effects. However, colic, including the development of steinstrasse, that requires intervention or emergency room visits is a complication and discussed later in the chapter.

## Complications

### Steinstrasse

Steinstrasse is an accumulation of stone fragments or stone gravel in the ureter, which does not pass within a reasonable period of time and interferes with the passage

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of urine [12, 13]. Steinstrasse occurs in 4–7% of cases following SWL [14–16], and the major risk factor for the formation of steinstrasse is stone size [15].

Although Coptcoat's classification of steinstrasse exists (Type I, fragments <2 mm in diameter; Type II, leading fragment 4–5 mm tailed by 2 mm particles; and Type III, consisting of large fragments), it is not widely used [13].

Clinically, steinstrasse can be symptomless or present with combinations of flank pain, fever, nausea and vomiting, or bladder irritation. Steinstrasse can cause obstruction of the ureter, which can be silent in up to 23% of cases [15] and can lead to failure of the function of the kidney [17]. In solitary kidneys anuria occurs in 5% of cases [15]. The insertion of a ureteral stent before ESWL might prevent formation of steinstrasse [18].

When steinstrasse is not symptomatic, conservative treatment is an initial option, depending on patient preference and the willingness to comply with a close surveillance schedule. Medical expulsive therapy might significantly increase stone expulsion rate and decrease need for endoscopic intervention [19, 20]. The patient should be informed about the controversial literature on medical expulsive therapy using alpha-blockers as well as its off-label use [21].

In cases where spontaneous passage is unlikely and interventional treatment becomes necessary, several options apply: SWL is one of the options in asymptomatic or symptomatic cases with no evidence of urinary tract infection, when large fragments of stones are presented [22]. There is an 80% chance of clearance of the steinstrasse [14].

Ureteroscopy is more effective but more invasive than SWL in treating steinstrasse (73–90%) [22–24].

Placement of a percutaneous nephrostomy tube is indicated in cases of symptomatic ureteric obstruction with or without urinary tract infection, and it is effective in 83% cases [14].

## Colic needing intervention

When conservative treatment of renal colic fails intervention therapy is indicated. Choosing the treatment method in cases when signs of urinary tract infection are not presented is based on size, location, and X-ray density of the blocking stone fragment. As in the treatment of ureteric stones, SWL or ureteroscopy is indicated [25]. Insertion of double-J stent or percutaneous nephrostomy tube is indicated in cases complicated by urinary tract infection.

## Infectious complications

Infectious complications of SWL are caused by renal trauma and vascular damage during SWL, facilitating bacteria to migrate into the blood vessels. Duvdevani et al. [26] showed in a prospective evaluation of 15 000 SWL treatments that bacteriuria after SWL occurred in 5.1% in spite of preoperative sterile urine. The most common pathogens were *Escherichia coli* (35.1%), *Pseudomonas aeruginosa* (16%), *Klebsiella pneumoniae* (12.8%), *Proteus mirabilis* (11.7%), *Enterococcus faecalis* (8.5%), and *Enterobacter cloacae* (4.3%). The risk of fever >38 °C, however, was only 1.4%. The probability of fever and bacteriuria is increased when an untreated or symptomatic urinary tract infection is present, a double-J catheter or nephrostomy tube is inserted, or when treating struvite stones (17.7 vs. 2.1%, $P < 0.05$) [27].

No standard antibiotic prophylaxis before SWL is recommended. However, in view of the abovementioned risk factors prophylaxis is recommended in the case of internal stent placement ahead of anticipated treatments and in the presence of increased bacterial burden (e.g. indwelling catheter, nephrostomy tube, or infectious stones) [28–30].

## Hematoma

On using computerized tomography routinely after SWL, perinephric soft-tissue stranding and fascial thickening were seen in up to70%. In addition, hematomas may be detected in 15%, being big in 2% [31], and using magnetic resonance subcapsular or perinephric fluid can be seen in up to 26% of cases [32]. Routine ultrasound after SWL detects hematomas in approximately 4%. The probability of developing a hematoma increases significantly with patient age. However, most of these changes remain asymptomatic [33]. The effect might depend on the lithotripter being used [34, 35].

Potential risk factors for hematoma development are any kind of coagulopathy including that induced by medication, hypertension, diabetes mellitus, coronary artery disease, obesity, and obviously age [35, 36].

In most cases hematomas are, or become, asymptomatic and might resolve within 2 years. Krishnamurthi and Streem followed 19 patients with post-SWL hematomas found on routine ultrasound for up to 61 months (mean 19.6 months). They showed a complete resolution of the hematoma in 85.7%, a significant reduction in 9.5%, and just one patient remained unchanged. There was no new onset or aggravation of pre-existing hypertension [37].

Stepwise voltage ramping can reduce the risk of developing hematomas (odds ratio 0.39, 95% confidence interval 0.19–0.80; $P = 0.01$) [38] in addition to considering the above mentioned risk factors [38].

## Cardiovascular complications

The incidence of cardiac of dysrhythmias varies from between 11 and 59% during ungated SWL [39, 40].

No correlation was mentioned between evidence of dysrythmias and type of lithotripter, number of shock waves, patient age, stone size and location, and type of anesthesia [39].

The incidence of morbid cardiac events or biochemical myocardial injury is extremely rare [41, 42].

Patients with a pacemaker can be treated with SWL, provided that appropriate technical precautions are taken; patients with implanted cardioverter defibrillators must be managed with special care (firing mode temporarily reprogrammed during SWL treatment). However, this might not be necessary with new-generation lithotripters [43, 44].

The SWL treatment in patients with aortic aneurysm is controversial. There are reports of rupture of aortic aneurysm due to SWL treatment [45, 46] and reports of safe treatment [47]. According to Tse et al.'s review of 18 SWL treatments in patients with aortic aneurysm, there is currently no high-level evidence to suggest that SWL in the presence of arterial aneurysm is unsafe [48]. However, an aneuryma in the vicinity of the stone and focal zone of SWL remain a contraindication for SWL treatment [36].

### Gastrointestinal complications related to SWL treatment

Gastrointestinal damage has been reported as a rare potential complication of SWL. The actual incidence is unknown. In a review, Maker and Layke reported 62 cases of gastrointestinal damage of 3423 patients (1.81%); only 28 (0.82%) were symptomatic, including nine bowel perforations [49]. The etiology of gastrointestinal damage is unknown; however, the majority of cases were reported in patients treated in prone position and with a higher number of applied shock waves [49].

Gastric and duodenal erosions recorded by pre- and post-ESWL endoscopy was found in 80% of the patients [50]. Ureterocolic fistula due to SWL [51] and dehiscence of gastrointestinal anastomosis [52] are reported, too.

Hepatic hematoma and spleen hematoma are rare complications of SWL. There were only 13 cases reported of hepatic [53] and seven of spleen hematomas [54, 55]. Due to the situation that the liver and spleen are intraperitoneal organs that lack a tough fascia, the need of surgical intervention is higher than in patients suffering post-SWL renal hematomas.

Elevation of serum amylase and lipase is presented in patients with acute pancreatic trauma. Only Kirkali et al. found significant elevation (but within physiological levels) of amylase and lipase in patients who underwent SWL of upper tract stones compared to patients treated for lower ureter stone [56]. There was no change recorded when treatment on newer generations of lithotripters was performed [57–59].

Case studies describe formation of a pancreatic abscess following SWL treatment for right renal stone [60] and pancreatitis after treatment in right and left kidney [61–63]. However, there is only a very limited number of cases described worldwide. A systematic review focusing on chronic calcified pancreatitis treated with SWL included 17 out of 31 studies and did not show any negative sequelae of SWL, like new onset of abscesses, although SWL was focused on pancreatic tissue [64].

## Long-term effects

### Diabetes mellitus

Looking at long-term effects, 19 years after SWL treatment Krambeck et al. performed a questionnaire-based evaluation of their patients treated in 1985 ($n = 578$, reponse rate 58.9%) and found an association of SWL treatment and the development not only of hypertension but also diabetes mellitus compared to a cohort of conservatively treated patients with nephrolithiasis [65]. This reflects the technology used 1985, however, and might differ from later research. In 2015 a systematic review on new-onset DM was performed including three case-control and two cohort studies out of 55 studies of a comprehensive search; a statistical association of SWL with new-onset of DM could not be found in the overall analysis [66].

### Effect on reproduction organs and pregnancy

Animal studies could not show any detrimental effect on sperm morphology [67]. A retrospective study following 84 women in reproductive age after SWL of distal ureteral stones suggests that SWL does not affect female fertility or lead to increased teratogenic risk [68]. SWL is contraindicated during pregnancy. Animal studies in mice showed decreasing number of surviving fetuses in proportion to increasing number of shock waves applied on the fetus, in particular during late pregnancy [69]. Shock waves targeted into the fetus of rabbits where fatal as well for the fetus in another study; however, fetuses outside the focal zone were vital and free of lesions; embryotoxic or teratogenic sequalae could not be shown in this study [70]. Case reports of successful delivery of healthy babies even when inadvertently treated with SWL because of distal ureteral [71] or renal [72] stones underline the importance of further research.

### Hypertension

Results of retrospective studies suggest an increase on developing diastolic hypertension following SWL

[73, 74], which is in contrast to prospective studies. Prospective observational studies were published in 1992 including 68 patients followed for 36 months after SWL treatment using a modified Dornier HM3 lithotripter; compared to first measurements 15 days prior to SWL-treatment no significant increase of mean diastolic blood pressure was seen [75]. Jewett et al. randomized patients with asymptomatic calyceal stones smaller than 2 cm to receive immediate SWL versus observation and followed them for a longer period (mean 22 months); they found no difference in new onset of hypertension. In contrast they demonstrated a decrease of mean diastolic blood pressure in the treatment group ($P < 0.03$); the results were independent of patient's age [76] and the SWL energy source used was electromagnetic. In a similar study Elves et al. randomized patients with stones up to 15 mm and followed 200 of them for at least 1 year, and a mean of 2.2 years. They found no evidence that SWL treatment causes changes in blood pressure; they used two different lithotripters [77].

Another prospective study used 24 hour ambulatory blood pressure monitoring; they studied 60 kidney stone patients and 30 patients with distal ureteral stones, all treated with SWL (Dornier HM4) and another group of patients with ureteral stones treated with ureteroscopy. After 1 year of follow-up they found a significant decrease in blood pressure values in the patient group treated for kidney stones, which was related to the power and number of shock waves. The authors speculated that these changes possibly were caused by alterations in intrarenal metabolism [78].

According to a meta-analysis including 11 studies, published by Yu et al., no statistical significance was detected between SWL and new-onset hypertension (relative risk 1.06, 95% confidence interval 0.83–1.35) [79].

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# SECTION 5

# Stone Management in Urology

# Part 1 General Principles

## 63

# Natural History of Stones

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## Introduction

Technologic advances in the surgical and medical therapy of urinary stone disease over the last three decades have allowed urologists to offer numerous treatment options for symptomatic and asymptomatic upper tract urinary stones. As with any disease, one of the options to be entertained is that of active surveillance/observation for asymptomatic stone disease. Observation is a reasonable approach and an often desired treatment option by the patient to limit costly and potentially painful interventions. However, before choosing observation physician and patients alike must be aware of the potential ramifications of leaving upper tract stones untreated in a variety of different clinical scenarios. In order to assist the urologist in best advising their patient on the risks and benefits of observation, this chapter discusses the natural history of urinary stones, both naturally occurring stones and the residual fragments present after prior treatment.

## Natural history of asymptomatic renal stones

The worldwide increase in the incidence and prevalence of stone disease has been attributed, in part, to the incidental detection of asymptomatic calculi secondary to escalating utilization of three-dimensional radiographic imaging [1, 2]. For example, an Icelandic population study found the annual incidence of stones among the population increased significantly from 108 to 138 per 100 000 over a 5 year period. However, the increase entirely was due to an increase in incidental stones detected at the time of imaging for a concurrent illness, from 7 to 23 per 100 000 with no significant increase in symptomatic stones [2].

Other observational studies have demonstrated a nearly 10% incidence of asymptomatic stones in the general population and thus some insights into the prevalence of asymptomatic renal stones can be obtained from these screening studies. In a series of 5000 patients undergoing screening computed tomography (CT) colonography urinary stones were found in 7.8% of patients, with a mean size of 3 mm and an average of two stones per patient [1]. Similarly, in a series of 2000 CT scans of kidney donors 9.7% harbored asymptomatic stones [3]. Although not the best imaging study for stone evaluation, a prospective renal ultrasound screening trial of 201 patients in Pakistan without a known genitourinary disease found a 3% rate of asymptomatic renal stones [4].

Once the incidental diagnosis of an asymptomatic stone is made, patients will require counseling regarding the implications and clinical relevance. At least ten studies have reported the outcomes of observing asymptomatic renal stones [1, 5–13] (see Table 63.1). These studies vary in population size and demographics, as well as stone location and number. Follow-up periods for the studies ranged from 1.6 to 10.0 years (median 3.4 years), but collectively they observed the outcome of more than 1800 asymptomatic renal stones, providing significant insight into the natural history of asymptomatic upper tract urinary stones.

Interval growth determined by follow-up imaging was reported in four studies (see Table 63.1). Hübner and Popaczy looked at 62 patients in 1990, with a mean follow-up of 7.4 years. Interval stone growth was seen in 28 (45%) patients and eight (13%) developed into staghorn

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**Table 63.1** Growth of asymptomatic renal stones treated with observation therapy.

| Study | *n* | Portion of stones that grew (%) | Average growth among growing stones (mm/year) | Spontaneous passage (%) | Symptomatic stone events (%) | Surgical intervention (%) | Follow-up (years) |
|---|---|---|---|---|---|---|---|
| Hübner and Popaczy [5] | 62 | 45 | – | 16 | 51 | 40 | 7.4 |
| Glowacki et al. [6] | 107 | – | – | 15 | 32 | 17 | 2.6 |
| Keely et al. [7] | 288 | – | – | 17 | 21 | 10 | 2.2 |
| Burgher et al. [8] | 300 | – | – | – | 45 | 26 | 3.3 |
| Inci et al. [9] | 24 | 33 | 1.7 | 13 | 11 | 11 | 4.3 |
| Boyce et al. [1] | 395 | – | – | – | 21 | – | 10.0 |
| Yuruk et al. [10] | 94 | – | – | 3 | 19 | 19 | 1.6 |
| Koh et al. [11] | 50 | 46 | 0.7 | 20 | 24 | 7 | 3.8 |
| Kang et al. [12] | 347 | – | – | 29 | 54 | 5 | 2.6 |
| Dropkin et al. [13] | 160 | 21 | – | 8 | 28 | 17 | 3.4 |

**Table 63.2** Summation of risk factors for clinical progression of asymptomatic stones.

| Risk factor | Stone growth | Spontaneous passage | Symptomatic stone event | Surgical intervention |
|---|---|---|---|---|
| Male gender | – | – | ↑ | – |
| Advanced age | – | ↓ | – | – |
| Larger stone size | ↑ | ↓ | ↑ | –/↑ |
| Upper pole/interpolar location | – | ↑ | ↑ | – |

stones [5]. Inci and colleagues followed 27 renal units with 2–12 mm stones every 2 years with a CT scan and found that 30% of stones grew by a mean of 4.4 mm (98% increase in size) at 2 years. Furthermore, 33% had grown by a mean of 7.2 mm (132% increase in size) at last follow-up (mean 4.3 years) [9]. In contrast, a study by Koh and colleagues found that 46% of stones grew, but only by 2.8 mm over 3.8 years [11]. Dropkin and colleagues reported 21% of stones grew by more than 50% of their initial size in 2 years [13]. Thus, the studies demonstrate varying degrees of stone growth over time, with some demonstrating significant stone size increases. When looking at risk factors for stone growth, two studies found no significant association between initial stone size or location and stone growth [9, 11], whereas the third found stones larger than 15 mm to grow at a slower rate than smaller stones [8]. In summation 21–46% of stones are found to grow on repeat observation. Average growth rates range from 0 to 2 mm per year [9].

In the patient with asymptomatic renal calculi undergoing observation, subsequent development of renal colic, flank pain, or other symptoms prompting further medical intervention has been recognized and is of significant concern. In 10 studies, the rate of such symptomatic stone events was 11–54% (follow-up range 1.6–10.0 years) [1, 5–13] with a cumulative event rate of 33% (see Table 63.1). Glowacki et al. estimated the risk of a symptomatic stone episode or need for intervention to be approximately 10% per year, culminating in 49% of patients having a stone event 5 years after their initial diagnosis of an asymptomatic renal calculi [6]. Spontaneous stone passage rates were recorded in eight studies and ranged from 3 to 29% (median 16%, cumulative rate 18%) [5–7, 9–12]. Surgical intervention rates were 5–40% between studies (median 17%, cumulative rate 15%) [1, 5–7, 9–13]. Specifically, the study by Burgher et al. found that 25% underwent surgery at 5 years and 50% at 7 years [8].

The observed differences in reported rates of spontaneous passage versus surgical intervention (e.g. from 3% passage and 19% intervention [10] to 29% passage and 5% intervention [12]), are in part due to differences in patient population such as age, gender, and stone size. Therefore, some work has gone into identifying risk factors of disease progression in asymptomatic renal stones. Studies focusing on risk of symptomatic stone events in patients with incidentally detected renal stones are summarized in Table 63.2.

## Demographic factors

Kang et al. looked at demographic factors affecting subsequent symptomatic stone events in patients with asymptomatic stones. Age, stone history, stone location (laterality and calyceal location), multiplicity, familial history, and body mass index were not found to be significant risk factors; however, men were more likely to have symptomatic stone events then women (hazard ratio 1.52). Furthermore, younger patients were more likely to spontaneously pass stones than older patients [12].

## Size

Stone size appears to be a significant factor for disease progression. Burgher et al. found that 100% of stones over 15 mm at time of detection would grow (71%), cause pain (57%), or necessitate surgery (29%). They also found that stones greater than or equal to 4 mm were 26% more likely to fail observation than smaller stones [8]. Another study found that stones measuring 5 mm or less were significantly more likely to spontaneously pass compared to stones that were larger in size (28 vs. 4%) [11, 12]. However, the authors found no association between stone size and need for intervention [11].

## Location

Prior studies have failed to identify any significant association between stone location and stone symptoms, spontaneous passage, or need for intervention. However, a more recent study by Dropkin et al. reported that upper pole and interpolar renal stones were more likely than lower pole stones to become symptomatic (40.6 vs. 24.3%) and more likely to pass spontaneously (14.5 vs. 2.9%) [13].

## Observation versus treatment

Raman and Pearle conducted a meta-analysis seeking optimum management of lower pole calculi. Their study revealed that patients with lower pole stones larger than 2 cm treated with percutaneous nephrolithotomy experienced less morbidity than those treated with other modalities. However, consistent with other previous studies, they also concluded that lower pole stones less than 1 cm may be observed with equivalent morbidity outcomes as shock-wave lithotripsy (SWL) and ureteroscopy with laser lithotripsy. The authors also noted observation to have the least cost and surgical risk of the available management strategies [14].

It should be noted that while the vast majority of interventions are performed for symptomatic events, not all events were symptomatic. In one study 2% of patients with asymptomatic renal calculi treated with observation developed silent obstruction and hydronephrosis identified on surveillance imaging leading to intervention [13]. Such findings, although rare, support the role for continued imaging observation for patients with asymptomatic renal calculi treated with conservative management. At a minimum, periodic renal ultrasound will provide information on the presence of hydronephrosis with minimal risk and no radiation exposure to the patient.

Although observation is an attractive treatment option for the above-noted reasons, the American Urological Association (AUA) guidelines on the surgical management of stone disease state that there are certain settings for which observation of asymptomatic renal calculi should not be considered. These settings include: cases of associated infection, vocational reasons in which an acute stone event would be detrimental (such as airline pilots, military), and poor access to contemporary medical care [15]. In such clinical scenarios consideration should be given to active surgical intervention to remove the stone.

## Natural history of staghorn calculi

A staghorn calculus is a term used for stones that occupy all or most of the renal collecting system in a branching fashion. These large branching stones are relatively rare, accounting for 1% of all symptomatic first-time stone events [16]. Staghorns most often involve the renal pelvis and extend into the infundibula and calyces [16]. Branched stones that occupy only a part of the collecting system are called branched stones or partial staghorns. Unlike the non-staghorn, nonbranched asymptomatic stones discussed earlier in the chapter these branching stones are often associated with infection and have quite an ominous natural course. If left untreated, a staghorn stone has a high likelihood of resulting in a nonfunctioning kidney, severe systemic infections, malignancy, or even patient death [15, 17–19].

Compelling observational data exist from before the current era of endourology. A study from 1976 looked at 60 staghorn patients treated with observation alone. The overall mortality rate in these staghorn calculi patients treated with observation was 28%, of which nine (15%) patients died of renal failure, four (7%) developed renal pelvis carcinoma, and 16 (27%) life-threatening pyonephrosis [17]. Another study from the same era found that nine of 30 (30%) patients treated conservatively for a staghorn calculus died of renal failure or urosepsis [18]. In a pathology-focused study, examination of kidneys removed due to staghorn stones found that 49% demonstrated significant renal parenchyma pathology. The findings included pyonephrosis (20%), xanthogranulomatous pyelonephritis (8%), severe or end-stage pyelonephritis (13%), end-stage hydronephrosis (7%), and perinephric abscesses (5%) [19]. A more recent study from the early 1990s of patients with conservatively treated staghorn stones found that 36% developed chronic renal failure and 11% died from uremia [20]. Furthermore, in a study from 1995, the early era of endourology, found none of 77 patients treated for staghorn stone and rendered stone-free died of renal disease at a mean follow-up of 7.7 years, compared to one of 35 (3%) with residual stone fragments after treatment and two of three (67%) of those treated conservatively [21].

In light of this unequivocal evidence against observation of staghorn calculi, published guidelines have since strongly advised for the complete surgical removal of staghorn stones in all patients fit to undergo surgery [15, 22].

A caveat in discussing the natural history of staghorn stones is that the most extensive data come from an era where the majority (59–68%) of staghorn stones were infection-stone compositions such as struvite. More contemporary series indicate that metabolic stones now account for 56% of staghorn stones, with calcium phosphate accounting for the majority [19, 23–25]. The natural history of metabolic stones may potentially be different from that of infection stones, and thus the natural history in the current era could differ from decades ago.

A 2015 study looked prospectively at 22 minimally symptomatic or asymptomatic staghorn stone patients who were treated conservatively, either because they were unfit or unwilling to undergo surgery. Among the

17 patients who had a unilateral staghorn stone, recurrent urinary tract infections occurred in seven (41%) patients, one (6%) required dialysis, and none died of renal disease or renal-related conditions at a median follow-up of 6 years. Such observed outcomes are notably better than in prior series. However, among five patients with bilateral staghorn stones, 80% had recurrent urinary tract infections, 20% required dialysis, and 40% died of renal disease [26]. The contemporary results can be compared to a recent series reporting long-term outcomes of percutaneous nephrolithotomy for staghorn stones in patients with reduced renal function at presentation. The authors found that 20% of patients had a decline in renal function postoperatively, but only three of 262 (1.8%) of patients developed end-stage renal failure at 3 years of follow-up [27]. Despite the more recent promising results of observation for staghorn calculi, active treatment is still recommended by the AUA and Endourology Society if the patient is healthy enough for surgical intervention [15]. The guideline recommendations are based on the fact that minimally invasive treatment of staghorn calculi with percutaneous nephrolithotomy is highly successful with minimal morbidity in most scenarios.

## Natural history of asymptomatic ureteral stones

While the renal pelvis and calices are capacious and can frequently accommodate stones without causing significant obstruction, the ureter is smaller in diameter and a stone in this location would be more likely to result in symptoms and/or obstruction. In fact, only 1.1–5.3% of all treated ureteral stones are silent [28, 29]. As previously mentioned, silent ureteral stones have been subsequently found in 2% of patient undergoing surveillance imaging who were on observation for asymptomatic renal stones. The population incidence of silent ureteral stones among subjects without a history of known stone disease is low. Among 5047 patient undergoing screening CT colonography only six (0.1%) were found to have an incidental silent ureteral stone [1]. Given their rare presentation, very limited data exist regarding spontaneous passage rates among asymptomatic ureteral stones with one study reporting one of 40 (2.5%) patients passing their stone before a scheduled surgery date [28]. Wimpissinger and colleagues [30] prospectively looked at 14 asymptomatic ureteral stones. They found 11 (76%) kidneys to be associated with hydronephrosis on imaging and on MAG3 scintigraphy and of the 11 kidneys with hydronephrosis, five (36%) were unobstructed, seven (50%) were obstructed, and two (14%) had no excretory function. There was a positive correlation between stone size and likelihood of obstruction, with larger stones more likely to result in complete obstruction or no excretory function [30]. Based on this limited data, most physicians should consider only a short trial of passage, 6 weeks or less per AUA and Endourology Society guidelines [15], with scheduled follow-up imaging to assess for definitive stone passage if observation is chosen for the asymptomatic ureteral calculi.

## Natural history of symptomatic ureteral stones

Symptomatic ureteral stones often call for intervention given infections, intractable pain, or adverse effects on renal function. It is, however, well documented that a large portion of ureteral stones pass spontaneously. Ample data exist from control arms of trials for medical expulsive therapy on the natural history of passage of symptomatic ureteral stones. A meta-analysis reported in the 2016 AUA and Endourology Society guidelines on surgical management of stone disease looked at 25 studies conducted from 2002 to 2015 on medical expulsive therapy for distal ureteral stones less than 10 mm in size. Combined, 1100 stone patients were in the control arms and underwent trial of passage without medical expulsive therapy. The cumulative stone passage rate in the control arms was 57% (range 4–88%, median 53%). Follow-up in the majority of studies was most commonly 4 or 6 weeks [15]. Fewer data were available on proximal and mid-ureteral stones and thus the guideline panel could not make strong conclusions based on the use of medical expulsive therapy for such stones. However, studies comparing stone passage based on ureteral location found that spontaneous passage occurs in 12–48% of proximal stones, 22–81% of mid-ureteral stones, and 45–96% of distal stones [31–34]. Stones at the ureterovesical junction pass in 43–79% [33, 35].

Stone size is also known to affect likelihood of passage. Ueno and colleges in 1977 [36] correlated stone size on plain X-ray by 1 mm increments with stone passage rate and Coll and colleagues in 2002 [33] similarly correlated the maximal stone diameter in the axial plane on helical CT with passage rates (see Table 63.3).

Factoring in stone size and location, Ahmed and colleges identified that at 45 days the passage rate for stones less than or equal to 5 mm was 50, 93, and 97% for proximal, mid, and distal ureter respectively and for stones greater than 5 mm it was 25, 65, and 95% for the same ureteral segments [31–34].

Additional CT imaging findings, such as higher three-dimensional stone volume and axial surface area, as well

**Table 63.3** Likelihood of ureteral stone passage based on size on imaging.

| | Passage rate (%) | |
|---|---|---|
| Stone size (mm) | Ueno et al. [36], abdominal X-ray | Coll et al. [33], CT |
| 1 | 100 | 87 |
| 2 | 93 | 72 |
| 3 | 87 | 83 |
| 4 | 78 | 72 |
| 5 | 57 | 60 |
| 6 | 35 | 72 |
| 7 | 28 | 74 |
| 8 | 14 | 56 |
| 9 | 0 | 33 |
| 10 | 0 | 27 |

as perinephric fat stranding and tissue-rim sign (potentially signs of stone impaction), have been reported to translate into a lower likelihood of spontaneous stone passage [34, 37–40]. However, data on the effect of hydronephrosis and elevated markers of inflammation on stone passage have provided inconsistent results [34, 38, 41, 42].

Hydration appears to have a limited effect on stone passage. While canine research data suggested that renal increased hydrostatic pressure was a primary driver for stone expulsion, a clinical study on forced intravenous fluid hydration have shown no improvement in spontaneous stone passage rates compared to normal hydration status [43, 44]. Limited data suggest that spontaneous stone passage is less likely in tobacco smokers, especially for stones larger than 4 mm [45]. Finally, a single series suggests that sexual intercourse three or four times a week increases stone passage rate for smaller distal stones [46]. The symptomatic ureteral stone has numerous treatment options including observation, medical expulsive therapy, SWL, and ureteroscopy. As with asymptomatic ureteral stones, if observation is chosen, a scheduled follow-up imaging to assess for definitive stone passage is needed to avoid the serious downstream effects of an obstructing asymptomatic stone [15].

## Natural history of ureteral stones after stent placement

In various clinical scenarios, such as in the setting of an obstructing stone with concomitant infection or deterioration of renal function, insertion of a ureteral stent with planned delayed stone removal is considered the standard of care. In rare instances the obstructing stone may pass while the temporizing ureteral stent is in place; however, such scenarios are not common and limited clinical data exist. Animal studies have shown that the presence of ureteric stents is associated with ureteric dilatation, diminished ureteric peristalsis, and impaired stone passage [47, 48]. Taha et al. report a clinical series where patients were stented for a mean of 3 months for acute obstructing stone indications. A CT scan was performed at follow-up prior to definitive stone treatment. Notably, 41% of the stones were no longer present on follow-up imaging. All the disappearing, or spontaneously passed stones were smaller than 6 mm and 70% were radiolucent on initial CT scout film imaging and thus were potentially uric acid stones. Patients on urinary alkalization therapy were not excluded and therefore stone dissolution may account for some of the missing stones. Among radiopaque stones, only 22% passed, all of them smaller than 6 mm [49]. Such stone passage rates are significantly lower than the 57% or higher spontaneous passage rates among ureteral stones on observation (see Table 63.3) [33, 36]. Thus, it can be concluded that in most scenarios placement of a ureteral stent hinders stone passage.

## Natural history of residual calculi after shock-wave lithotripsy

Treatments of stone disease are among the most common urological interventions, and for ureteral stones shock wave lithotripsy (SWL) is one of the most widely utilized treatment modalities. Therefore, the natural history of residual stone fragments after surgical intervention is of significant concern. As with incidentally identified asymptomatic stones treated with observation, residual fragments after surgical intervention are subject to growth, symptomatic events, and possible need for further surgical interventions. To date, the most data on residual fragments after surgical intervention exist for SWL. SWL by design does not remove stones and leaves the patient prone to residual fragments. SWL fractures the stone into small fragments that must then be expelled naturally down the ureter. Most stone fragments are expelled; however, in the best treatment scenarios at 3 months' follow-up 23–36% of patients will still harbor residual fragments [50–52]. Residual fragments are often treated, with an average of 1.26–1.34 treatments needed to reach a stone-free state, based on size and location [15]. Some authors historically advised for observation of fragments less than 4–5 mm [50].

Of these patients with remaining fragments at 3 months' postprocedure follow-up, the likelihood of eventual stone fragment clearance is low. In fact, Candau and colleagues found that of patients with a 4 mm stone or less at 3 months, 66% still had a stable or larger residual fragment 40 months later [53]. It had been suggested that the presence of non-infection, nonobstructive, asymptomatic postprocedural residual fragments <4 mm could be managed metabolically in order to prevent stone growth adequately, sometimes referred to as "clinically insignificant fragments." However, based on data from Candau and other authors the idea of clinically insignificant fragments should be considered a misnomer [53–55].

At least seven studies have looked at fragment growth after SWL in adult populations (see Table 63.4), with follow-up ranging from 15 to 89 months. Depending on the study, regrowth or increase in size occurred in 2–55% of patients (median 18%) [51, 53, 55–59]. When compared to other surgical interventions such as percutaneous nephrolithotomy or ureteroscopy, symptomatic stone recurrence rates appear to be higher after SWL for similar-sized stones [60]. It has been postulated that high recurrence rates after SWL may be the results of microscopic stone particles migrating to dependent calyces and acting as a nidus for new stone formation. Thus, by increasing the surface area of the original stone, SWL may favor new stone growth through heterogeneous nucleation and crystal aggregation by exposing the stone area to a lithogenic environment [61]. Accordingly, numerous reports suggest that controlling metabolic factors post-SWL substantially affect stone recurrence rates [52, 62, 63].

In addition to contributing to stone recurrence, sizeable residual fragments may cause clinically significant events. As with recurrence numbers, reported symptomatic events and complication secondary to residual stone fragments after SWL range widely from 0 to 59% (see Table 63.4) [4, 57]. In a review by Khaitan and colleges of 75 patients with less than or equal to 4 mm residual stone fragments 3 months after SWL, 24% passed them spontaneously and 17% remained stable, whereas 59% developed one or more complications. Within the 59% with complications, 35 had pain, five had recurrent urinary tract infections, four had ureteric obstruction, and two hematuria [57]. By contrast Osman and colleges followed 175 with less than 4 mm fragments and reported that 21% required subsequent intervention, but all interventions were for stone fragment growth [55]. In a contradictory report by Buchholz and colleges "no patient reported any serious discomfort caused by the residual during the follow-up period" [56]. The differences among studies are likely in part explained by the timing and nature of the follow-up, as design differed notably between the studies. With regards to intervention, not all studies clarify whether interventions were done for a symptomatic event, asymptomatic presence of fragments, regrowth, or combination thereof.

Most prior studies have focused on the outcome of residual fragments less than 4 mm in size, possibly given that this size has been considered "clinically insignificant" and a residual fragment of such size is considered a success after SWL. A more recent study looked at the clinical significance of even smaller fragments. This study compared residual fragments less than or equal to 2 mm to those 2–4 mm after SWL [56]. At 3 months, all fragments 2 mm or less passed spontaneously without a need of an emergency department visit as compared to 76% stone-free rate among 2–4 mm fragments. Furthermore, 19% of the patients with residual fragments 2–4 mm in size presented to the emergency department for treatment of renal colic [64]. The number of stones treated, as well as their size, understandably affects the likelihood of fragment passage [57].

**Table 63.4** Symptoms, intervention, stone-free rates, and stone regrowth after shock-wave lithotripsy.

| Study | Remained asymptomatic without intervention (%) | Symptomatic events (%) | Required intervention (%) | Stone-free (%) | Stone regrowth (%) | Months of follow-up |
|---|---|---|---|---|---|---|
| Streem et al. [59] | 57 | 43 | 28 | 36 | 18 | 89 |
| Zanetti et al. [51] | NR | NR | NR | 56 | 7 | 24 |
| Buchholz et al. [56] | 100 | 0 | 0 | 87 | 2 | 30 |
| Candau et al. [53] | NR | NR | 22 | 33 | 37 | 40 |
| Khaitan et al. [57] | 41 | 59 | 32 | 24 | 55 | 15 |
| Osman et al. [55] | NR | NR | 21 | 79 | 10 | 60 |
| El-Nahas et al. [58] | 52 | 15 | 48 | 13 | 34 | 31 |
| Sahin et al. [64] | 79 | 19 | 21 | 79 | NR | 3 |

NR, Not reported.

Factors other than residual fragment size can affect the eventual clinical outcomes. Residual fragment location on postoperative imaging after SWL also appears to affect the likelihood of fragment passage. Zanetti and colleges found that patients with lower pole fragments after SWL only becomes stone free in 39% of cases at 12 months of follow-up as compared to 59% of interpolar calyx fragments and 70% of upper pole calyx fragments [51]. Similarly, looking at residual fragments 5 mm or less, Buchholz and colleges found that 2.5 years after SWL 12.5% of patients still harbored residual fragments. All upper pole, interpolar, and renal pelvis stones had cleared and two-thirds of the remaining stones were in lower pole calyces and one third were in the proximal ureter.

Finally, expulsion of fragment is inherently dependent on the absence of distal obstruction, such as another stone or ureteral stricture. In fact, the AUA/Endourology Society guidelines statement on the surgical management of stone disease states that SWL should not be performed in the presence of distal of obstruction.

## Natural history of residual calculi after ureteroscopy

Although SWL has historically been the most frequently utilized treatment modality for upper tract stone disease, due to high single treatment success rates and low overall morbidity, ureteroscopy has overtaken SWL as the preferred treatment modality. With ureteroscopy, stones are extracted, fractured, and extracted or dusted with the fragments left to pass spontaneously similar to SWL. Based on ureteroscopic technique as well as timing and type of follow-up imaging, stone-free rates have been reported anywhere from 53 to 97% [65]. Given the potential for deleterious effects observed for post-SWL residual fragments, it is important to identify if the same concerns hold true for postureteroscopy residual fragments. Unlike SWL where multiple studies are available, limited data exist on the fate of residual fragments after ureteroscopy (see Table 63.5).

Rebuck and colleagues looked at 51 patients with fragments of 4 mm or less after ureteroscopy followed with routine serial CT scans over 19 months. The authors found that 22% of the patients spontaneously passed their residual fragments, 19% had a symptomatic event, and the remaining 59% retained their fragments without symptoms. The patients who developed symptomatic events had interval growth of fragments on CT scans leading up to the event, whereas those who remained asymptomatic had no interval growth [66]. Chew and colleges performed a multi-institutional retrospective study on 232 patients with any size of fragment after ureteroscopy. The authors reported higher symptomatic event and intervention rates than previous studies. Despite no difference in the likelihood of passage when comparing fragments smaller or larger than 4 mm, the larger fragments were more likely to grow with time, were associated with significantly more complications and required more re-interventions. Fragments smaller than 2 mm were less likely to grow compared to larger fragments, but were just as likely to pass, cause complications, or lead to interventions. Of note, the authors found that dusting versus active extraction of fragments did not statistically affect the risk of re-intervention [67]. Based on these findings, removal of residual fragments after ureteroscopy noted on follow-up imaging should strongly be considered if they are 4 mm or larger in size.

## Natural history of residual calculi after percutaneous nephrolithotomy

Percutaneous nephrolithotomy offers the highest stone-free rate of any procedure [15]. When residual fragments are identified with postoperative imaging they are frequently removed with a second-look percutaneous nephrolithotomy or ureteroscopy. However, despite the surgeons' best efforts, residual fragments after percutaneous nephrolithotomy do occur. Ganpule and Desai reported a series of 187 patients with residual fragments after percutaneous stone removal, of which 67% of patient passed their fragments in the first 3 months. Fragments less than 25 mm$^2$ in size and those situated in the renal pelvis had the best chance of clearance [68]. Other studies have looked at the longer-term clinical

**Table 63.5** Symptoms, interventions, and stone-free rates after ureteroscopy.

| Study | Remained asymptomatic without intervention (%) | Symptomatic events (%) | Interventions (%) | Stone-free (%) | Months of follow-up |
|---|---|---|---|---|---|
| Rebuck et al. [66] | 81 | 19 | 12 | 41 | 18.9 |
| Chew et al. [67] | 56 | 44 | 29 | 27 | 16.8 |

**Table 63.6** Symptoms, intervention, and stone-free rates after percutaneous nephrolithotomy.

| Study | Remained asymptomatic without intervention (%) | Symptomatic events (%) | Interventions (%) | Stone-free (%) | Stone growth (%) | Months of follow-up |
|---|---|---|---|---|---|---|
| Ganpule and Desai [68] | – | – | – | 33 | – | 3 |
| Raman et al. [71] | 57 | 43 | 26 | – | – | 41 |
| Altunrende et al. [70] | – | 26 | – | 8 | 21 | 28 |
| Xin et al. [69] | – | 31 | – | – | – | 31 |

sequelae of residual fragments after percutaneous nephrolithotomy, with symptomatic events occurring between 26 and 43% of cases (see Table 63.6) [68–71]. Raman and colleagues identified that on multivariate analysis only maximum residual fragment size larger than 2 mm and location in the renal pelvis or ureter independently predicted a symptomatic stone event. In the same study 8% of patients with residual fragments less than 2 mm in size underwent surgical retreatment compared to 53% of patients with residual fragments greater than 2 mm. Thus, they concluded that second look flexible nephroscopy may be of benefit in patients with residual fragments larger than 2 mm or in those with fragments located in the renal pelvis or ureter [71]. Xin and colleagues verified these findings regarding residual fragment size after percutaneous nephrolithotomy and need for subsequent intervention. Interestingly, the authors added that in addition to residual stone fragment size, a past history of SWL increased the risk of symptomatic stone events for residual fragments after percutaneous nephrolithotomy [69].

Only one study has reported stone regrowth rates after percutaneous nephrolithotomy. In the study by Altunrende and colleagues stone regrowth after percutaneous nephrolithotomy occurred in 21% of patients followed over 28 months [70]. These findings are consistent with a study comparing new stone formation after either SWL or percutaneous nephrolithotomy, which found 22% of patients developing new renal stones within 2 years of the procedure [60].

## Natural history of asymptomatic stones and residual fragments in children

The bulk of the abovementioned literature comes from adult patients; however, data are emerging on observation of asymptomatic stones in children. A retrospective study of renal ultrasound studies found that asymptomatic renal stones in children will neither grow nor cause symptoms in (21%), not pass spontaneously (5%) or require intervention (25%) [72].

Recently two studies have also been published on residual fragments after stone treatment in children. Dincel and colleges followed 22 children aged 1–17 years (mean 9 years), who had residual fragments of 4 mm or less after SWL, percutaneous nephrolithotomy, or ureteroscopy. Spontaneous passage of the residual fragment occurred in 26% of the children regardless of the primary treatment. Acute symptoms occurred in 40% of children with residual fragments after surgical intervention. Stone growth occurred in 21%. Subsequent surgical intervention was needed in 29% of the children for either acute symptoms or stone regrowth [73]. Similarly, El-Assmy and colleges looked at 42 children with a median age of 6 years (range 1–14 years) who had less than or equal to 4 mm residual fragment after either SWL or percutaneous nephrolithotomy. While 69% of the children passed fragments spontaneously or had asymptomatic fragments without growth, 32% had an acute stone event or significant stone growth. Furthermore, secondary surgical procedures were required in 16% of the children [74]. Taken in total, it must be concluded that small residual fragments are quite clinically relevant in children and should be followed closely.

## Conclusion

The incidence of asymptomatic stones is increasing, most likely due to the wide availability of sensitive imaging techniques. Observation of asymptomatic renal calculi is a reasonable treatment option, but the patient and physician must be aware of the risks of stone growth, symptomatic events, and need for subsequent surgical intervention. The risk of the asymptomatic calculi becoming symptomatic in both the adult and pediatric population is dependent on many factors, which must be weighed when determining if observation is appropriate. Likewise, when residual fragments are noted after surgical intervention, there is a risk of subsequent stone regrowth or symptomatic events. However, with appropriate counseling and follow-up the asymptomatic stone can be safely observed in the appropriately selected patient.

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# 64

# Initial Choice of Therapy in the Stone Patient

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## Introduction

Urolithiasis is a prevalent condition, afflicting nearly 10% of the US population [1]. Cost estimates for stone management range from US$2 billion to $10 billion annually in the American healthcare system [1, 2]. As the front line in managing stone disease, the urologist is armed with numerous tools to manage a patient presenting with a urinary stone. This chapter will focus on adult patients with "normal" renal anatomy, as stones in aberrant urinary systems are discussed in Chapters 67–71. Since the focus is elective stone management, patients presenting with sepsis, renal failure, or intractable pain are not discussed, as these situations dictate urgent urinary tract decompression with either ureteral stenting or percutaneous nephrostomy and are described in Chapter 66. The prime modalities discussed are shock-wave lithotripsy (SWL), ureteroscopy/ureterorenoscopy (URS), percutaneous nephrolithotomy (PCNL), medical expulsive therapy (MET), and observation.

## Overall approach

Most urologists confront ureteral stones acutely and renal stones in a less urgent fashion. As such, the primary issue facing the urologist treating a patient with a ureteral stone, after insuring appropriate pain management, renal function, and that systemic inflammatory response syndrome (SIRS)/sepsis is not an issue, is to determine if spontaneous passage is likely or not. When faced with a renal stone, decision-making is often less pressed and selecting the optimal surgical approach is paramount to assure the best chance of success.

A recent *New England Journal of Medicine* article by Smith-Bindman et al. provided some insight into the rate of urgent intervention needed when patients present to the emergency department with renal colic [3]. Nearly 10% of patients seen initially for renal colic require hospital admission for pain management and/or surgical intervention. In the month following initial evaluation, another 10–15% will present back to the emergency department and one-third of these patients will require hospital admission [3]. This highlights that although some patients need urgent intervention, many will semi-electively end up seeing a urologist where a plan for observation or intervention will be created.

## Ureteral stones

Although some data have come to light questioning the efficacy of MET [4], the general paradigm for managing ureteral stones involves observation with or without MET for most stones and if that fails proceeding to a URS or SWL. Rarely will an antegrade/percutaneous or laparoscopic/robotic/open approach be needed for these stones.

### Distal ureteral stones

Stones in the distal ureter are among those with the highest rate of spontaneous passage [5, 6]. The ureterovesical junction (UVJ) remains a common site for stones to become lodged, as it is the narrowest part of the ureter (Figure 64.1a). Generally speaking, smaller stones that are further along the ureter have a greater chance of spontaneous passage than larger stones in a

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Companion website: www.wiley.com/go/smith/textbookofendourology

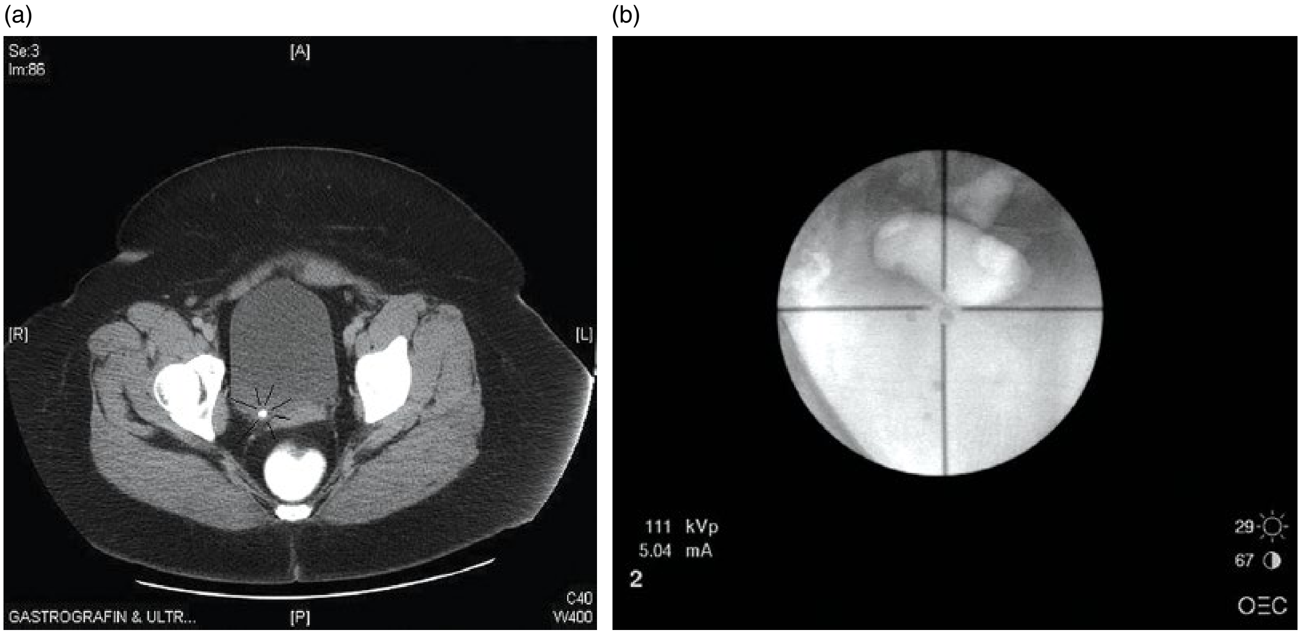

**Figure 64.1** (a) Computed tomography (CT) of right distal ureteral calculus at the UVJ (demarcated by lines). (b) Fluoroscopy of right distal ureteral stone localized at the F2 focal point for shock-wave lithotripsy.

more proximal location. Although it is difficult to tell the exact fate of any given stone, there is ample evidence that the majority of stones under 4–5 mm often pass [5, 6]. Additionally, stones that have not passed within 4–6 weeks seldom do so [5].

A trial of MET is warranted in nearly all patients with an uncomplicated distal stones under 1 cm. Two meta-analyses support the role of both alpha-antagonists and calcium channel blockers (CCBs) to increase the number of stones passed and to hasten the speed of stone passage [7, 8]. A review from Hollingsworth et al. suggests a 65% increased rate of stone expulsion with either agent, and the number needed to treat to lead to one additional stone expulsion was four [7]. A study from the emergency medicine literature, pooling data from 16 alpha-blocker studies and nine CCB studies, shows a 59% greater rate of passage with alpha-blockers and a 50% greater rate of passage with CCBs [8]. The number needed to treat in this study for alpha-blockers was 3.3 and for CCBs it was 3.9 [8]. Based upon their own analysis of the data, the American Urological Association (AUA) suggests alpha-blockers are the preferred agent for MET, primarily due to their lower rate of side effects than CCBs [6].

Recently, a well-powered study from the United Kingdom suggested that MET with either alpha-blockers or CCBs provides minimal benefit over observation [4]. This study randomized over 1100 patients to placebo, nifedipine, or tamsulosin and showed that 80% of patients in each arm did not require surgical intervention. Interestingly, this trial accrued patients with stones in all ureteral locations while prior work has focused on the distal ureter, and had only one-third of enrolled patients with stones >5 mm in size [4]. This high-quality trial is the best-powered study to date on MET; however, there are some legitimate criticisms of the study design. Given the familiarity urologists have with alpha-blockers and their excellent safety profile, it seems a trial that is both well powered and with a patient population similar to the prior studies with equivalent percentages of distal stones >5 mm may be needed to curtail the practice of MET.

Two sets of AUA guidelines on the surgical management of stones have clearly demonstrated that URS is the most efficacious means of managing a distal ureteral stone [5, 6]. Success rates for URS are well over 90% in most series and SWL has a clearance rate much lower, often in the 60–70% range: this is clearly dependent on a number of factors including the lithotripter used. Overall, a patient undergoing a SWL for a distal stone will require 1.3 procedures for clearance, as compared to a patient undergoing a URS [5, 6]. Both procedures are relatively safe, with URS associated with a <5% risk of several ureteral injury in modern series [6]; however, the common use of ureteral stents after URS is a continuing source of morbidity and often dreaded by patients who are recurrent stone formers.

Given this information, it seems apparent that a trial of MET is appropriate in many patients with uncomplicated distal ureteral stones. If MET fails, the choice of

URS or SWL for a distal ureteral stone lies with the available expertise and equipment, and with the patient after an informed discussion of the risks and benefits of each modality. Armed with the knowledge that both modalities lead to high rates of stone clearance, additional factors such as the potential need for stenting, type of anesthetic used, and complication profile of each procedure can be used to guide the choice of therapy.

## Proximal and mid-ureteral stones

Optimal management of these stones depends heavily upon the size and density of the calculus in question [9]. As described above, larger and more proximal stones are associated with a lower rate and longer time to spontaneous passage than smaller and more distal stones [5, 6]. Management of mid- and proximal ureteral stones is slightly different from that of distal stones, with the largest difference being the lack of evidence for MET in mid- and proximal ureteral stones as it has not been thoroughly tested. A study by Pickard et al. would suggest there is no role for MET in these stones, although it also suggested no role for MET in distal stones [4]. Operative intervention consists primarily of SWL or URS, although there is a select role for antegrade approaches to large and complex proximal calculi.

Once again, pooled data from multiple studies are provided by the 2007 and 2016 AUA guidelines delineating outcomes in the management of proximal and mid-ureteral stones [5, 6]. Overall, URS is associated with improved stone-free rates in both locations, with nearly 90% success in many studies, while SWL again has a lower stone-free rate in the 70–85% range [5, 6]. This relationship holds until stones get over 1 cm in size and then outcomes begin to converge, with roughly 80% stone-free rates for both modalities [5, 6]. The rate of secondary procedures is higher when SWL is used for stones under 1 cm, as in the distal ureter [5, 6].

One unique issue with SWL in the mid ureter involves the bony pelvis interfering with visualization and treatment of the stone (Figure 64.2). In some lithotripters, a prone position must be used to ensure the stone is in the ideal position for treatment, and localization of the stone may be challenging due to the bony structures.

An additional consideration to aid in selecting optimal initial therapy for proximal ureteral stones focuses on the costs incurred with treatment. A cost analysis from Lotan et al. shows that URS is less costly than SWL for proximal stones when performed primarily [10]. When considering the higher rate of adjunctive procedures for SWL compared with URS, the cost differential is even greater and is something to potentially consider when deciding how to approach the patient with such a stone [10].

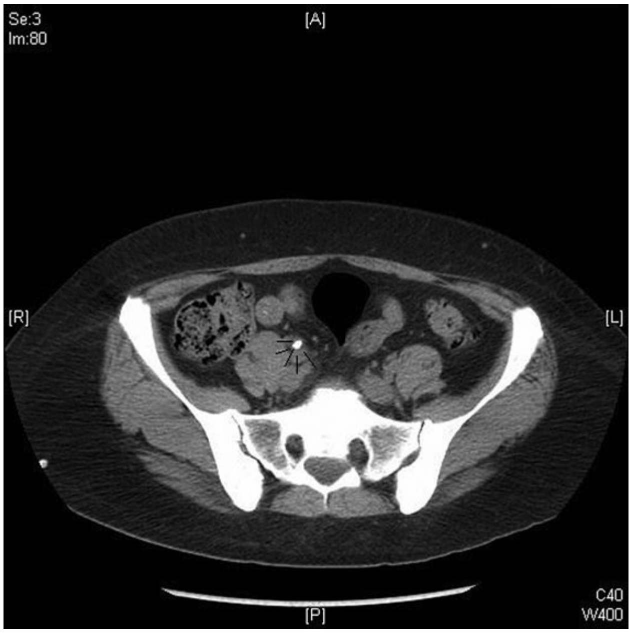

**Figure 64.2** CT of right mid-ureteral stone (demarcated by lines). Note the presence of the sacrum and iliac bones posterior, which can interfere with shock transmission.

In select cases of very large stones in the proximal ureter, or stones which are heavily impacted and do not permit retrograde access, a patient can be offered an antegrade procedure for clearance [11]. Both rigid and flexible nephroscopy can be used to approach the ureteropelvic junction and proximal ureter. In addition, following treatment of the stone, fragments can be removed via the percutaneous tract, obviating the need for passage.

### Summary

The patient with an uncomplicated ureteral stone is best managed initially with a period of observation, with or without MET. If surgical therapy is indicated, URS generally leads to higher stone-free rates than SWL, though is associated with a higher rate of complications and is more invasive. A frank and informed discussion about the risks and benefits of each surgical approach, individual patient factors, and consideration of stone composition, size, and location, are the optimal means of choosing the most appropriate surgical stone therapy (Figure 64.3).

## Renal stones

As in the ureter, both stone size and location are critical to the choice of optimal initial therapy in the renal stone patient. Unlike the ureter, where anatomy is generally straightforward and of little consequence for surgical

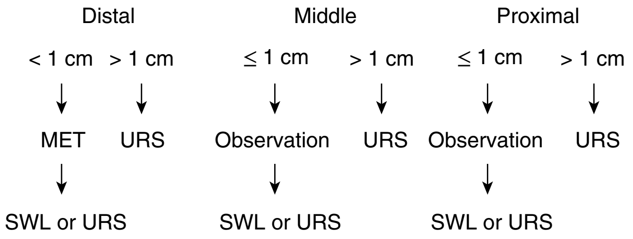

**Figure 64.3** Ureteral calculi: optimal initial management strategy.

planning, intrarenal anatomy and patient body habitus can play significant roles in deciding which treatment options are best for each patient. Additionally, stone composition is vitally important, as it heavily impacts the outcomes of SWL, in particular. Here the choice of management will generally range from observation to SWL, URS, and PCNL.

For renal stones 1 cm or smaller that are asymptomatic, non-obstructing, and not associated with infection, a reasonable strategy is one of observation. Periodic assessment of the patient for symptoms and the stone for growth with a plan for deferred management is reasonable. Following the stone with plain radiography, renal ultrasound, both, or a low-radiation-dose computed tomography (CT) at semi-annual or annual intervals is a sensible approach. A recent study from the Dartmouth group suggested that stones in the lower pole are substantially less likely to become symptomatic than in all other renal locations: 24% for the lower pole versus 41% for the remainder of the kidney [12]. Given that roughly 30% of patients in this study became symptomatic or needed intervention over an average of 41 months of follow-up, this may allow better risk stratification among patients on surveillance.

## Renal stones 1 cm or smaller in size

There are three options for managing a renal stone up to 1 cm in size: SWL, URS, and PCNL. We will consider lower pole stones separately later in the chapter (Figure 64.4). SWL is still a first-line option for these stones, especially for a stone of low attenuation on CT scan (<800–900 Hounsfield units density), in an interpolar, upper pole, or renal pelvic location, and in a calyx with a normal infundibulum [9, 13–15].

Highest clearance is achievable with stones in the renal pelvis, with reported success rates of 80–90% [13–15]. Although CT does not perfectly predict the composition of stones, stones with higher Hounsfield units are less susceptible to management with SWL, and this is a reasonable means of stratifying treatment [15, 16]. Additionally, body habitus in terms of the skin–stone distance is a critical factor in appropriate patient choice for SWL, with a skin–stone distance of over 10 cm associated with poorer outcome for that procedure [15, 16].

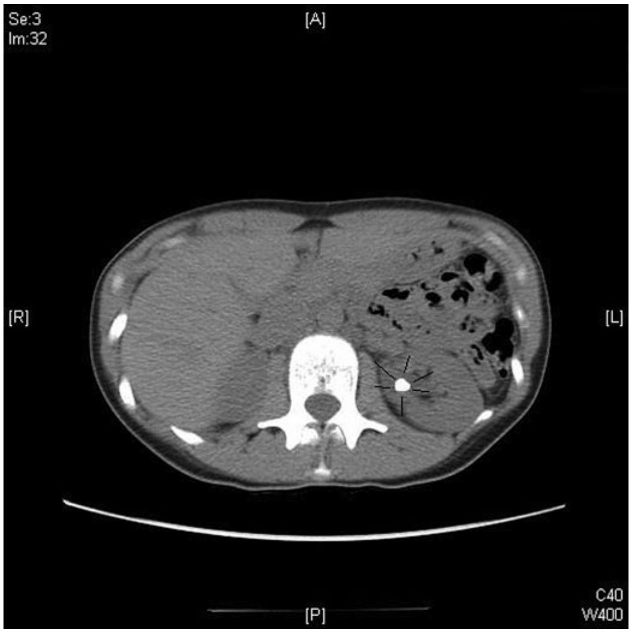

**Figure 64.4** CT scan of left renal pelvic stone (demarcated by lines).

URS is a reasonable choice for many renal stones, as modern ureteroscopes can reach the entire collecting system and displace a stone to a readily accessible location for lithotripsy or basket removal. This achieves equivalent outcomes to SWL for calculi located within the kidney across all stone compositions, with very low morbidity [15]. Stone-free rates of approximately 80% can be expected for renal stones of 1 cm or smaller in size treated by URS [15]. In the patient with a high-attenuation stone or a large skin–stone distance, URS is preferred to SWL as the difference in success rate is significant [15].

Finally, PCNL yields very high clearance rates for small renal calculi, but may be an overly morbid procedure for a stone of 1 cm or less considering the success rates achieved with less invasive procedures [15]. In general, PCNL should not be considered as optimal initial management in renal stones of 1 cm or less, unless extraneous factors such as associated conditions or abnormal anatomy are at play.

## Renal stones 1–2 cm in size

For renal stones, SWL remains a treatment option in this size range. A nomogram developed by Kanao et al. offers good estimates of stone clearance and can help guide decision-making [17]. For a renal pelvic stone, the chances of clearance at 3 months after a single SWL session are 43% for stones of 16–20 mm and 64% for stones of 11–15 mm in size [17]. For stones located in a calyx, the comparable stone-free rates are 35 and 57%, respectively [17].

As already stated, advances in equipment for stone management over recent years mean that virtually any location in the kidney can be readily accessed with flexible ureteroscopes. Concomitantly, there has been an effort to manage larger renal calculi with URS to assess its role compared with the more invasive PCNL (Figure 64.5). Several studies have sought to compare URS and PCNL in this size range, confirming that the stone-free rate is higher with PCNL, as expected, as is the complication rate [18–20].

When deciding how to manage these stones, the decision should largely rest on the patient's goals of therapy and possible complications of treatment. For example, if the patient's priority is to be stone free with the greatest degree of success in the face of high stone density or lower pole location, PCNL would be the ideal choice. Yet if the stone has favourable characteristics that might favor a less invasive alternative, such as renal pelvis location, low Hounsfield units density, and – in the case of SWL – low skin-to-stone distance, SWL or URS may offer a better alternative. Unfortunately, established Level 1 evidence is somewhat lacking, so to definitively answer the question for the population of patients with this stone size cannot be readily done; as a result, individual patient and

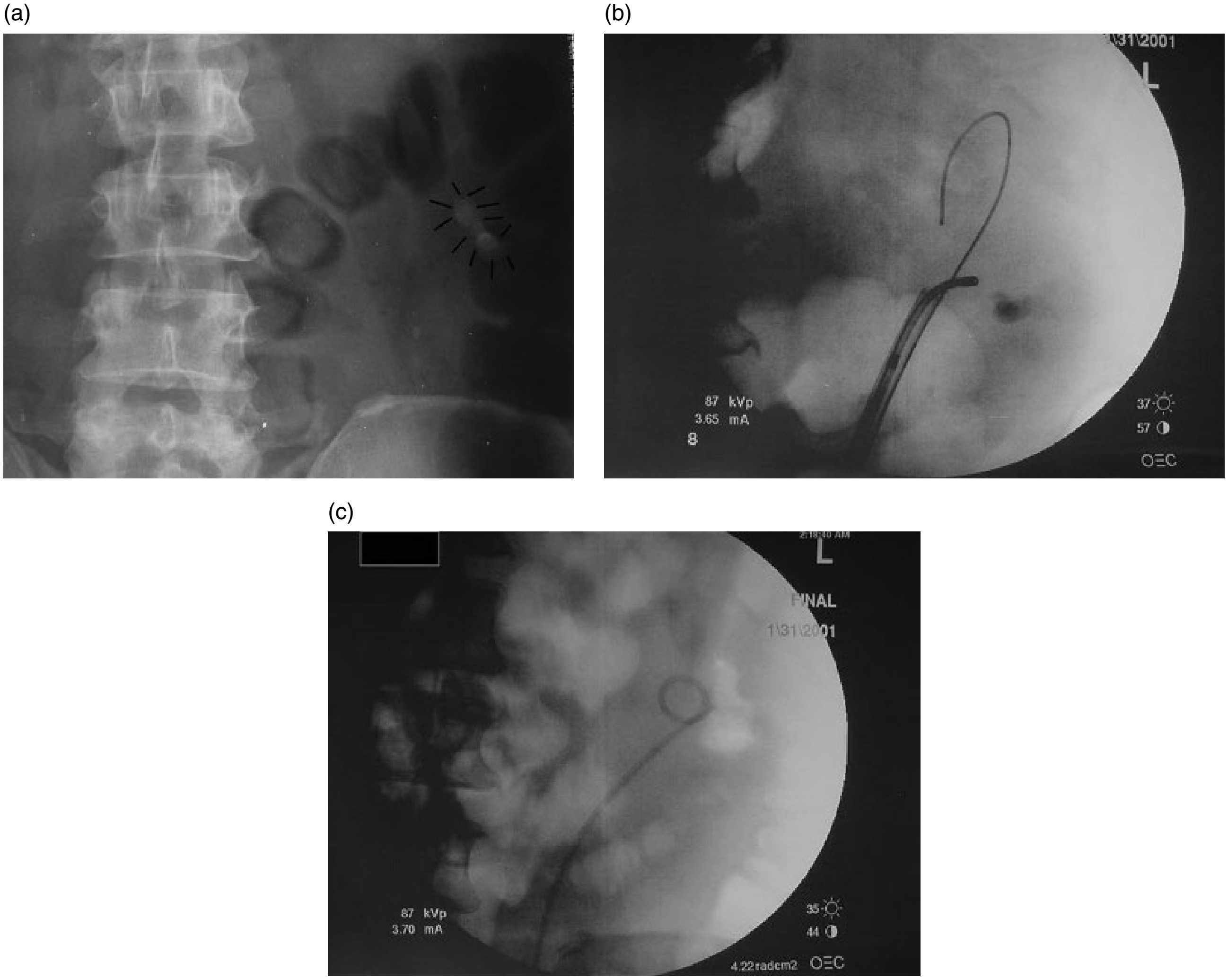

**Figure 64.5** (a) Fluoroscopy of left partial staghorn renal stone (demarcated by lines). (b) Fluoroscopy during URS of left partial staghorn renal stone. Mid procedure, note clearance of stone is underway. (c) Fluoroscopy during conclusion of URS with stent in position and stone cleared from lower pole.

stone factors are the critical data points to consider when counseling patients and determining therapy.

## Renal stones greater than 2 cm in size

When approaching stones greater than 2 cm in size, the success rate of PCNL is unparalleled compared with the alternatives. Both SWL and URS have been utilized with stones of this size, but clearance often requires multiple procedures to achieve stone-free status, whereas PCNL still has a high rate of success with one procedure.

The nomogram by Kanao et al. suggests clearance for renal stones greater than 2 cm in size using SWL is 30% for renal pelvic stones and 23% for calyceal stones [17]. Likewise, for URS stone clearance is feasible for stones over 2 cm in size, but this requires an average of 2.3 URS procedures per patient [19]. In the Lower Pole I cohort, six of seven patients with stones greater than 2 cm in the lower pole were cleared with PCNL, whereas only one in seven patients were cleared with SWL (Figure 64.6) [20].

Clearly, for staghorn calculi and assuming that adequate renal function is present, PCNL is the mainstay of treatment, and can involve multiple access tracts and/or flexible nephroscopy to achieve ultimate success. Procedures such as laparoscopic and open pyelolithotomy/nephrolithotomy are typically reserved for unique situations in the current era, including aberrant anatomy or lack of appropriate instrumentation (Figure 64.7). Stone-free rates approach nearly 80% with a single percutaneous procedure even for such complex cases [21], and can reach up to 95% when flexible scopes and laser lithotripsy are included in the procedure [21].

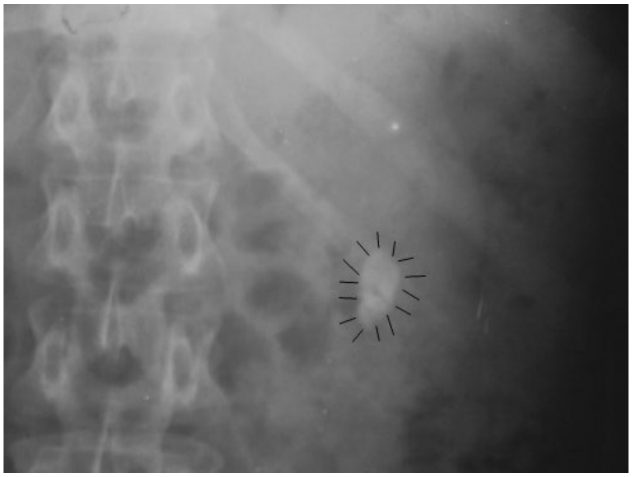

**Figure 64.6** Fluoroscopy of large left lower pole stone (demarcated by lines).

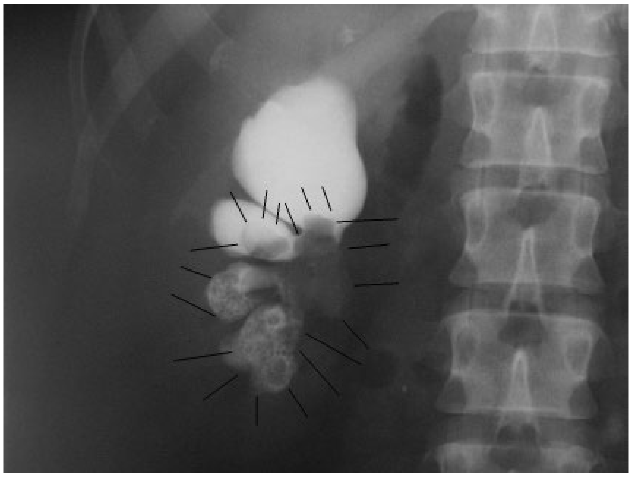

**Figure 64.7** Fluoroscopy during intravenous urography showing large right staghorn renal calculi (demarcated by lines) manifesting as filling defect occupying lower and mid calyces, and renal pelvis.

## Lower pole stones

The lower pole presents a unique anatomic entity in many renal units. Factors such as the width and length of the infundibulum and the angle between the infundibulum and the pelvis can greatly influence surgical outcomes. Although SWL, URS, and PCNL can all be used to manage stones in this location, there are a few broad themes that resonate throughout several trials focusing on this unique location [22]:

1) SWL is associated with the worst outcomes of all modalities.
2) PCNL is associated with the highest stone-free rates of all modalities.
3) URS can compete with PCNL for many stones under 2 cm in size; however, as stones get larger, PCNL is clearly the dominant modality.

## Summary

For renal stones, several variables contribute to the decision as to which stone therapy is optimal for initial management. For asymptomatic stones of 1 cm or smaller in size, a trial of observation is certainly reasonable, although patients should be aware that stones often require treatment or become symptomatic with the passage of time. For stones of 1 cm or smaller in size that warrant treatment, SWL and URS are associated with fair-to-moderate clearance rates and relatively low morbidity. As stones increase in size, especially with a lower pole location, PCNL becomes the most important means of treatment. As stones increase in size over 2 cm, PCNL is the preferred means of management (Figure 64.8).

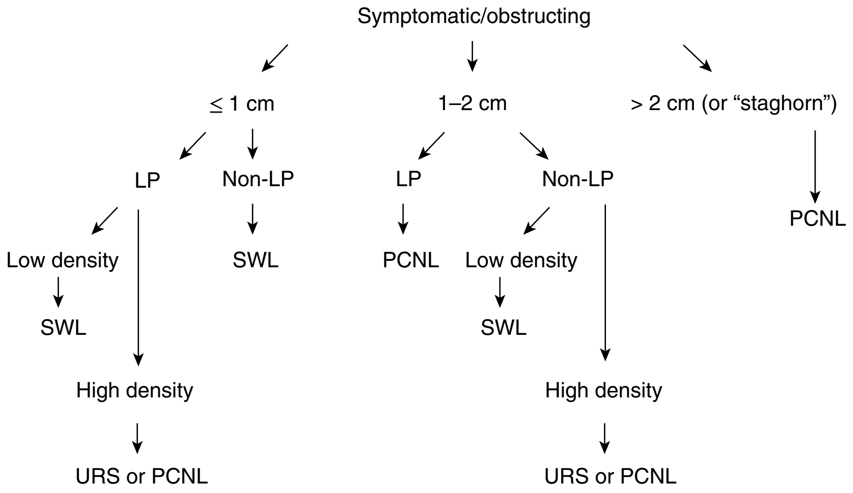

**Figure 64.8** Renal calculi: optimal initial management strategy. LP, lower pole.

## Stones in calyceal diverticula

Stones presenting in a calyceal diverticulum are an infrequent occurrence, and may or may not be symptomatic. Treatment options available for these calculi include SWL, URS, PCNL, and laparoscopic approaches [23–26]. Since this condition is relatively rare, robust data comparing treatment modalities are lacking. Generally SWL will be the least successful means of managing these stones, as the narrow diverticular neck will often preclude passage of all but the smallest fragments. Still, there is a recognized symptomatic improvement in some cases managed by SWL in which colic is the presenting symptom. URS is also efficacious, especially when the diverticulum has a narrow and stenotic neck, hindering passage of fragments after SWL [24, 26]. Using both the flexible ureteroscope and the holmium laser, many of these diverticula can be cleared of their stone burden, with smaller stones again being more amenable to successful clearance.

In the case of a posterior diverticulum, PCNL is an excellent means of accessing the diverticulum, as well as clearing its stone burden and possibly ablating the lining of the diverticulum [23, 26]. Finally, in the event of an anterior diverticulum, a laparoscopic approach has been successfully applied and thus offers an additional treatment option to the percutaneous approach [23, 26].

## Laparoscopic and open stone surgery

The advent of SWL, smaller ureteroscopes, and PCNL has essentially rendered conventional stone surgery obsolete. Nonetheless, circumstances do arise, though rarely, where a laparoscopic or open approach is indicated [27]. For ureteral calculi, operative intervention is rarely needed; however, large impacted stones that fail SWL, URS, or antegrade removal would be candidates [26]. For such stones a laparoscopic/robotic approach can be utilized in lieu of an open ureterolithotomy [27].

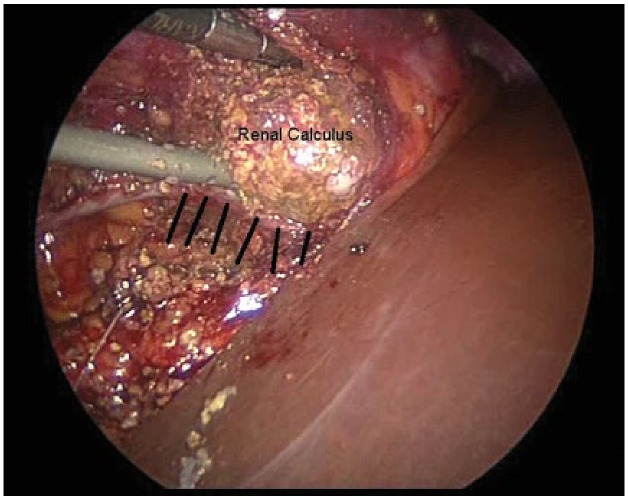

**Figure 64.9** Intraoperative view during laparoscopic pyelolithotomy. The stone is visible as it is being extracted, while the lines demarcate the edge of the pyelotomy incision.

For renal stones, an open or laparoscopic approach can be considered in select circumstances as well (Figure 64.9). In the event of failed PCNL, SWL, or URS, especially after multiple procedures, there is a role for formal operative intervention [27]. Additionally, in the event of a staghorn calculus where clearance seems unlikely in a reasonable number of minimally invasive procedures, open or laparoscopic surgery is an option [27]. Occasionally concomitant surgery on an unrelated organ system would be an indication to perform an open procedure on a large renal stone, as would concurrent surgery to repair a ureteral stricture [27]. Finally, some patients' body habitus precludes fluoroscopy, endoscopy, or positioning for SWL and thus leaves the surgeon with no choice but an open or laparoscopic approach to a urinary stone [27].

## Conclusions

The modern urologist has a wide range of operative and nonoperative tools at his disposal to manage renal and ureteral stones. Nearly all ureteral stones can initially be observed, with or without MET. For distal stones, URS provides the highest stone-free rates, while in the upper ureter SWL competes with URS, especially as stones get larger. In the kidney, SWL is still a useful technique, especially when patients are well selected for therapy. URS is a versatile means of managing many renal stones, although as stones get larger, PCNL maintains a dominant position in having the best stone-free rates, especially in the lower pole.

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# 65

# Management of Urolithiasis in Pregnancy

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## Anatomic changes during pregnancy

Pregnancy induces a number of anatomic changes within the urinary tract. Renal size increases secondary to an increase in renal vascular volume and an increase in the renal interstitial space. Hydronephrosis of varying severity is experienced by approximately 90% of pregnant women by the third trimester. The hydroureter extends to the sacral promontory and is typically absent more distally. The hydroureteronephrosis of pregnancy results primarily from compression of the gravid uterus [1]. Physiologic hydronephrosis can affect 90% of right kidneys and up to 67% of left kidneys [2]. The hydroureter is more prevalent and severe on the right side, secondary to uterine dextrorotation, as well as a pressure-reducing effect of the sigmoid colon on the left side. The ureteric smooth muscle relaxation due to increased levels of progesterone has also been implicated in the development of gestational hydronephrosis [3, 4]. However, this mechanism may contribute to the early development of hydronephrosis, between 6 and 10 weeks of gestation, while the mechanical factor remains the major cause thereafter. Support for a primarily mechanical theory includes absence of urinary tract gestational ureteral dilation below the pelvic brim in patients with a pelvic kidney and in those who have undergone previous urinary diversion. The bladder is displaced anterosuperiorly by the gravid uterus, bladder capacity increases, and the detrusor muscle becomes relatively hypotonic and has decreased sensation (Table 65.1). The urothelium becomes congested and hyperemic.

## Physiologic changes during pregnancy

Pregnancy induces physiologic changes in many organ systems, including the renal system (Table 65.2). Glomerular filtration rate (GFR) and renal plasma flow increase by 40–65% and 50–85%, respectively [5], secondary to an increase in the cardiac output and decrease in the renal vascular resistance. Creatinine clearance increases by up to 50% [6], leading to lower serum creatinine and urea levels, a higher level of filtered glucose and glucosuria, and higher level of urine sodium, calcium, uric acid, citrate, magnesium, and glucosminoglycans. Enhanced renal filtration additionally affects dosing of antibiotics as well as anesthetic agents. Other nonrenal systems undergo physiologic changes as well.

## Mineral metabolism and stone formation during pregnancy

The homeostasis of urolithiasis-promoting and -inhibiting factors is altered in pregnancy. Placental 1,25-dihydroxycholecalciferol increases intestinal resorption of calcium as well uptake of calcium from bone. The increase in absorbed calcium is offset by an increase in GFR and subsequent increased filtered load of calcium. Parathyroid hormone secretion is decreased, suppressing the tubular resorption of calcium. Thus, serum calcium levels generally remain unchanged and hypercalciuria occurs. Uric acid and oxalate excretion is increased due to increased GFR, and fetal and dietary factors [6–8]. Hypercalciuria,

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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 65.1** Anatomic changes in the genitourinary tract during pregnancy.

| System | Anatomic changes |
|---|---|
| Kidney | Renomegaly<br>Hydronephrosis |
| Ureter | Hydroureter |
| Bladder | Anterosuperior displacement<br>Increased capacity |
| Urethra | Urothelial hyperemia and congestion<br>Squamous metaplasia |

**Table 65.2** Physiologic changes during pregnancy.

| System | Physiologic changes |
|---|---|
| Genitourinary | |
| Kidney | ↑ Blood flow and vascular volume<br>↑ Glomerular filtration rate<br>↑ Proteinurea, uricosuria, calciuria, and citraturia<br>↓ Serum creatinine and blood urea nitrogen |
| Bladder | ↓ Sensation and relative hypotonia |
| Cardiovascular | ↑ Cardiac output<br>↑ Heart rate and stroke volume<br>↑ Blood volume<br>↓ Systemic vascular resistance<br>↓ Cardiac output near end of pregnancy<br>↓ Venous return<br>↓ Hematocrit |
| Respiratory | ↑ Consumption of oxygen<br>Hypoxemia<br>Hypoventilation<br>↓ Functional residual capacity |
| Hematologic | Hypercoagulable state<br>↑ Factors VII, VIII, and X<br>↑ Fibrinogen<br>↓ Fibrinolytic activity |
| Gastrointestinal | ↓ Gastrointestinal motility<br>Relaxation of gastroesophageal sphincter |

uricosuria, and oxaluria all create a favorable environment for renal calculus formation.

Pregnancy, however, is not associated with an increased incidence of urolithiasis compared to the nonpregnant population [9, 10]. This is most likely explained by the increase in filtered citrate, magnesium, and glycosaminoglycans [6–8], all of which are known inhibitors of crystal aggregation and growth.

Renal calculi during pregnancy are documented to be composed primarily of calcium phosphate (74%) and calcium oxalate (26%) [11].

Calcium supplementation during pregnancy is associated with a reduction in the risk of preeclampsia, maternal morbidity and mortality, and preterm labor [12–14]. There is evidence that calcium supplementation during pregnancy may however be associated with a slight increased risk of urolithiasis [14].

## Incidence

The incidence of symptomatic urolithiasis in pregnancy is between 1 in 244 and 1 in 2000 pregnancies [15–17]. The overall incidence of urolithiasis is uncertain, but is estimated to be higher, as some asymptomatic renal calculi may remain undetected. There are no observed differences in the rate of urolithiasis between pregnant and nonpregnant women [18, 19].

The average age of presentation is 27 [20] with 80–90% of cases detected during the second and third trimesters. Urolithiasis seems to be higher in multiparous women, in white patients, and in patients with a history of hypertension and renal disease [20, 21]. Ureteral calculi present twice as often as renal calculi [22, 23]. Up to 30% of patients have a history of stone disease [24].

## Presentation

Symptomatic pregnant patients may present with abdominal or flank pain (85–100%), gross (15–30%) or microscopic hematuria (95–100%), lower urinary tract symptoms, urinary tract infection, preeclampsia, and premature labor [25–27]. Nausea and vomiting are invariably present as well. A comprehensive differential diagnosis of abdominal pain during pregnancy is given in Table 65.3.

Acute abdominal or flank pain in pregnancy presents a unique diagnostic challenge. The clinician has to consider anatomic alterations induced by pregnancy that can lead to various conditions mimicking each other. For example, the appendix can be displaced superiorly after the first trimester and appendicitis may mimic pyelonephritis or cholecystitis [28].

## Diagnostic tests

### Imaging and radiation exposure

Accurate diagnosis of abdominal pain in pregnancy largely depends on diagnostic imaging. The necessity of diagnostic imaging and exposure to ionizing radiation is commonly anxiety-provoking for both patients and clinicians. Use of the ionizing radiation needs to be avoided whenever possible, due to its potential teratogenic effects. When its use is unavoidable, a detailed discussion with patients is required, carefully explaining the

**Table 65.3** Differential diagnosis of acute abdominal pain in pregnancy.

| Urologic causes | Gynecologic and obstetric causes | General surgical causes |
|---|---|---|
| Urolithiasis<br>Pyelonephritis | Premature labor<br>Placental abruption<br>Chorioamnionitis<br>Ectopic pregnancy<br>Ovarian torsion<br>Pelvic inflammatory disease | Appendicitis<br>Cholecystitis<br>Diverticulitis<br>Intestinal obstruction<br>Gastroenteritis<br>Hernia<br>Pancreatitis<br>Mesenteric lymphadenitis |

potential risks associated with its use. Application of techniques to reduce radiation dose is mandatory. The delivered dose of radiation should be as low as possible, while maintaining the quality of diagnostic image that is useful for diagnosis. Effects of ionizing radiation on the fetus can be categorized into four classes: intrauterine fetal death, fetal malformation, disturbance of growth and development, and mutagenic/carcinogenic effect [29, 30]. The risk of exposure is also dependent on the dose of the radiation and fetal gestational age [31].

The radiation dose is measured in Gray units (Gy, SI system), representing the amount of ionizing radiation absorbed by tissue. Previously, the radiation dose was measured in rads (1 Gy equating to 100 rads), representing the radiation dose delivered and not necessarily absorbed by the tissues. The delivered fetal dose for each diagnostic imaging procedure varies according to the technique used (Table 65.4) and maternal body configuration. Most diagnostic procedures deliver fetal doses below 50 mGy [32]. This dose of radiation has not been associated with an increase in fetal anomalies or pregnancy loss [33]. The American College of Obstetricians and Gynecologists recommends that "women should be counseled that the X-ray exposure from a single diagnostic procedure does not result in harmful effects" [33].

The effects of radiation depend on the fetal gestational age [31]. Fetal tissues are most susceptible to ionizing radiation during the first trimester when organogenesis is occurring. Use of ionizing radiation should be avoided during this period. The teratogenic effects of radiation are summarized in Table 65.5. In addition, ionizing radiation has a potential to induce development of childhood cancers such as leukemia. Historic studies raised concern that *in utero* radiation exposure may increase the incidence of childhood malignancy by 1.3–2 times [31, 34]. However, more recent investigations have reputed this evidence [35]. The National Radiological Radiation Board concluded that the majority of diagnostic radiologic procedures performed in an individual pregnancy presents no substantial risk and carries a less than 1 in 5000 chance of developing a fatal childhood cancer (1 in 33 000 per mGy). Additionally, the risk is less than 1 in 10 000 for development of induced inheritable disease (1 in 40 000 per mGy) [36, 37].

**Table 65.4** Fetal radiation doses for radiologic tests.

| Procedure | Fetal dose (mGy) |
|---|---|
| CT scan (conventional) | 8.0–49 |
| CT scan (limited) | 0.244–1.372 |
| IVU | 1.7–10 |
| KUB | 1.4–4.2 |
| Nuclear renogram (MAG3 or DTPA) | 0.2–4.0 |
| MRI | No radiation, no known adverse effects |
| Ultrasonography | No radiation, no known adverse effects |

CT, computed tomography; IVU, intravenous urography; KUB, kidney–ureter–bladder plain film; MAG3, mercaptoacethyltriglycine; DTPA, diethyltriamine penta-acetic acid; MRI, magnetic resonance imaging.

**Table 65.5** Effects of significant radiation exposure on the fetus.

| Gestational age (weeks) | Radiation effect |
|---|---|
| 2–4 | All lethal or no impact on fetus, without any malformations present |
| 4–10 (organogenesis) | Microcephaly, growth retardation, gross malformations |
| 10–17 (peak neurologic development) | Microcephaly, mental retardation, growth retardation and sterility in adult life |
| 17–40 | Adverse effects seen rarely, if ever |

## Ultrasound

Ultrasonography (Figure 65.1) is the most useful initial test when acute abdominal or flank pain in pregnancy is investigated. The appeal of ultrasound derives from the lack of ionizing radiation and absence of harmful effects, documented over many years of use. Ultrasonography can effectively evaluate the renal parenchyma, pelvicalyceal system, and dilated ureter, and to some extent visualize renal and ureteral calculi.

The accuracy of ultrasonography in the detection of renal calculi is reported to be between 34 and 86% [20–22]. This wide variation in the reported accuracy most likely derives from the fact that ultrasound is operator-dependent. Additionally, ultrasonography is very nonspecific and often

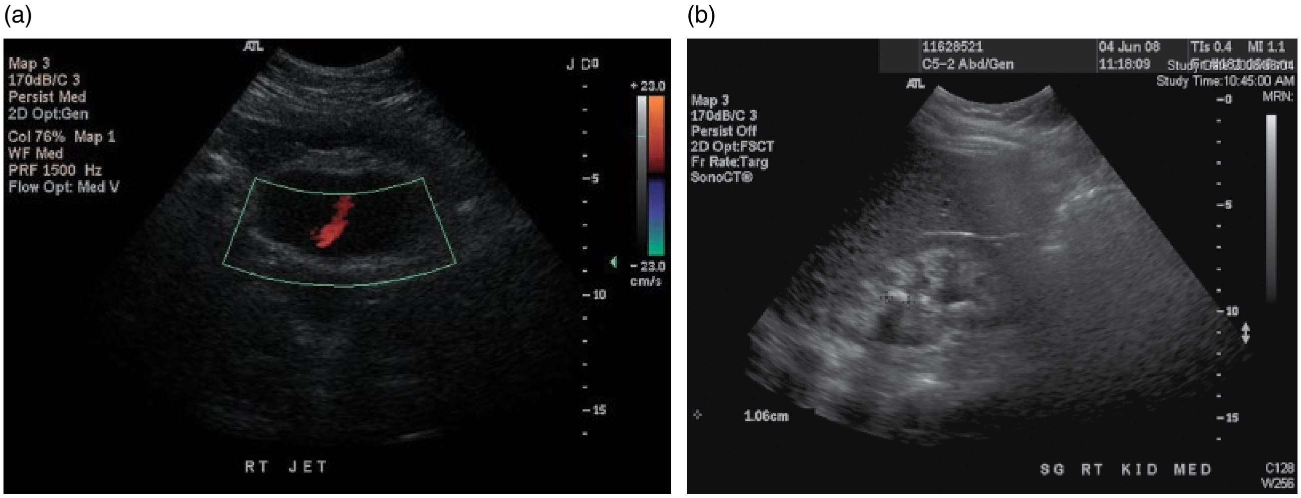

(a)
Map 3
170dB/C 3
Persist Med
2D Opt:Gen
Col 76% Map 1
WF Med
PRF 1500 Hz
Flow Opt: Med V
+23.0
−23.0
cm/s
RT JET
(b)
11628521
C5-2 Abd/Gen
04 Jun 08
11:18:09
Study Time:10:45:00 AM
MRN:
Map 3
170dB/C 3
Persist Off
2D Opt:FSCT
Fr Rate:Targ
SonoCT®
1.06cm
SG RT KID MED
C128
W256

**Figure 65.1** Ultrasound images. (a) Bladder (Doppler) demonstrating an absence of left ureteric jet, in a 30 year-old pregnant woman, G1P1 GA 30 weeks. (b) Kidney with a right renal stone in a 31 year-old pregnant woman, G2P2 GA 28 weeks.

cannot distinguish between hydronephrosis of pregnancy and that secondary to calculi.

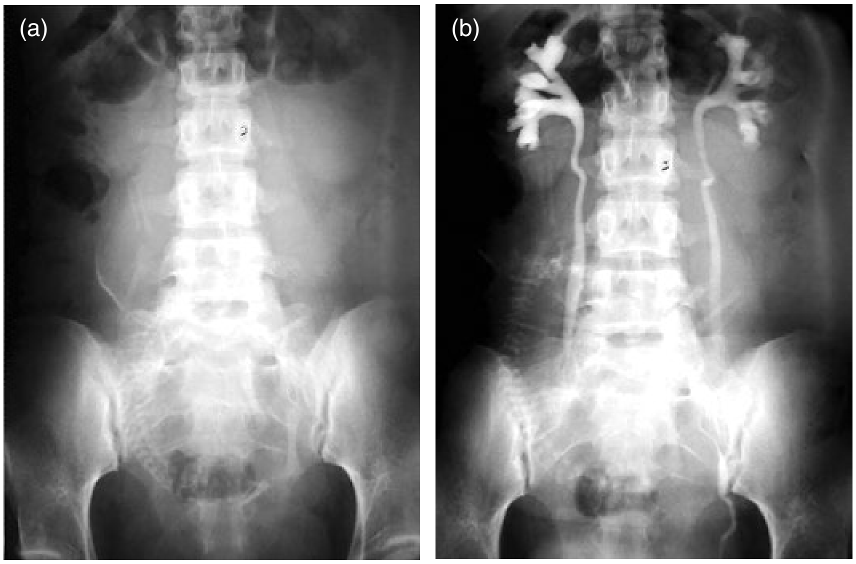
Several modifications to ultrasonography have attempted to improve its accuracy. Transvaginal ultrasound was demonstrated to be effective in the detection of distal ureteral calculi [38]. Detection of hydroureter below the pelvic brim, with any ultrasound approach, may alert the operator to the presence of distal ureteral calculi [39]. The presence of ureteral jets on ultrasound or Doppler ultrasound can exclude complete ureteral obstruction in 80–100% of cases [40].

Resistive index (RI) measurements may increase the accuracy of ultrasonogarphy in distinguishing between the physiologic dilation and calculus-related obstruction [41]. An RI of 0.70 was demonstrated to have 87% accuracy, 45% sensitivity, and 91% specificity for diagnosis [41, 42]. Additionally, a difference in RI values (ΔRI) between the affected side and the normal contralateral kidney of 0.06 increases the sensitivity of ultrasonography to 95%, with specificity of 100% and accuracy of 100% [42]. This type of ultrasonography adjunct was demonstrated to be limited by pre-existing renal disease, nonsteroidal anti-inflammatory drugs (NSAIDs) and acute onset of obstruction (<6 hours).

## Intravenous urography

Intravenous urography (IVU) (Figure 65.2) is effective in describing anatomy and function of the collecting system, along with the site and degree of potential

**Figure 65.2** (a, b) Kidneys, ureters, and bladder intravenous urogram demonstrating a right ureteral calculus in a 30 year-old pregnant woman, G1P0 GA 29 weeks.



obstruction. IVU can be considered as a second-line investigation for hydronephrosis of pregnancy. Small published series report relatively high specificity in diagnosing renal calculi in pregnancy [20, 43]. If needed, a limited three-shot protocol should be used: a scout film, 15–20 minute film, and a selected delayed image at 2 hours. Fetal shielding should be used at all times [44].

IVU, if considered, should be used judiciously due to potential risks of intravenous contrast and fetal radiation exposure. Intravenous contrast was demonstrated to cross the placenta in small quantities, but without any described teratogenic effects [45]. However, exposure to iodinated intravenous contrast during late pregnancy can lead to fetal thyroid suppression, and requires screening for neonatal hypothyroidism [45].

A limited IVU delivers 0.5 mGy of radiation to the fetus, which is below the 5 mGy safety point. Fetal shielding and films obtained in a prone position can further reduce the dose.

## Computed tomography

A traditional computed tomography (CT) scan (Figure 65.3) remains contraindicated in pregnancy due to the high dose of ionizing radiation delivered. Recently, however, a low-dose CT scan protocol has been described for the detection of renal calculi during pregnancy. A low-dose CT scan protocol uses a pitch of 1.5 (from 0.75 in regular CT), 120 kV, and a mean of 109 mA. With these modifications the mean delivered fetal radiation exposure is 705.5 mrad (range 244–1372 mrad), although this is probably an overestimate due to maternal changes in body geometry. Obese patients receive a higher estimated dose on average. The resulting CT images are of much lower quality in comparison to traditional scans, but this investigation still provides high sensitivity and specificity for detection of renal and ureteral calculi.

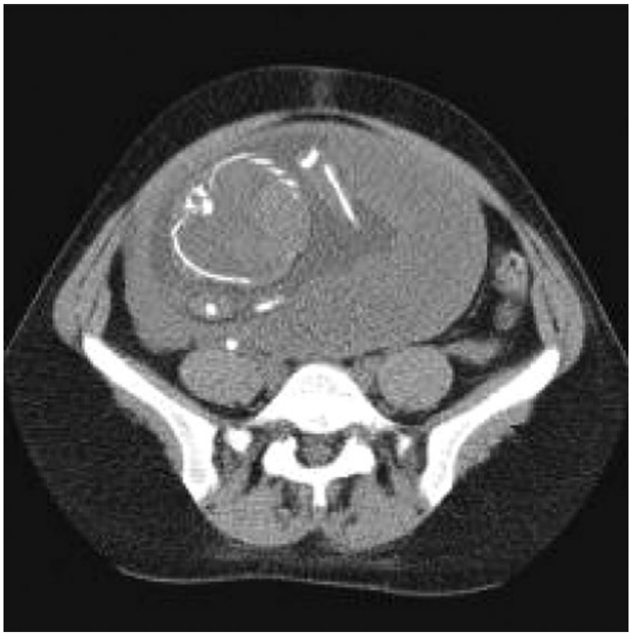


**Figure 65.3** Low-dose CT scan demonstrating a right ureteral calculus in a 29 year-old woman, G1P0 GA 27 weeks. *Source:* [46]. Reproduced with permission of Mary Ann Liebert, Inc.

Based on the finding of a small Research Ethics Board (REB)-approved study, the authors concluded that a low-dose CT scan is more sensitive than ultrasound and improves decision-making [46]. In another recent study, the positive predictive value of low-dose CT scan was the highest (95.8%) compared to renal ultrasound alone (77%) or magnetic resonance imaging (MRI) (80%) in the diagnosis of urolithiasis during pregnancy [47]. The rate of negative ureteroscopies was the lowest in pregnant patients who had low-dose CT scan as part of their preoperative evaluation (only 4.2%) [47]. Thus, the judicious use of low-dose CT scans in pregnant women with flank pain and negative initial ultrasound is advocated

## Magnetic resonance

MRI in pregnancy produces high-quality images of urinary tract anatomy. Heavily weighted T2 MRI pulse sequences or use of intravenous gadolinium can produce precise urograms, comparable to those produced by IVU. The accuracy of MRI in delineating pathologic obstruction from hydronephrosis of pregnancy ranges from 93 to 100% [48]. MRI's diagnostic accuracy can be enhanced by combining it with Doppler ultrasonography and nuclear renography [49]. To date, no harmful effects have been reported with the use of MRI in pregnancy [50]. Experience with gadolinium is limited, but gadolinium-based contrast agents can cross the placenta and remain within the amniotic fluid during pregnancy, raising theoretical concerns over the possible risk of nephrogenic systemic fibrosis [51]. The National Radiological Radiation Board recommends avoiding gadolinium in the first trimester of pregnancy. The main limitation of MRI remains the inability to visualize the stone. The presence of the stone has to be inferred from several soft signs such as "signal voids," "double kink," and perinephric and periureteral edema. Additional limitations include the time-consuming nature of performing MRI (although this continues to improve with new-generation scans), its lower availability, and high costs. Patients afflicted with claustrophobia also will not be able to undergo this diagnostic procedure.

## Management

### When to intervene?

Figure 65.4 shows a suggested management plan for urolithiasis during pregnancy. The rate of spontaneous stone passage in pregnancy is between 64 and 84% [20, 24]. Up to 50% of the remaining stones will pass in the postpartum period [20]. Based on these data, the guiding principle of therapy remains that of conservative management. Conservative management requires hydration, antibiotics, antiemetics, analgesics, and close daily follow-up during the symptomatic period. Straining of urine is also advised. Medical expulsive therapy (MET) drugs, including alpha-blockers and calcium-channel inhibitors, are classified as group B drugs during pregnancy [52]. The safety of tamsulosin was examined during pregnancy in a study including 27 pregnant women [53]. It was not associated with any increase in adverse maternal or fetal outcomes; however, two infants in the MET group died of sudden infant death syndrome within 6 months of birth compared to none from the control group [53]. Thus, further studies are needed to determine the long-term safety of MET drugs during and after preganancy.

Conservative management of urolithiasis will fail in approximately 15–30% of pregnant women [54]. Indications for intervention in symptomatic pregnant patients are the same as in the nonpregnant population. These include sepsis, renal failure from obstruction of a solitary kidney or bilateral obstruction, uncontrolled pain, premature onset of labor, preeclampsia, and poor access to expert urologic care.

### Anesthetic risks

Use of anesthesia for nonobstetric surgery during pregnancy has a potential for inducing fetal congenital malformations, spontaneous abortion, and premature labor [55]. Thus, nonemergency surgery during pregnancy

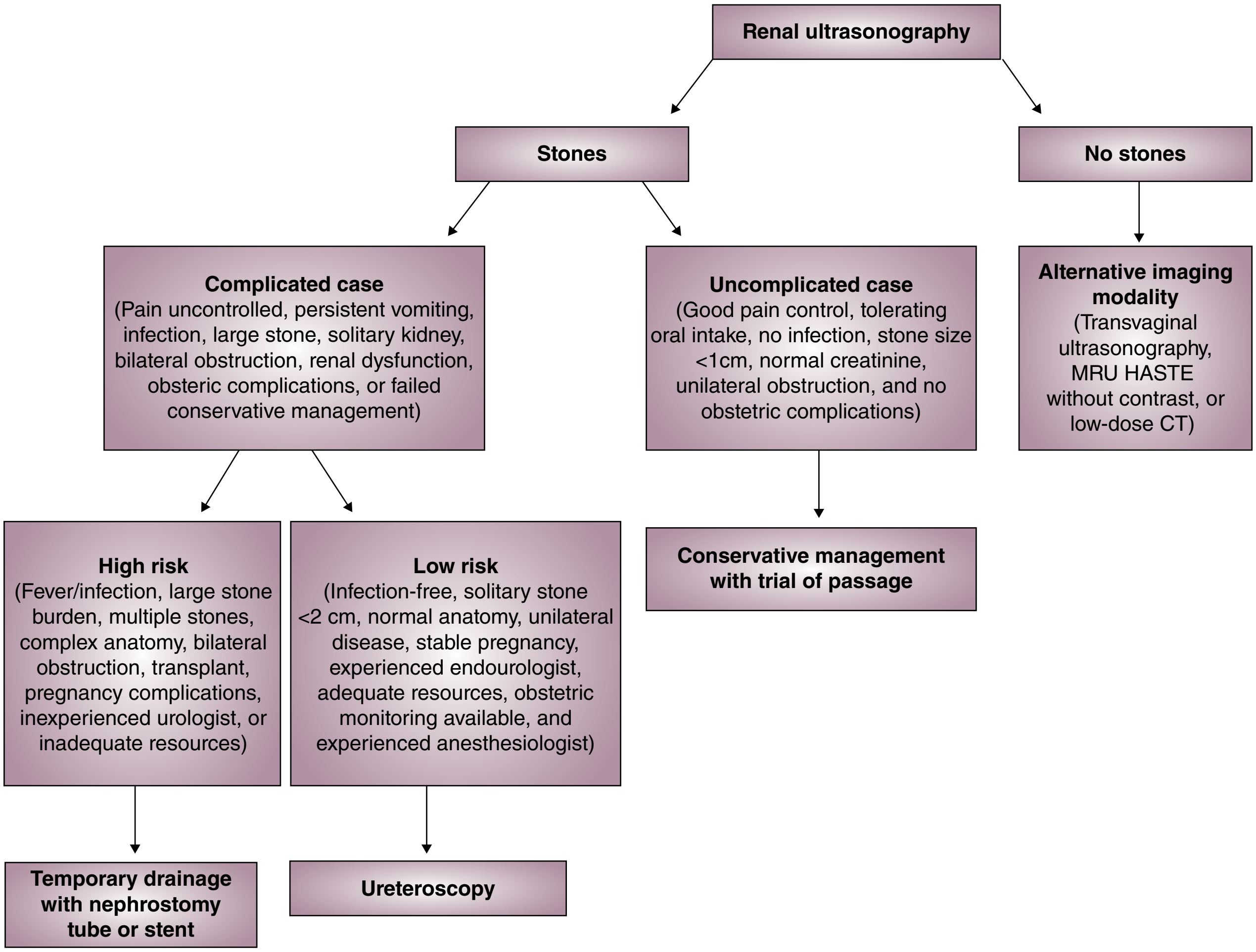

Renal ultrasonography
Stones
No stones
Complicated case (Pain uncontrolled, persistent vomiting, infection, large stone, solitary kidney, bilateral obstruction, renal dysfunction, obsteric complications, or failed conservative management)
Uncomplicated case (Good pain control, tolerating oral intake, no infection, stone size <1cm, normal creatinine, unilateral obstruction, and no obstetric complications)
Alternative imaging modality (Transvaginal ultrasonography, MRU HASTE without contrast, or low-dose CT)
High risk (Fever/infection, large stone burden, multiple stones, complex anatomy, bilateral obstruction, transplant, pregnancy complications, inexperienced urologist, or inadequate resources)
Low risk (Infection-free, solitary stone <2 cm, normal anatomy, unilateral disease, stable pregnancy, experienced endourologist, adequate resources, obstetric monitoring available, and experienced anesthesiologist)
Conservative management with trial of passage
Temporary drainage with nephrostomy tube or stent
Ureteroscopy

**Figure 65.4** Suggested management plan of pregnant patients with urolithiasis. *Source:* [97]. Reproduced with permission of Nature Publishing Group.

should not be performed. Open surgery should be considered only as treatment for septic patients who have failed to respond to any other therapeutic options and when endourologic expertise or equipment is not available [54, 56]. Performing any surgery during the first trimester was found to increase risk of miscarriage [57] and in the third trimester of premature labor [58]. The optimal time for performing nonobstetric surgical intervention during pregnancy is the second trimester [58].

In general, the dosing of both general and locoregional anesthetics during pregnancy is decreased [59, 60]. The increased levels of progesterone and endorphins that have been documented in pregnancy probably play a role in decreasing the minimal alveolar concentrations of the inhalational agents halothane and isofulrane [59], whereas progesterone has also been reported to enhance neuronal membrane sensitivity to local anesthetics [60], thereby diminishing the dose. Drug dosing for spinal and epidural anesthesia was reported to diminish even further in the later stages of pregnancy due to compression of the cerebrospinal space and subsequent epidural venous congestion [61].

Any surgical intervention during pregnancy should involve the obstetric team for monitoring of the fetal heart rate and uterine activity. Fetal monitoring should continue for 24 hours postintervention [62]. NSAIDs should not be used for analgesia as they may induce premature closure of the fetal ductus arteriosus [63].

## Endourologic interventions

### Ureteric stenting

Ureteral stenting represents a temporizing measure, with definitive management deferred until the postpartum period. This approach minimizes or eliminates the requirement for anesthesia, but has several drawbacks. Stent insertion can be accomplished using either fluoroscopy or ultrasound. Fluoroscopy is preferable, but is associated with exposure to ionizing radiation. If using fluoroscopy, fetal shielding and pulsed imaging can reduce radiation exposure. Ultrasound-guided insertion of a ureteric stent eliminates radiation exposure completely [64].

The main drawbacks of ureteric stenting during pregnancy are stent discomfort and stent encrustation. Stent discomfort is similar to that in the nonpregnant population and can manifest as an increase in urinary frequency and urgency, dysuria, mild gross hematuria, and flank pain. Stent discomfort in pregnancy is usually heightened secondary to the presence of overactive bladder symptoms that many women experience in the later stages of pregnancy. The risk of stent encrustation during pregnancy is increased secondary to hypercalciuria and hyperuricosuria of pregnancy. This increased risk necessitates frequent stent exchanges, every 4–6 weeks [21, 65]. The cumulative risks of frequent stent exchanges may exceed that of a single definitive procedure.

### Indications for a percutaneous nephrostomy

A percutaneous nephrostomy (PCN) tube is also a temporizing measure that provides immediate and efficient decompression of the urinary tract. PCN insertion can be achieved with ultrasound guidance and under local anesthesia (usually inserted by an interventional radiologist). The main advantages of this treatment modality are absence of ionizing radiation, minimal anesthesia requirements, avoidance of ureteral manipulation, and very effective drainage of the urinary tract. It also establishes a percutaneous tract for later definitive management of calculi. These attributes often make PCN insertion a preferred option for treatment of septic patients or patients during the first trimester [21, 56].

The main disadvantages of PCN tubes are the risk of bleeding during insertion, bacterial colonization, tube dislodgement, blockage by debris, and tube discomfort. PCN tube blockage, encrustation, and dislodgement necessitate PCN exchanges every 6–8 weeks as a preventative measure.

### Ureteroscopy

At present, ureteroscopy is considered the procedure of choice in the management of symptomatic urolithiasis in pregnancy, following the failure of conservative management. Safe and successful ureteroscopic management requires modern endoscopic equipment and sufficient endourologic expertise.

The safety and effectiveness of ureteroscopy in pregnancy has been demonstrated in a number of small series [66–85] (Table 65.6). A recent meta-analysis of published reports has documented the safety of ureteroscopic stone extraction or intracorporeal lithotripsy in pregnant women to be equal to that in the nonpregnant population, and complication rates have been low (0–20%) [86].

Ureteroscopy can be performed under general or spinal anesthesia. Intravenous sedation with fentanyl and propofol has also been described. The patient is positioned in the modified dorsal lithotomy position [67–69]. Both rigid and flexible ureteroscopes can be used, with instruments sized 8 Fr or smaller, which do not require the dilation of the ureteric orifice [70–72]. Ureteroscopy can be performed either with ultrasound guidance or with pulsed fluoroscopic imaging and mandatory fetal shielding. Performing ureteroscopy in pregnancy is not considered technically difficult, as physiologic dilation of the ureter helps with the manipulation of flexible ureteroscopes [73].

The holmium:YAG laser has emerged as the preferred and safest intracorporeal lithotripter utilized in pregnancy

**Table 65.6** Summary of studies of ureteroscopic management of urolithiasis during pregnancy.

| Study | Number of patients | Lithotripter used | Number stone-free (%) | Fetal or maternal complications | Level of evidence |
|---|---|---|---|---|---|
| Rana et al. [88] | 19 | Pneumatic | 15/19 (79) | None | 3 |
| Travassos et al. [72] | 9 | Basket | 9/9 (100) | None | 3 |
| Geavlete et al. [73] | 15 | Laser<br>Basket/grasper | 14/15 (93) | None | 3 |
| Akpinar et al. [71] | | Holmium:YAG laser | 6/7 (86) | None | 3 |
| Usai et al. [74] | 7<br>3 | Pneumatic<br>Basket/grasper | 3/3 (100) | None | 3 |
| Ulvik et al. [75] | 27 | Basket/grasper | 23/27 (71) | Ureteral perforation (1)<br>Preterm delivery (1)<br>Premature uterine contractions (2)<br>None | 3 |
| Watterson et al. [67] | 8 | Holmium:YAG laser | 7/9 (89%) | None | 3 |
| Lifshitz et al. [76] | 4 | Basket/grasper | 4/4 (100%) | None | 3 |
| Lemos et al. [70] | 14 | Ultrasound<br>Basket/grasper | 13/14 (93%) | None | 3 |
| Sharifi and Ahmandia [77] | 4 | Pneumatic/basket | 4/4 (100%) | None | 3 |
| Banon et al. [78] | 8 | Basket/grasper | 8/8 (100%) | Fever (2) | 3 |
| Tekerlekis et al. [79] | 16 | Basket/grasper | 12/16 (75%) | Premature uterine contractions (1) | 3 |
| Shokeir et al. [69] | 8 | Ultrasound<br>Basket/grasper | 5/8 (63%) | Maternal UTI (2) | 3 |
| Bozkurt et al. [80] | 32 | Pneumatic<br>Holmium:YAG laser | Not reported | Sepsis (1)<br>UTI (4)<br>Renal colic (2) | 3 |
| Elgamasy et al. [81] | 15 | Pneumatic/basket | Not reported | Premature labor (1)<br>Stent migration (1) | 3 |
| Isen et al. [82] | 9 | Pneumatic | 9/9 (100%) | Mild hematuria (1) | 3 |
| Kader et al. [83] | 17 | Pneumatic | 17/17 (100%) | None | 3 |
| Wang et al. [84] | 64 | Holmium:YAG laser | 52/64 (81.2%) | None | 3 |
| Polat et al. [85] | 16 | Pneumatic | 11/16 (68.7%) | None | 3 |

UTI, urinary tract infection.

[74, 75]. The holmium:YAG laser has a wide safety margin due to its unique wavelength (2100 nm) and limited depth of penetration in a fluid environment (<0.5 mm from the tip of the probe). Use of the holmium:YAG laser was reported to result in an 89% overall stone-free rate [74]. A theoretical concern with its use is the production of cyanide during laser lithotripsy of uric acid stones. However, there are no published reports of cyanide toxicity to date [86, 87]. The risk of cyanide toxicity should be negligible, as any cyanide produced during the lithotripsy should be diluted out from the urinary tract with the irrigant.

Alternative intracorporeal lithotripters used in pregnancy include the ballistic or pneumatic lithotripter, ultrasonic lithotripter, and forceps crushers [88–90].

Ultrasonic lithotripsy is known to be very safe to the surrounding tissues [91], but there is a theoretical concern regarding fetal auditory development. However, there is evidence to suggest that the peak pressure of the sound emitted by all intracorporeal lithotripters within the ureter does not affect fetal auditory development [92]. The main limitation of ultrasonic lithotripsy remains the rigid nature of the probe that restricts its use to rigid or semirigid ureteroscopes.

The electrohydraulic lithotripter (EHL) has the lowest margin of safety for use in pregnancy. EHLs generate high peak pressures and the electrical energy generated from the probe poses a potential risk for fetal injury and induction of premature labor. It is not recommended for use in pregnancy [44, 93].

The potential risks of ureteroscopy are similar to those in the nonpregnant population and include urinary tract infection, sepsis, ureteral perforation, and ureteral avulsion. In experienced hands and with use of proper equipment the complication rates are very low (Table 65.6).

### Percutaneous nephrolithotomy

Percutaneous nephrolithotomy (PCNL) is not advised during pregnancy. The necessity of prolonged general anesthetic, prone positioning, and need for fluoroscopy make PCNL a high-risk procedure during pregnancy. Nonetheless, with recent advancements of technique, cases of PCNL during pregnancy were reported to be successful using supine or lateral flank position and performing the procedure under total ultrasound guidance [94, 95].

### Extracorporeal shock-wave lithotripsy

Extracorporeal shock-wave lithotripsy (SWL) is presently contraindicated in pregnancy due to the potential adverse effects of high-energy shock waves on the fetus and the ionizing radiation exposure. However, treatment of six unknowingly pregnant women was not found to result in fetal malformations or chromosomal anomalies in the children [96].

## Conclusions

The safe and effective management of calculi in pregnancy requires a thorough knowledge of anatomic and physiologic changes that occur with each stage of pregnancy. Both fetal and maternal health must be considered. The use of ionizing radiation has to be minimized. Clinicians must use a team approach and adhere to strict indications for intervention in order to maximize a successful outcome for the mother and fetus.

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## 66

# Management of Renal Colic and Triage in the Emergency Department

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## Introduction

Acute renal colic is probably the most painful event a person can endure. Renal colic affects approximately 1.2 million people each year and accounts for approximately 1% of all hospital admissions. Most active emergency rooms treat an average of at least one patient with acute renal colic every day, depending on the size of the hospital [1]. Renal colic is often the supposed diagnosis made in the emergency room in patients presenting with an acute onset of flank or loin pain. Often, multiple investigations are done before the diagnosis is confirmed. Frequently this causes a delay in appropriate management. It is up to the attending physician or urologist not only to make a prompt diagnosis but also to initiate effective pain control and identify potentially complicated renal colic.

## Classic presentation of renal colic: symptoms and signs

Patients with acute renal colic classically present with a sudden onset of severe pain originating in the flank. The initial presentation typically lasts 3–18 hours. The progression of pain has been described as having three clinical phases. The typical attack starts slowly and insidiously. The pain typically waxes and wanes in severity, and develops in waves or paroxysms that are related to movement of the stone in the ureter and associated ureteral spasm. Paroxysms of severe pain usually last 20–60 minutes. Pain is thought to occur primarily from urinary obstruction with distension of the renal capsule. The pain reaches its maximum 1–2 hours after the start. In the constant phase, the period of sustained maximal pain, the pain tends to remain constant until it is either treated or allowed to improve spontaneously. Most patients arrive in the emergency room during this phase of the attack. In the final phase of renal colic, relief can occur spontaneously at any time after the initial onset and most commonly lasts 1.5–3 hours.

The pain may localize at different sites of the abdomen depending on the exact position of the calculus in the urinary tract. Stones commonly become impacted in the urinary tract in a calyx, at the ureteropelvic junction, at the pelvic brim where the ureter begins to arch over the iliac vessels, at the broad ligament in females, and at the ureterovesical junction, which is the most common site of impaction. Pain from upper ureteral calculi tends to radiate to the flank and lumbar areas. Mid-ureteral calculi cause pain that radiates anteriorly and caudally. Distal ureteral calculi cause pain that tends to radiate into the groin or testicle in the male or labia majora in the female. If a calculus is lodged in the distal intramural part of the ureter, symptoms may mimic detrusor overactivity or cystitis. These symptoms include suprapubic pain, urinary frequency, urgency, dysuria, or pain at the tip of the penis in men.

On examination of the abdomen, the pain localizes to the costovertebral angle. The remaining examination findings are often unremarkable. The characteristic difference between patients with renal colic and those with an acute abdomen lies in the restlessness of patients with renal colic. Patients with an acute abdomen of surgical origin usually lie as still as possible. Rebound tenderness will be present in an abdomen with peritonitis. The pain is generally diffuse in an acute abdomen as opposed to renal colic where the patient can often point to the site of maximum tenderness, which is likely to be the site of the ureteral obstruction.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

Hematuria is often associated with renal colic. However, 15% of all patients with urinary calculi do not have hematuria [2]. Therefore, the lack of hematuria does not exclude the possibility of acute renal colic. Other clinical signs that may be encountered are fever, chills, nausea, vomiting, and tachycardia. The presence of pyuria, fever, leukocytosis, or bacteriuria suggests the possibility of a urinary infection and the potential for an infected obstructed kidney. This is a potentially life-threatening situation and should be treated as a surgical emergency.

## Mechanism of renal colic

Renal colic is the consequence of the acute dilation of the urinary tract proximal to an obstruction along with smooth muscle spasm at the site of the obstruction. High intrarenal pressure promotes local synthesis and release of prostaglandin E2 with subsequent vasodilation of the afferent arterioles, which promotes diuresis and a further rise in renal–pelvic pressure, potentially exacerbating the patient's pain. In addition, ureteral smooth muscle spasm is directly stimulated by prostaglandin E2 [3]. Most of the pain receptors of the upper urinary tract responsible for the perception of renal colic are located submucosally in the renal pelvis, calyces, renal capsule, and upper ureter. Acute distension seems to be most important in the development of the pain of acute renal colic. Muscle spasm, increased proximal peristalsis, and local inflammation at the site of obstruction may contribute to the development of pain through chemoreceptor activation and stretching of submucosal free nerve endings. Renal colic pain rarely, if ever, occurs without obstruction.

### Autoregulatory process associated with obstruction

The initial renal response to acute unilateral ureteral obstruction is the release of prostaglandins, especially E2, resulting in vasodilatation of the afferent arterioles and worsening of ureteral smooth muscle spasm. Subsequently, the dilation of the afferent arterioles results in an increase in renal blood flow and glomerular filtration rate [4]. As a consequence, more urine is produced, and the renal pelvis and ureter dilate further. Distension of the renal pelvis initially stimulates ureteral hyperperistalsis. Peak hydrostatic renal pelvis pressure is attained within 2–5 hours after a complete obstruction. The initial phase of obstruction lasts approximately 1.5 hours and is followed by vasoconstriction of the efferent arterioles with a resultant decrease in renal blood flow. Eventually, the afferent arterioles constrict and ureteral pressures fall [4]. By this time, intraureteral pressures have returned to normal, but the proximal ureteral dilation remains and ureteral peristalsis is minimal. The interstitial edema of the ipsilateral kidney enhances fluid reabsorption, which helps to increase the renal lymphatic drainage to establish a new, relatively stable, equilibrium. At the same time, renal blood flow increases in the contralateral kidney as renal function decreases in the obstructed kidney. The return of renal function after a period of complete unilateral ureteral obstruction is an important clinical concern for the urologist. The renal function recovery rate after 1 week of ureteral obstruction is 100%, but after 4 weeks only a 30% recovery can be expected [5]. If only a partial obstruction is present, the same changes occur, but to a lesser degree.

## Diagnosis

The diagnosis of renal colic is often made based on clinical symptoms alone, although confirmatory tests are usually performed. Additional tests are useful not only to confirm the diagnosis but also to facilitate in the decision-making process on further treatment. Before a decision on treatment can be made, a urologist must know the size, shape, orientation, radiolucency, and location of the stone. Other factors that may influence further treatment are kidney function and the presence of infection, as well as all other clinical information and comorbid conditions the patient may have.

### Laboratory investigations

#### Urinalysis

Patient history, physical examination, and urinalysis alone cannot help confirm or exclude urolithiasis with sufficient accuracy. In particular, hematuria testing has a sensitivity of 81–84% and a specificity and negative predictive value of 48 and 65%, respectively [6, 7].

In addition to the presence of blood in the urine, the presence or absence of leukocytes, crystals, and bacteria, and the urinary pH should be documented. A urinary tract infection should be suspected if the number of white blood cells (WBCs) in the urine is greater than 10 per high-power field. Determining urinary pH may be helpful in planning treatment. With a pH lower than 6.0, a uric acid stone should be considered. The observation of cystine, uric acid, struvite, or calcium oxalate crystals in the urine may be an indication of the type of calculus ultimately found.

#### Hematologic tests

While mild leukocytosis often accompanies a renal colic attack, a high index of suspicion for a possible infection should accompany any serum WBC count of 15 000/μl or higher in a patient presenting with an apparent acute kidney stone attack, even if afebrile. Urea, creatinine, and electrolyte testing may be helpful in identifying patients with renal function impairment as well as in giving some information on the hydration status of the patient, which may determine their further management.

## Imaging studies

### Plain abdominal radiograph

The historical cornerstone of the evaluation of renal colic was a radiograph of the kidneys–ureters–bladder (KUB). Not all urinary calculi will be visible on the KUB radiograph because of their small size, calculus radiolucency, or overlying bowel gas. Typically, 90% of calculi are radiopaque. However, many calcifications that can be observed on the KUB radiograph are not calculi, but phleboliths, vascular calcifications, calcified lymph nodes, or bowel contents. Typically the differentiation between a phlebolith and a urinary calculus becomes easier when the KUB radiograph demonstrates a lucent center, identifying the calcification as a phlebolith. However, this central lucency is not observed as often on computed tomography (CT) scans. The KUB radiograph is also quite accurate for helping determine the size and shape of a visible radiopaque calculus. It uses the same orientation and anatomic presentation that is observed on fluoroscopy images during endoscopic ureteral surgery. Also, the progress of the stone can be easily monitored with a follow-up radiograph. For these reasons, many urologists recommend a KUB in addition to a CT scan in the workup of renal colic (Figure 66.1).

### Renal ultrasound

Renal ultrasound is most useful in diagnosing relatively large calculi within the renal pelvis or kidney. However, it is less useful than other modalities for detecting ureteral calculi. One benefit is that it can easily diagnose any significant hydronephrosis. Ultrasound can also be used to diagnose other pathologic conditions such as abdominal aortic aneurysm or cholelithiasis, which can sometimes be mistaken for acute renal colic. Combining a renal ultrasound with a KUB radiograph can be adopted as a reasonable alternative when a CT scan cannot be performed.

### Intravenous urogram

Intravenous urography (IVU) has been the imaging modality of choice for investigating acute renal colic since Osborne et al. first described it in 1923 [8]. It provides detailed information about the anatomy of the renal collecting system and ureters, offers some information about renal function and the degree of obstruction, and is good for the planning of calculus surgery (Figure 66.2). When a patient has multiple pelvic calcifications, identifying the actual stone is simple with an IVU and it can also show nonopaque calculi as filling defects.

There are, however, limitations: adequate bowel preparation is necessary for good-quality studies, and there is a risk of contrast-related allergic and anaphylactic reactions (10 and 1% of patients, respectively) [9]. Also, in patients with renal failure and diabetes mellitus, the risk of contrast-induced nephrotoxicity is 25% [10]. A serum creatinine level of more than 2 mg/ml is a relative contraindication to the use of intravenous contrast. Furthermore, there may be a need for delayed films if

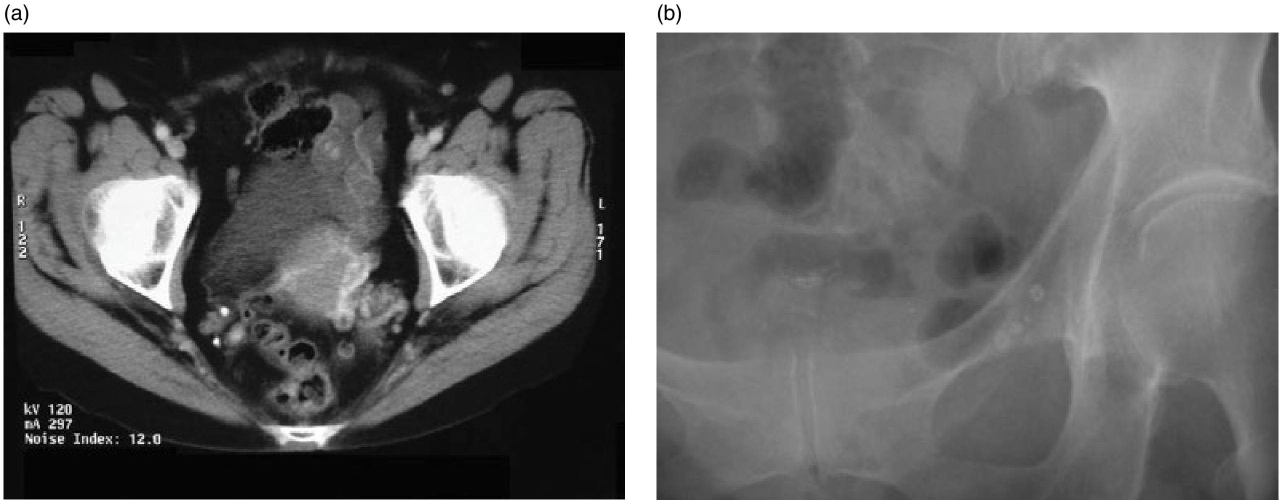

**Figure 66.1** (a) Distinguishing renal calculi from phleboliths in the pelvis can be intricate. This axial noncontrast CT demonstrates two phleboliths in the pelvis. One demonstrates the comet-tail sign, which is a soft-tissue attenuation leading to the phlebolith and represents a vein in which it is located. (b) On a KUB radiograph, a phlebolith classically demonstrates a central lucency whereas ureteral calculi do not.

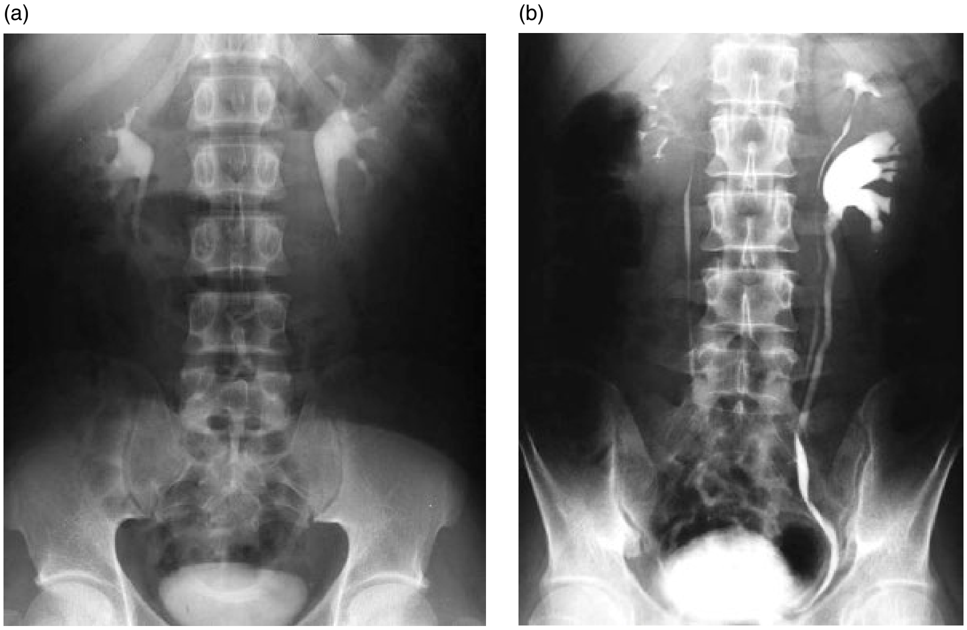

**Figure 66.2** (a) An IVU obtained in a patient with renal colic demonstrates a calculus <6 mm, normal anatomy, and no signs of obstruction, which makes for the ideal candidate for conservative management or medical expulsive therapy. (b) IVU image demonstrates a calculus >6 mm at the ureteropelvic junction in the lower moiety of a kidney with complete ureteral duplication. This represents a clear indication for a surgical intervention.

there is high-grade obstruction, which can lead to delays in diagnosis and treatment.

The classic finding of acute ureteral obstruction is a persistent nephrogram, caused by an increase in the intrarenal concentration of the contrast. Even without observing any specific calculus, the presence of a persistent nephrogram in one kidney with prompt contrast excretion by the contralateral kidney is highly suggestive of ureteral obstruction secondary to a calculus. There may also be columnization on the delayed films. Extravasation of contrast around the collecting system may be a sign of a ruptured fornix, while pyelolymphatic backflow indicates that contrast has entered into the renal lymphatic drainage system. Both are considered signs of a more severe ureteric obstruction.

### Computed tomography scan

The use of a noncontrast helical CT (NCCT) scan to assess patients with acute flank pain was first reported in 1995 by Smith et al. [11]. Recent studies have shown that NCCT is more accurate and reliable than IVU in making a diagnosis in patients presenting with acute flank pain. NCCT has both sensitivity and specificity of 94–100% compared with 60–94% for IVU, partly because NCCT clearly demonstrates both radiopaque and radiolucent stones, as well as detecting alternative causes for a patient's symptoms [12, 13]. Unrelated pathology may be detected by NCCT in 28% of patients [14]. Moreover, NCCT does not require special preparation or intravenous contrast, thus avoiding the risk of contrast-associated reactions and allowing imaging studies to be completed in a few seconds, which improves image quality by reducing respiratory motion and artifact [15, 16]. For these reasons, NCCT has displaced IVU to become the investigation of choice for acute flank pain in many institutions across North America, Europe, and Australasia [13, 17, 18].

Very finely spaced scans are taken through the kidneys and bladder areas, where symptomatic calculi are most likely to be encountered (Figure 66.3). A KUB radiograph is sometimes automatically included in a renal colic study, as mentioned.

Katz et al. found that CT scan estimates of stone size to be similar to those determined by plain film radiography [19]. Both the estimated mean stone diameter and the length were similar on CT and KUB. The limitation of this method is that if CT collimation is too large relative to the stone, the entire stone may not be scanned, leading to underestimation of stone length. This inaccuracy can be best compensated for by making sure that slices are small in relation to stone size. Therefore, 5 mm collimation is preferred to 10 mm collimation. In addition to verifying similarity of stone size estimates by CT and KUB, Katz et al. also found that the prediction of spontaneous stone passage was similar using the two imaging modalities. It is widely believed that transverse stone dimension is more important than length in predicting the likelihood of spontaneous passage. Interestingly, the

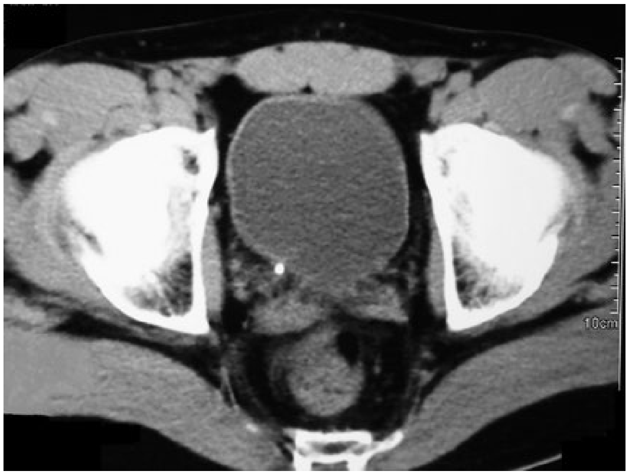

**Figure 66.3** Classic example of a calculus <6 mm in the intramural part of the ureter. Conservative management or medical expulsive therapy would be an appropriate course of action.

study demonstrated the measured anteroposterior stone diameter on CT to be wider in many cases than the measured transverse diameter on CT and plain film. This result could be explained by orthogonal imaging in curved portions of the ureter, where larger anteroposterior diameters were found irrespective of stone location. At any given point along the CT scan, the ureter is either ascending or descending; therefore, an anteroposterior cut would slice tangentially, and cause a wider anteroposterior than transverse diameter.

Phleboliths are often confused with ureteral calculi. On a KUB radiograph, the characteristic lucent center of a phlebolith is often visible, but is not present in a true calculus. Unfortunately, as mentioned above, CT scans usually fail to reveal this central lucency. The "rim sign," originally reported by Smith et al. in 1995, is described as a rim or halo of soft tissue, visible on CT scans, that completely surrounds ureteral calculi [11]. This effect is enhanced by the local inflammation in the ureteral wall with subsequent edema at the site of the calculus. The rim sign is generally incomplete with phleboliths. The rim sign is more likely to be present in small stones up to 5 mm in diameter.

Calculi, including relatively radiolucent uric acid calculi, and cystine and matrix stones, are easily identifiable on CT scan. While they do not contain calcium, they are still much denser than the surrounding soft tissue. The only exception is indinavir calculi, which are not visible on CT scans. These patients require an IVU that will demonstrate a filling defect.

Currently, CT scans can be used to estimate the relative density of the calculus and composition to some extent. The mean peak Hounsfield reading of uric acid calculi and calcium oxalate calculi are around 344 ± 152 and 652 ± 490 HU, respectively [20].

Secondary signs of obstruction may be visible on CT scans. In some cases, if the stone passed shortly before the study, these signs may be the only evidence that the patient had a stone. These secondary signs include ureteral dilation with hydronephrosis and renal enlargement with streaking of the perinephric fatty tissue [2]. Although NCCT is unable to provide direct information on function and drainage, the degree of obstruction can be assessed by secondary signs, such as the severity of hydronephrosis and ureteral dilation and the presence of perinephric fluid, indicating forniceal rupture. Smith et al. found a high correlation between secondary signs of obstruction and the presence of a ureteral calculus. In particular, the combination of collecting system dilation and perinephric stranding had a positive predictive value of 98%, while the absence of both of these secondary signs had a negative predictive value of 91% [21].

The biggest advantage of a CT scan over an IVU lies in its ability to diagnose other underlying pathology mistaken for renal colic, such as aortic aneurysms, pancreatitis, appendicitis, ovarian problems, and bowel disorders.

Disadvantages of a CT scan include difficulties in identifying a stone if the patient exhibits limited hydronephrosis with additional pelvic calcifications and the little information it gives on the renal function. Stone location can be described in anatomic terms, but the scan lacks the surgical orientation that most urologists prefer. Spiral CT scans can, however, allow for anatomic three-dimensional image reconstruction, which may be useful in the evaluation and pretreatment planning (Figure 66.4).

It is recommended to add a KUB radiograph when a renal colic CT scan study is performed for acute flank pain, especially when the CT scan findings are positive for urolithiasis. The KUB radiograph not only provides more precise information about the size and shape of a stone, but it also quickly reveals whether stones are radiopaque or radiolucent. Follow-up evaluations are easier because only a repeat KUB radiograph is needed for comparison.

## Differential diagnoses of renal colic

### Alternative urologic pathology

**Pyelonephritis**

Pyelonephritis is a common cause of flank pain, but the discomfort is usually described as a relatively mild dull ache rather than typical renal colic pain. Fever, chills, nausea, and vomiting are often associated symptoms. Flank and costovertebral angle tenderness are also present, but more severe than with renal colic.

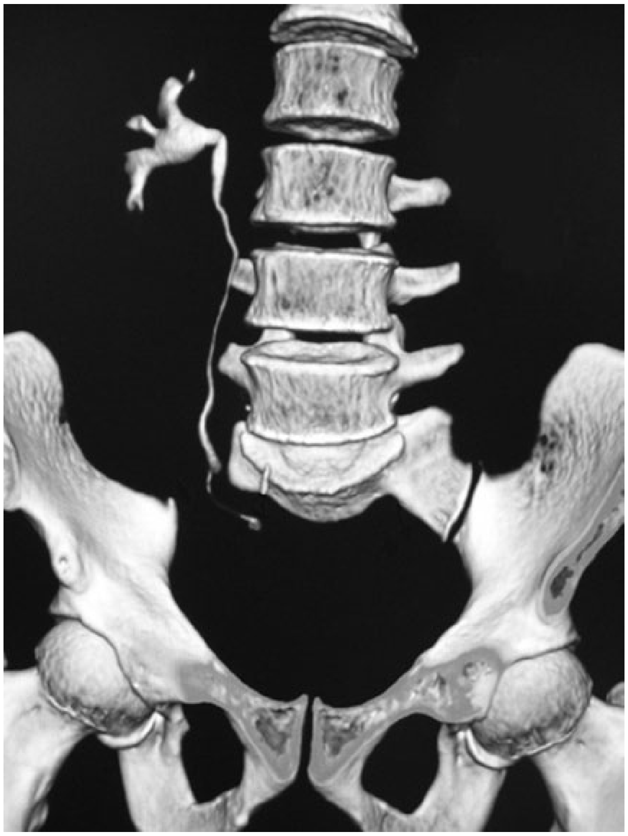

Figure 66.4 A three-dimensional reconstruction of NCCT of a patient with a single kidney with a calculus impacted at the pelvic brim. This imaging option can be a valuable adjunct in high-risk patients in choosing the most appropriate treatment option as well as planning the surgery.

**Renal abscesses**

Renal abscesses tend to cause pain similar to pyelonephritis rather than renal colic. Sometimes, a flank mass may be palpable. Urinalysis often demonstrates a urinary infection, but can be normal in some cases. Fever and chills are common. It is usually associated with patients who are immune compromised.

**Kidney tumors**

Kidney tumors may cause flank pain either from renal capsular stretching or by mechanical compression of large tumors. Primary tumor extension into the renal pelvis can cause urinary obstruction, although this is usually a slow process during which patients are often asymptomatic.

**Ureteropelvic junction obstruction**

Ureteropelvic junction obstruction is one of the more common causes of renal pain. The pain is similar to an acute ureteral obstruction and usually follows the intake of large amounts of fluid, which causes diuresis resulting in renal pelvic distension and colic. The pain is not as severe as renal colic and is recurrent in nature.

**Obstructive uropathy due to other causes**

Other obstructive causes include:

- blood clots
- renal papillary necrosis
- ureteral strictures
- renal cysts
- polycystic kidney disease
- pyelocalyceal diverticulum.

### Vascular pathology

**Abdominal aortic aneurysms**

Patients with an abdominal aortic aneurysm may present with symptoms of flank pain that mimic renal colic. Symptoms are generated from either a leaking or ruptured aneurysm. Large aneurysms may lie in close approximation to the ureter and cause hematuria from local ureteral inflammation. Abdominal aortic aneurysms are best diagnosed with ultrasound or a CT scan. CT scanning is particularly useful in cases of suspected renal colic in patients older than 50 years who are at risk for an aortic aneurysm.

### Gastrointestinal tract pathology

Causes include Crohn's disease, diverticulitis, appendicitis, cholecystitis, and pancreatitis.

### Gynecologic pathology

Causes include ectopic or tubal pregnancy, endometriosis, ovarian cyst, and pelvic inflammatory disease.

## Medical and surgical treatment

The management of acute renal colic is a problem commonly encountered by both urologists and emergency medicine physicians. One aspect of the medical treatment is the management of acute renal colic pain, a condition that demands rapid and effective analgesia. Currently, nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids are the best agents for acute renal colic, overshadowing other drugs such as antimuscarinics (i.e. hyoscine butylbromide) [22].

In addition to controlling the pain associated with obstructing calculi, drug therapy that promotes the expulsion of stones is an evolving aspect of medical therapy.

Observation with analgesia is most appropriate for patients without infection whose pain can be well-controlled with oral medications. Key factors contributing to stone retention include edema, ureteral spasm, and infection, all of which are potential pharmacologic targets. However, in cases of persistence, ureteral obstruction, or pain, other minimally invasive interventions are preferred [23].

Figure 66.5 shows an algorithm for the evaluation, triage, and further management of suspected renal colic.

## Triage

The majority of emergency departments (EDs) in the United States (87.4%) do not have guidelines regarding the treatment of patients who present with renal colic [1]. Having well-designed guidelines in the ED will not only facilitate and expedite diagnosis and enable appropriate treatment, but will also significantly decrease patient morbidity and channel patients with life-threatening conditions to the appropriate departments without delay. Such guidelines should help

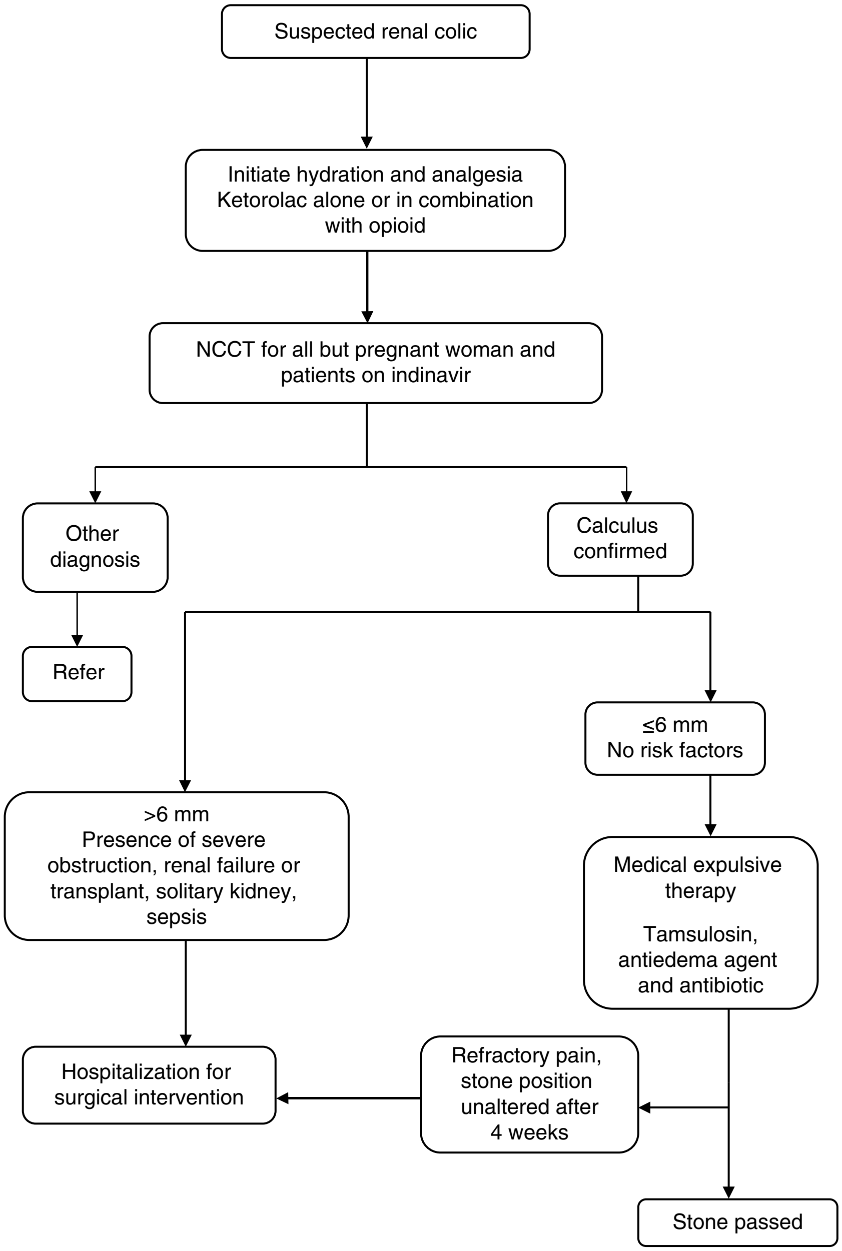
Suspected renal colic
Initiate hydration and analgesia Ketorolac alone or in combination with opioid
NCCT for all but pregnant woman and patients on indinavir
Other diagnosis
Calculus confirmed
Refer
≤6 mm No risk factors
>6 mm Presence of severe obstruction, renal failure or transplant, solitary kidney, sepsis
Medical expulsive therapy
Tamsulosin, antiedema agent and antibiotic
Hospitalization for surgical intervention
Refractory pain, stone position unaltered after 4 weeks
Stone passed

**Figure 66.5** Algorithm of the evaluation, triage, and further management of a patient with suspected renal colic.

acquire the most suitable imaging modalities, decide which patients should be hospitalized or referred to other departments, and facilitate in the triage and decision-making on conservative versus surgical therapy.

### Predicting spontaneous stone passage

Setting patient expectations with regard to the likelihood of spontaneous stone passage and the time to stone passage is critical to help guide the patient to make an informed decision between conservative management and surgical intervention. The management of patients with ureteral calculi relies on estimated stone size and the stone's potential for spontaneous passage. Several factors influence the likelihood of spontaneous stone passage, such as location and history of spontaneous expulsion. Indeed, with accurate information, more patients might select early intervention as opposed to expectant observation. In general, smaller calculi are more likely to pass spontaneously, but stone passage also depends on the specific anatomy of the upper urinary tract. Any anatomic abnormality could make the passing of even a small stone impossible.

Spontaneous passage of urinary calculi of less than 5 mm in diameter may occur in most patients, although the calculus may take 40 days or more to pass [24]. Prospective clinical trials have stratified the spontaneous stone passage rate and time to stone passage. Stones of 4 mm and smaller have a 94% chance of spontaneous passage, whereas stones of 4–6 mm in size will pass spontaneously 50% of the time. Average time to stone passage was 1 week for a stone of less than 2 mm, 2 weeks for a stone of 2–4 mm, and 3 weeks for a stone of 4–6 mm. Calculi of greater than 6 mm are unlikely to pass spontaneously [25–28].

Excluding complications related to stone disease, such as severe hydronephrosis, renal insufficiency, intractable pain, and infection, that mandate a more aggressive approach (ureteral stent, nephrostomy, retrograde intrarenal surgery, extracorporeal shock-wave lithotripsy), drug therapy is useful in the management of urolithiasis and represents an important adjunct to conservative therapy.

With regard to cost, observation represents the most cost-effective approach to ureteral calculi, but it remains unsatisfactory for recurrent stone-formers, in whom the high rate of recurrence precludes a conservative approach [29]. A cost-effectiveness model revealed that a conservative approach to ureteral stones is associated with lower cost than any invasive procedures only if it is followed by stone expulsion [30].

It is suggested that a conservative approach to larger ureteral stones should not be extended for longer than 2 weeks in order to avoid renal function impairment, urosepsis, and intractable pain [31]. Many urologists have adopted the conservative treatment plan of 4 weeks proposed by Hubner et al. [28]. This is safe if the stone is 6 mm or smaller in the absence of severe hydronephrosis.

### Hospitalization

The decision to hospitalize a patient with a stone is usually made based on clinical grounds rather than on any specific finding on a radiograph. Watchful waiting for spontaneous stone passage is certainly the least invasive management option; however, several signs and symptoms may prohibit such a course of action. Fever, chills, or other sign of infection are the most urgent scenarios prohibiting watchful waiting. Evidence of renal insufficiency or frank anuria similarly necessitates urgent intervention. Poorly controlled renal colic pain and vomiting are more subjective indications. Other than extreme cases necessitating inpatient management, clinical scenarios that may warrant acute intervention include inability to perform routine activities safely and reliably, upcoming travel plans, job restrictions, etc. [32]. Patients with obstructing ureteric stones of greater than 6 mm are seldom likely to pass their stone spontaneously, and early admission for procedural therapy may be prudent [2]. Most patients with acute renal colic can be treated on an ambulatory basis. Hospitalization for an acute renal colic attack rarely lasts for longer than 24 hours, after which the patient can go home.

### Surgical intervention

The presence of urosepsis in a patient with an obstruction from stone disease is a true surgical emergency. This condition requires hospital admission with intravenous fluids, antibiotics, and, most importantly, early drainage of the affected kidney using either retrograde-placed double-J stents or percutaneous nephrostomy.

Retrograde endoscopy should be reserved for relatively mild cases that are medically stable. Double-J stents virtually guarantee drainage of urine from the kidney and bypass the obstruction. This relieves patients of their renal colic pain even if the actual stone remains.

In patients with pyonephrosis in association with an obstructing calculus, retrograde endourologic procedures, such as retrograde pyelograms and double-J stent placement, may worsen the infection by pushing infected urinary material into the obstructed kidney and may exacerbate the systemic sepsis. These situations clearly indicate the need for a percutaneous nephrostomy, especially in patients who are hemodynamically unstable. Later, when the infection is under control and the patient is no longer septic, a more definitive procedure can be performed to remove or fragment the obstructing stone.

Approximately 10–20% of all kidney stones may cause the patient enough problems to require surgical removal.

If there is no evidence of movement or passage of a ureteral stone that has been treated conservatively for 3–4 weeks or if pain is intractable, surgical intervention is warranted. Other conditions that may require a more expedited approach are the presence of unusually large stones, high-risk medical conditions, uncontrollable pain, renal failure, solitary kidneys, renal transplants, and pregnancy.

## Hydration

Initial treatment of a renal colic patient in the ED starts with obtaining intravenous access to allow fluid, analgesic, and antiemetic medications to be administered. Some patients may be dehydrated from nausea and vomiting. Some believe hydration may increase the speed of passage of a stone through the urinary tract. Traditionally, patients were aggressively hydrated intravenously or were told to increase their oral hydration to promote stone passage [33]. This practice stems from the thought that the stone might pass spontaneously if forced hydration is utilized. Using hydration as a therapy to assist stone passage remains controversial.

Some urologists worry that the extra fluid only increases the hydrostatic fluid pressure inside the blocked renal unit, exacerbating the pain. In addition to this, diuresis may be detrimental to the ipsilateral renal unit by potentially causing forniceal rupture [34, 35]. Therefore, fluid restriction may be more advantageous to the patient.

Maintenance intravenous fluids are as efficacious as forced hydration with regard to patient pain perception and narcotic use. Moreover, it appears the state of hydration has little impact on stone passage [36].

Intravenous hydration during an episode of renal colic is necessary in patients who are unable to tolerate liquids by mouth. It is therefore recommended that patients who have been vomiting or have laboratory values suggesting dehydration receive appropriate replacement fluids plus their normal maintenance requirements.

## Pain relief

The two principal classes of drugs used for analgesia in renal colic are NSAIDs and opioids. The combination of these drugs is currently the preferred treatment of renal colic at most EDs.

### Narcotics and opioids

The mainstay of medical therapy for patients with acute renal colic is parenteral narcotic analgesics. These medications work primarily on the central nervous system (CNS) to reduce the perception of pain. When considering a medication and dosage range, it must be remembered that acute renal colic is probably the most painful episode to affect humans. Morphine, meperidine, and tramadol are the most commonly used drugs.

Morphine is the principal opium alkaloid product. As a potent narcotic analgesic, morphine sulfate controls severe pain primarily through a CNS mechanism. Adverse effects include respiratory depression, drowsiness, nausea, and vomiting. The usual dose of morphine sulfate is 10 mg/70 kg of body weight intramuscularly every 4 hours. For more rapid results, morphine sulfate can be administered intravenously in doses of 4–10 mg, but it must be administered slowly to avoid excessive adverse effects and respiratory depression.

Similar to morphine sulfate, meperidine is a potent parenteral narcotic analgesic. Doses of 1 mg/kg should be adequate to bring relief to a patient with renal colic. Meperidine offers a slightly more rapid onset of action and slightly shorter duration of analgesic activity than morphine sulfate. The dosage is usually 1 mg/kg intramuscularly every 4 hours. This dosage is reduced by at least 50% when administered intravenously. The actual effective dosage varies according to the source of the pain and the individual's tolerance. As with morphine sulfate, intravenous administration should be performed slowly.

Tramadol is a synthetic cyclohexanol derivative used since the late 1970s. It is a centrally acting analgesic with inhibition of serotonin and norepinephrine reuptake. Fewer side effects are seen with tramadol, although it is less effective for severe pain [37]. Negligible cardiac and respiratory depression has been shown, and reported side effects are minor: mainly nausea and emesis, usually preventable by slow injection of the drug and prophylactic administration of an antiemetic.

For long-lasting pain relief, intravenous opioids titrated to effect are recommended. However, on-demand intravenous titration of drugs is difficult to organize in a busy ED, especially if patients have to leave for the medical imaging department. A continuous intravenous tramadol drip, on the other hand, proved to offer superior analgesia and greater patient satisfaction without an increase in reported side effects [37].

### Nonsteroidal anti-inflammatory drug therapy

NSAIDs have a direct action on the underlying cause of the pain by inhibiting prostaglandin synthesis, and subsequently reduce vasodilatation with a drop in intrarenal pressure, inhibit ureteral smooth muscle contraction, and reduce urinary tract inflammation [38].

There are various NSAIDs available for either intramuscular or intravenous use. The most common intravenous NSAID used in the USA is ketorolac, which works at the peripheral site of pain production rather than on the CNS. It has fewer adverse effects and often provides dramatic improvement in pain symptoms. The dosage is an initial 30–60 mg intramuscularly or 30 mg intravenously, followed by 30 mg intravenously or intramuscularly every 6–8 hours. Ketorolac has been shown to be as effective in the treatment of renal colic as the narcotic meperidine [39, 40].

In more severe cases, ketorolac can be combined with narcotic analgesia with better analgesic effect than either one administered individually. Once the acute episode has been dealt with, an oral NSAID can be used. Of the various enteral NSAIDs, ketorolac, ibuprofen, or the newer oral cyclo-oxygenase-2 inhibitors are equally effective for pain management in outpatients. Chemically, ketorolac and ibuprofen are similar to aspirin and may increase the prothrombin time when administered with anticoagulants. They should be avoided in patients with peptic ulcer disease, renal failure, or recent gastrointestinal bleeding.

#### Antidiuretics

Desmopressin (DDAVP), a potent antidiuretic medication that is essentially an antidiuretic hormone, can dramatically reduce the pain of acute renal colic in many patients. It is thought to work by reducing the intraureteral pressure, but it may also have some direct relaxing effect on the ureteral musculature. Whether this therapy significantly affects eventual stone passage is unknown [41]. It is available as a nasal spray (usual dose 40 μg) and as an intravenous injection (4 μg/ml). Generally, only one dose is administered. While some human studies lack adequate controls and further studies must be conducted, desmopressin therapy currently appears to be a promising alternative to analgesic medications in patients in whom narcotics cannot be used or in whom the pain is unusually resistant to standard medical treatment.

### Antiemetics

Because nausea and vomiting frequently accompany acute renal colic, antiemetics often play a role in renal colic therapy. Metoclopramide is a well-known agent in the treatment of renal colic. Its antiemetic effect stems from its dopaminergic receptor blockage in the CNS. The effect after intravenous injection of 10 mg is rapid; within 3 minutes the patient experiences relief. Other medications commonly used as antiemetics include promethazine and prochlorperazine. Antiemetics are recommended when patients with renal colic have been vomiting actively or report nausea sufficient to interfere with oral therapy.

### Medical expulsive therapy

As discussed above, stone size affects expulsion times, but other factors such as stone shape and edema around the stone may also have an effect. Additionally, the sympathetic nervous system modulates ureteral activity, as demonstrated by the presence of adrenergic receptors in the ureter. Various medications or combinations thereof have been used to facilitate and expedite the passage of ureteral stones. The rationale for the combination of an anti-inflammatory drug (NSAID or steroid) with a smooth muscle relaxant (nifedipine or tamsulosin) is that the former will reduce edema while the latter will inhibit stone-induced ureteral spasm, thus maintaining peristaltic rhythm [30, 42, 43].

However, medical expulsive therapy (MET) should only be used in favorable conditions for spontaneous stone passage. Patients who elect for MET should have well-controlled pain, no clinical evidence of sepsis, and adequate renal functional reserve. Patients should be followed with periodic imaging studies to monitor stone position and to assess for hydronephrosis. Since patient complaints and stone size do not predict future renal function loss and time to permanent renal injury cannot be easily estimated, intervention should be recommended for any patient with persistent obstruction, failure of stone progression, or recurrent colic pain.

#### α-Adrenergic antagonists and calcium channel blockers

The presence of α- and β-adrenergic receptors has been demonstrated in human ureters. α1-Adrenergic receptors, particularly subtype α1d, are present in high density in the lower ureteral segment and may play an important role in lower ureteral physiology [44]. Norepinephrine is the main alpha-agonist and exerts a positive chronotropic and inotropic effect on the ureter. As a result, stimulation of α-adrenergic receptors decreases the volume of urine flow through the ureter.

α-Adrenergic antagonists are able to inhibit the basal tone and peristaltic frequency, dilating the ureteral lumen and facilitating in stone passage [45]. Several investigators have shown the utility of α1-blockers and their spasmolytic action in the active expulsion from the distal ureter [31, 46]. Tamsulosin may increase the urine bolus, and thus the pressure, above the stone; at the same time, the agent may decrease peristalsis, and thus the intraureteral pressure, below the stone. The net effect is an increased intraureteral pressure gradient around the stone, which ultimately results in a stronger expulsive force [35].

Yilmaz et al. evaluated tamsulosin, terazosin, and doxazosin alone compared with watchful waiting and found a significant increase in spontaneous stone passage with all three alpha-blockers (79, 78, 76, and 53%, respectively) [47]. A recent meta-analysis of 11 randomized clinical trials in more than 900 patients concluded that alpha-blockers increase the rate of spontaneous stone passage by 44% [48].

Moreover, α1-blockers reduce the need for analgesia by decreasing the frequency of peristaltic contractions in the obstructed ureteral tract, thus decreasing the frequency of ureteral colic [49]. There may be a double action of tamsulosin on the control of pain associated with ureteral colic; one on the smooth muscle, preventing spasm, and a second on C-fibers or sympathetic postganglionic neurons, which also block pain conduction to the CNS [50]. In addition, tamsulosin drastically decreases the need for hospitalization (10 vs. 27.5%), as well as the need for endoscopic procedures (0 vs. 13%) [31].

Calcium channel blockers such as nifedipine represent a valid and well-established pharmacologic treatment for urolithiasis owing to their spasmolytic action on the ureter.

The primary functional anatomic unit of the ureter is the smooth muscle cell, which functions in response to changes in calcium ion concentration. At the most fundamental level, an increase in calcium concentration results in relaxation. Ureteral stones induce ureteral spasm, which results in arrest of stone passage. Studies in both animal and human ureters show that calcium antagonists, namely nifedipine, inhibit the quick phasic contractions without affecting tonic activity [42].

Porpiglia et al. showed that medical treatment with nifedipine and deflazacort was both safe and effective, as evidenced by increased stone expulsion rate, decreased expulsion time, and reduced need for analgesic therapy [42]. Borghi et al. may have provided the most compelling evidence for the isolated effect of nifedipine when they compared nifedipine plus methylprednisolone with prednisolone alone in ureteral stones of up to 15 mm, and reported a success rate of 87% in the nifedipine arm compared with 65% in the control arm [51].

Two studies have compared alpha-blockade with calcium channel blockade with regard to spontaneous stone passage, with both finding an advantage for tamsulosin. Dellabella et al. evaluated patients with ureteral stones of greater than 4 mm and found tamsulosin to be the most effective, with a 97% success rate and an average of 72 hours to passage compared with 77% for nifedipine, with an average of 120 hours to passage [50]. Porpiglia et al. compared tamsulosin plus deflazacort with nifedipine plus deflazacort in a control group. Although not as significant as the findings in the study by Dellabella et al., there was a slight advantage of tamsulosin over nifedipine for overall effect (85 vs. 80%) and days to passage (7.7 vs. 9.3 days) [52].

Nifedipine blocks all ureteral contraction, while tamsulosin significantly reduces it, but still maintains some baseline activity. Thus, both agents work well to block the disorganized counteractive contractile activity associated with ureteral spasm, but the possibility of maintaining some degree of antegrade peristalsis allowed by alpha-blockade may explain the slight advantage [32]. Therefore, it is advocated to use tamsulosin as a first-line approach for the outpatient management of patients with distal ureteral stones.

Other studies that have been recently published, challenging the use of both alpha-adrenergic antagonist and calcium channel blockers. One of the studies by Robert Pickard established that neither an alpha-blocker, tamsulosin, nor the calcium channel blocker, nifedipine, showed any clinically useful benefit for expediting the spontaneous passage of stones and thereby decreasing the number of surgical interventions [53]. This multicenter trial was randomized with 1167 participants and they found by 4 weeks 80% of the patients taking placebo, 81% of the patients taking tamsulosin, and 80% of the nifedipine group did not need surgical intervention. However, there is enough evidence that clearly proves the beneficial effect on pain control of tamsulosin to make it useful in treatment of renal colic as part of a combination treatment strategy.

### Combination therapy

Based on data that suggest a higher rate of spontaneous stone passage, fewer days lost from work, and fewer surgical procedures, some urologists advocate a more aggressive medical approach. This treatment plan is intended for short-term use only but may benefit selected patients who can take medications reliably. A combination of drugs can be used together to improve the chances of spontaneous stone passage and alleviate renal colic discomfort.

A typically used combination therapy to facilitate spontaneous expulsion of urinary calculi consists of:

- ketorolac or similar NSAID for 5 days
- tamsulosin or nifedipine for 7 days
- levofloxacin or trimethoprim/sulfamethoxazole for 7 days
- an oral opioid pain medication as needed for breakthrough pain
- metoclopramide or prochlorperazine as needed for control of nausea.

Most ED physicians (76%) use ketorolac for pain management in renal colic, either alone (42.3%) or in combination with morphine (33.7%) [1]. A double-blind, randomized controlled trial demonstrated that the combination of intravenous ketorolac and morphine was superior at reducing pain scores and the need for rescue morphine compared with single-agent therapy [54].

Combination therapy may also increase the efficacy of expulsive therapy. Both ureteral spasm and edema play a role in preventing stone passage. In this regard, the combination of nifedipine (an antispasmodic) and a corticosteroid (antiedema agent) is recognized to be well-tolerated and effective in promoting ureteral stone passage [30].

Because it is widely recognized that infection within the ureter is a possible cause of calculus retention, it seems advisable to include an antibiotic in the standard approach to the patient with a symptomatic ureteral stone. One week of levofloxacin 250 mg could be an appropriate and reasonable measure in this setting [31].

**Straining the urine**

Stone analysis is extremely important in the evaluation of a patient with urolithiasis for stone preventive therapy. Knowing when a calculus is going to pass is impossible, regardless of its size or location. Therefore, straining of the urine of patients on MET should be continued until the stone is actually collected.

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# Part 2 Management of Stones in Abnormal Situations

## 67

## Management of Stones in Horseshoe Kidneys

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### Introduction

Renal fusion anomalies can be broadly divided into two distinct types: horseshoe kidneys and cross-fused ectopia. Horseshoe kidneys are the commonest type of renal anomaly and have been reported to have an incidence of 1 in 400–700 live births in both autopsy and radiographic data [1, 2]. There is a male preponderance for this condition with a male-to-female ratio of 2:1. No genetic predisposition is known and horseshoe kidneys are frequently diagnosed incidentally and in isolation for adult patients, but may be part of a syndrome in the pediatric population, where it is estimated that 23% of patients with horseshoe kidney have other severe associated malformations, which may be gastro- intestinal, musculoskeletal, neurological, or most commonly urogenital anomalies [3]. There are several syndromes that are commonly linked to horseshoe kidneys including Down's syndrome, Turner's syndrome, and Trisomy 18.

### Development

Normal kidney development occurs at the fourth week of gestation from the fusion of the ureteric bud and metanephric blastema. The kidney is originally formed in the pelvic location and ascends with the growth of the body, in particular the sacral and lumbar regions during fourth to ninth weeks of gestation. Primitive renal vessels that originate from the pelvic aorta degenerate as the vascular supplies gradually arise from the proximal aorta. As the kidneys ascend through the arterial fork, they may be pushed together too closely and become fused at the lower poles. A more recent theory suggests that fusion may be the result of abnormal migration of the posterior nephrogenic cells which then fuse with the lower poles of the kidneys, forming an isthmus [4]. Notochord is necessary for correct positioning of the metanephric kidney and the axial sonic hedgehog (*ASH*) gene signal is essential step for kidney positioning along the mediolateral axis. Kidney fusion may occur with disruption of notochord or the *ASH* gene [5]. The ascent of the fused lower pole kidneys terminates just below the inferior mesenteric artery and oftens lie between the L1 and L4 vertebral levels (Figures 67.1 and 67.2).

Horseshoe kidneys are located anterior to the aorta and inferior vena cava. The fused lower poles of horseshoe kidneys are bridged by either functional renal tissue or fibrous tissue. As a consequence of the fusion at the lower poles, the renal pelvis fails to rotate medially and consequently remains ventrally located. This results in the ureter exiting the renal pelvis ventrally and more superiorly, and the longitudinal renal axis converges medially [6]. Matusmoto et al. [7] classified horseshoe kidneys into five types: Type A (a), fused at the upper poles; Type A (b), fused at the lower pole; Type B (a), fused by fibrous tissue; Type B (b), fused directly; and Type B (c), fused by mediators. Graves [8] proposed a classification system (Table 67.1) with six basic patterns of arterial supply for each horseshoe kidney segment.

A horseshoe kidney by itself is asymptomatic; however, due to the anatomy of high ureteric insertion, the presence of the isthmus, and the ventral orientation of the renal pelvis such kidneys are more prone to certain complications which include recurrent infections [9], renal stones, pelviureteric junction obstruction, vesicoureteric reflux [10], and renal tumor.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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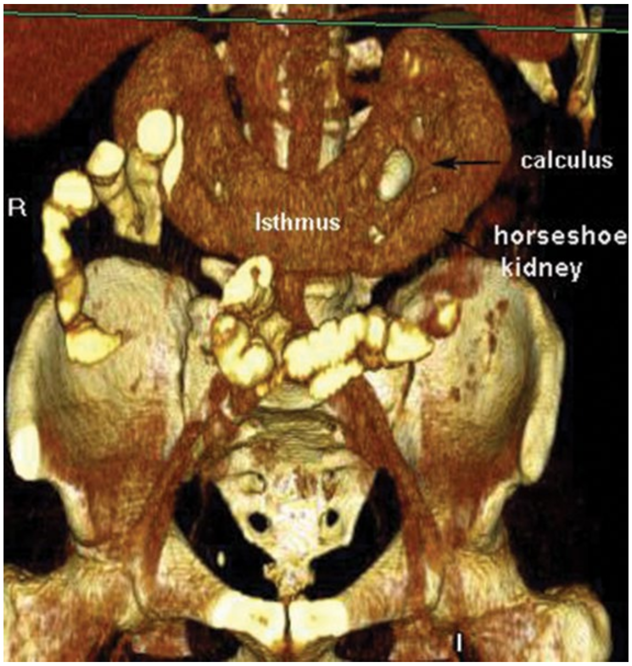

**Figure 67.1** Coronal view of the horseshoe kidney; three-dimensional reconstruction with a calculus in the left moiety.

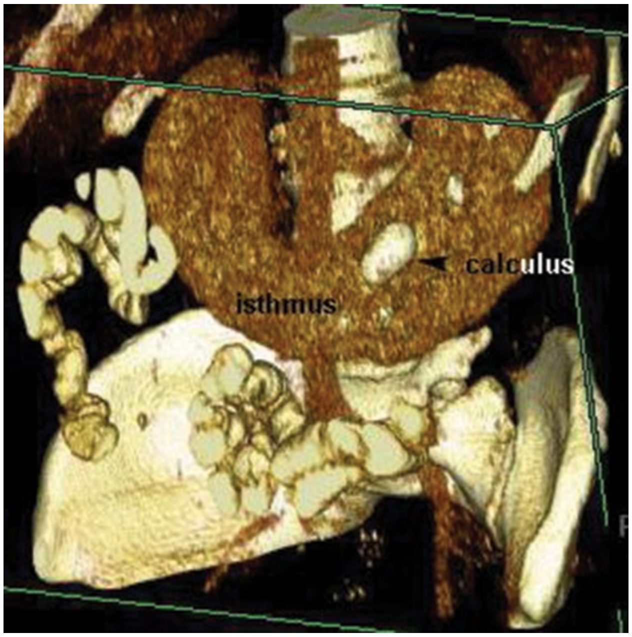

**Figure 67.2** Coronal oblique view with three-dimensional reconstruction showing the ventrally orientated lower pole and isthmus.

**Table 67.1** Arterial vascular pattern of horseshoe kidneys.

| | |
|---|---|
| Type 1 | The arterial supply may follow the normal pattern with a single renal artery supplying the upper, middle, and lower segments. |
| Type 2 | Upper and middle segments may be supplied by a single renal artery with a branch from the aorta entering each lower segment. |
| Type 3 | The arteries to the lower segment arise from the aorta by a common trunk and upper and middle segments are supplied by a single renal artery on either side. |
| Type 4 | All three segments are supplied by separate arteries arising from the aorta. |
| Type 5 | The isthmus may be supplied by arteries arising above or below the isthmus; these may be unilateral or bilateral and may originate from the aorta, independently, or by a common trunk. |
| Type 6 | The fused lower segments may be supplied by arterial branches from the common iliac artery or rarely from the internal iliac artery (hypogastric) or middle sacral artery. |

**Table 67.2** Endourological considerations in horseshoe kidney.

| Anatomic variations | Effect of variations | Therapeutic adjustments |
|---|---|---|
| Incomplete rotation | Medially directed calyces | May require more medial percutaneous puncture |
| Abnormally oriented calyces | Acute angle at infundibulum | Difficult or incomplete access to collecting system |
| Lack of ascent | Low-lying kidney | Lower puncture may be necessary |
| Lack of usual pararenal support | Mobile kidney | Percutaneous puncture more demanding |
| Renal pelvis anterior | Increase distance from skin | Long instruments necessary |
| Arteriovenous variations | Single renal artery in 30% | Vascular hazards |

## Urolithiasis

Urolithiasis is the commonest complication related to horseshoe kidney and is estimated to be 21–60% [11]. This is likely to be a consequence of impaired urinary drainage leading to stasis and infection predisposing to calculi formation. The treatment of urolithiasis poses a unique challenge due to the variable vascular and renal anatomy and the predisposition to multiple and large staghorn-like calculi [3]. The abnormal orientation of the renal pelvicalyceal system further increases the potential complexity for stone management (Table 67.2).

Minimally invasive intervention for the treatment of urolithiasis in a horseshoe kidney is now widely accepted with good stone-free results and low complication rates [12, 13]. However, the clinical decision making process must balance the likelihood of stone-free rates against the intervention risk and potential for complications.

## Extracorporeal shock-wave lithotripsy

Extracorporeal shock-wave lithotripsy (ESWL) has revolutionalized the treatment of renal stone disease. ESWL has been advocated as the primary treatment modality for stones less than 20 mm [11]. Sheir et al. retrospectively reviewed 198 patients with anomalous kidneys and showed that ESWL is a safe and reliable method of treatment with a stone-free rate of 72% [14]. This is comparable with the stone-free rate of a solitary stone, in a normal kidney, at an average of 72.8%; however, the reported range for stone-free rates in horseshoe kidneys is 33–79% [14, 15].

The anatomy and orientation of a horseshoe kidney presents a challenge to the use of ESWL as the renal pelvis is ventromedially orientated and approximately a third may have a concomitant ureteropelvic junction obstruction. Locating these calculi can be difficult as the vertebrae may act as an obstacle and in some patients there may be associated vertebral anomalies. The skin-to-stone distance may also be increased, resulting in difficulty in positioning focal point (Figure 67.2). Prone position and "blast path" may need to be used to target these awkwardly positioned calculi [16]. A better stone-free result can also be achieved when a second-generation lithotripter is used [14]. Concerns have also been raised, due to the high ureteric insertion of the ureter, as to whether fragments post-ESWL are able to pass spontaneously. The most important predictor for failure of ESWL or significant residual calculi needing retreatment is location, stone density, size, and number. Various studies have reported a stone-free rate of 39–66% (Table 67.3). Ancillary procedures may need to be used pre-ESWL such as percutaneous nephrostomy, double-J ureteric stents, or ureteral catheterization and these should be decided on a case-by-case basis. It is important to emphasize that there have been no prospective studies comparing the different treatment modalities in this group of patients but ESWL may be beneficial in patients with small calculi.

Complications post-ESWL in horseshoe kidneys are similar to those performed in normal kidneys. Renal colic, mild haematuria, and urinary tract infection are considered mild and may be treated conservatively and medically. Steinstrasse is rare but a known complication post-ESWL which can result in ureteric obstruction requiring endoscopic retrieval of these calculi. The risk factors for steinstrasse post-ESWL in a normal kidney are stones greater than 2 cm in a dilated system, proximal located calculi, and the use of high kV for disintegration [20].

## Percutaneous nephrolithotomy

Percutaneous nephrolithotomy (PCNL) is a well-established technique in the treatment of urolithiasis in normal kidneys and often widely used as first-line treatment in horseshoe kidneys, especially when calculi are larger than 2 cm or after failed ESWL.

As described, the horseshoe kidney lies lower than a normal kidney. The renal pelvis is ventrally orientated and in most cases the lower poles are connected by an isthmus which may be fibrous or viable renal tissue. The long axis of the kidney is orientated in the sagittal plane, such that the posterior calyces are orientated dorsomedially and the frontal row points dorsolaterally. Thirty percent of horseshoe kidneys have a single renal artery on either side [21] but the blood supply is variable with accessory vessels arising from any part of the abdominal aorta, bifurcation, or iliac arteries and inserting into the renal hilum (see Table 67.1). There are no accessory vessels in the dorsal aspect of the horseshoe kidney [22].

Taking all the above anatomical factors into consideration, percutaneous access of horseshoe kidney is relatively safe and often best approached via the most superior calyx (see Chapter 18 and Video 18.1 on upper pole PCNL). Inadvertent damage to the pleura is uncommon with an upper pole puncture in a low-lying horseshoe kidney. The posterior calyx is relatively easily

**Table 67.3** Main outcomes of extracorporeal shock-wave lithotripsy.

| Study | Study period | No. of patients | Mean stone burden (cm$^2$) | Stone free (%) | Significant fragment (%) | Auxiliary treatment rate (%) |
|---|---|---|---|---|---|---|
| Tunc et al. [17] | 1990–2002 | 45 | 2.24 ± 0.6 | 66.7 | 22.2 | – |
| Ray et al. [18] | 1994–2010 | 41 | 0.91 ± 0.716 | 39.1 | – | 72.7 |
| Torrecilla Ortíz et al. [19] | 1988–1999 | 32 | – | 54 | 30 | – |

accessible with a direct puncture in a dorsoventral direction and the puncture site more medially located in comparison to normally orientated kidney. Apart from several accessory vessels to the isthmus, there are no major blood vessels arising from the dorsal aspect of the kidney. The risk of access-related major vascular hemorrhage is no higher than in normal kidneys.

Access for PCNL can be performed under ultrasound, fluoroscopic, or computed tomography (CT) guidance. The basic principle of achieving an atraumatic puncture of the renal calyx should be adhered to if possible, regardless of the modality used. The safest point of puncture is the middle of the calyx following Brödel's line. However, the superior calyx is usually the chosen puncture site for a staghorn calculus or stones within multiple calyces. This is because the anatomic access with a posterior puncture allows increased maneuverability of the nephroscope within the collecting system and the option to use flexible instrumentation to access stones in peripheral calyces.

Ultrasound can be used to guide puncture into the superior calyx if the collecting system is hydronephrotic or predilated with fluid/contrast retrogradely. However, the lower pole is also often poorly delineated and as a consequence the view of the calyx may be suboptimal for guiding access puncture [23].

Fluoroscopically guided puncture is the standard technique used in our institution. After placing a ureteric catheter. The patient is then turned to the prone position with the C-arm placed vertically. The pelvicalyceal system is distended with contrast media and the C-arm can be rotated +30 to −30° to evaluate the calyceal anatomy. An 18G sheath needle is used to puncture the skin and advanced into the desired calyx under fluoroscopic guidance (Figure 67.3). The needle is advanced in increments and aims at the calyceal cup. When the needle is moving with respiration, the C-arm is then rotated obliquely to an angle such that the length of needle is visualized and the needle is advanced under fluoroscopic guidance. The needle should be advanced ideally to puncture the epicenter of the calyx and the needle tract should be in the orientation of the infundibulum. As the tract may be longer for a horseshoe kidney, longer instruments may be necessary. The lower pole and pelvis are more anteriorly facing than is usual; lower pole lateral entry may damage the large anterior division arteries or accessory branches from the iliac artery [24]. Therefore, lower pole calyx puncture is avoided in our practice unless there is no other alternative. Once the puncture site is secured, an Amplatz super-stiff guide wire (0.035 in, 180 cm; Boston Scientific) is advanced, preferably down the ureter (Figure 67.4), and the tract is dilated using a NephroMax™ High Pressure Balloon (Boston Scientific) catheter and a 30 Fr PTFE sheath. The inflated balloon catheter is advanced over the Amplatz super-stiff guidewire until the distal tip of the balloon is positioned in the calyx. The other option is to dilate the tract serially with telescopic metal dilators (Keymed; Olympus) to accommodate a 26 Fr (up to 30 Fr) Amplatz sheath (Cook Urology) (Figure 67.5).

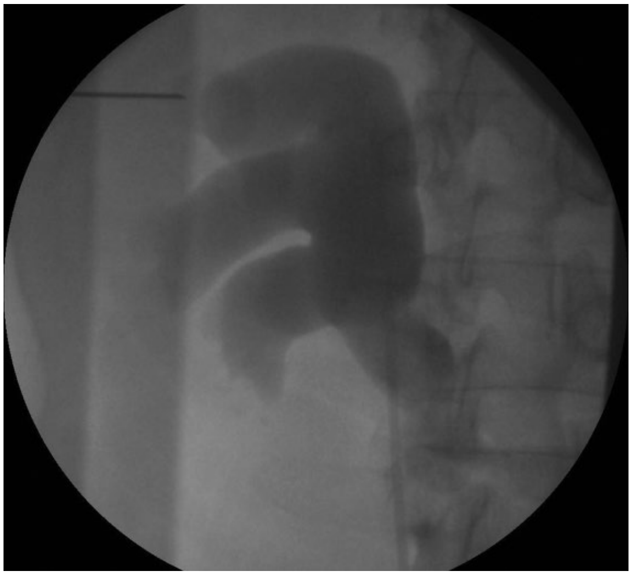

**Figure 67.3** The 18G-sheathed needle is aiming at the calyceal cup.

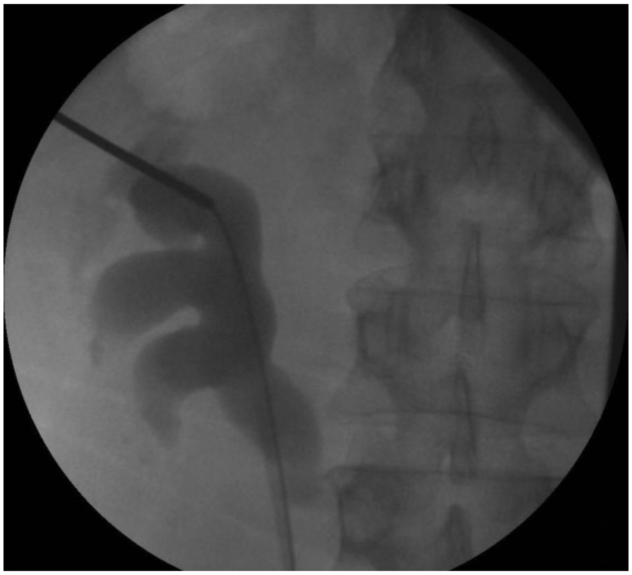

**Figure 67.4** The telescopic metal dilator is inserted within the upper pole calyx with Amplatz superstiff guidewire in the ureter to anchor the tract.

A rigid nephroscope is used to remove the calculi using either an ultrasonic or lithoclast lithotripter to disintegrate the stones. Having a flexible cystoscope or nephroscope may allow access to abnormally located calyces. Stones can be removed sequentially through the tract with various

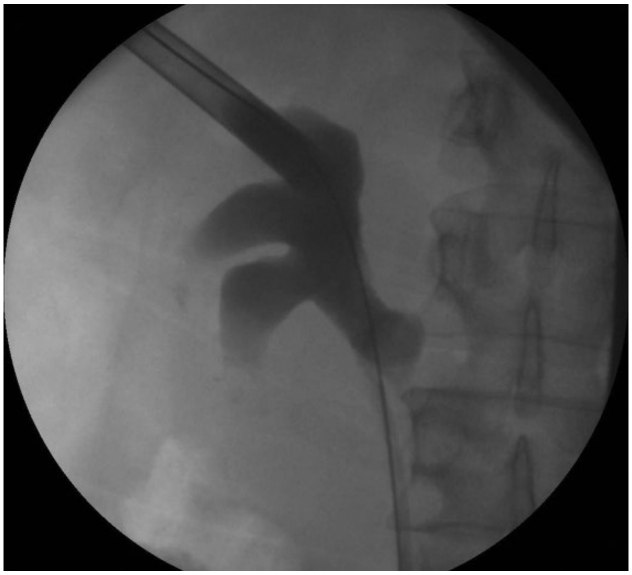

**Figure 67.5** A 26 Fr amplatz sheath is inserted into the upper pole calyx.

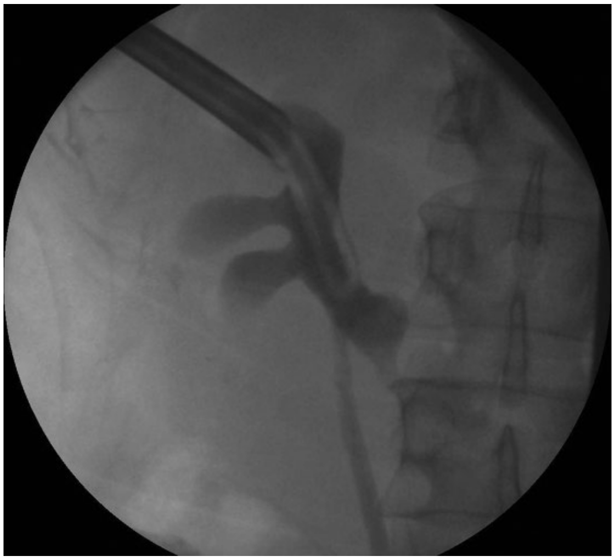

**Figure 67.6** A Foley catheter is sited as a covering nephrostomy at the end of the procedure.

stone-grasping devices. At the end of the procedure, we usually site a Foley catheter (20 Fr) as a covering nephrostomy to tamponade the tract for at least 24 hours (Figure 67.6). This will then be clamped and if the patient is asymptomatic the nephrostomy will then be removed on the ward. A post-procedural nephrostogram will only be performed if there is concern with regard to injury or potential distal ureteric stones causing obstruction.

CT-guided access is reserved for complex situations resulting in challenging access due to the patient's associated vertebral anomaly (e.g. severe kyphoscoliosis), extreme obesity, or hepatosplenomegaly. CT is normally acquired in a *prone* position and can also be used for surgical planning prior to PCNL. Retrorenal or posterolateral displacement of the bowel can be associated with horseshoe kidney and the bowel may occasionally act as an obstacle to percutaneous access. In these situations, an initial unenhanced CT abdomen and pelvis with 2 mm reconstruction (CT kidney–ureter–bladder) may be performed as an overview. Subsequent images for CT-guided procedure can be acquired by obtaining a volume of area of interest and reconstructed with 3 mm slice thickness. It is paramount in this case that the patient will be able to tolerate a prolonged prone positioning. Once access is obtained, a nephrostomy tube can be left *in situ* for subsequent access and the tract can be dilated as described above under general anesthetic.

The stone-free rate post-PCNL in the treatment of renal calculi in horseshoe kidney is similar to that in a normal kidney at 80%. The complication rates reported are also comparable with that of normal renal PCNL with minor complications such as hematuria and infection reported at 15%. Major complications, for example hydropneumothorax requiring insertion of a chest drain, have an incidence of 2% [24] (Table 67.4).

## Ureteroscopy

Retrograde digital flexible ureteroscopy is becoming a more frequently used modality, especially for stones less than 15 mm in diameter, using holmium:YAG laser for stone disintegration. However, reported case numbers are small and retrospective and there may be issues relating to ureteric access requiring prestenting. These cases will generally require use of an access sheath and postoperative stent insertion. In addition, access to the lower pole may be difficult in some patients and relocation of the stone from the lower pole to the upper pole may be necessary. To date such cases have generally been managed in specialist stone centers that can offer the full range of stone management [31]. A recent systematic review identified three studies. A success rate of 78% was noted in 41 patients. A ureteral access sheath was used in all patients [32].

## Laparoscopic pyelolithotomy

While most stones can be efficiently managed using endourologic techniques, the use of laparoscopy for the management of urolithiasis has a limited role. Laparoscopy has been used alone or in combination with other endoscopic procedures. Delineation of vascular anatomy by preoperative CT angiography/urography is recommended before surgery as it helps in surgical

**Table 67.4** Percutaneous nephrolithotomy outcomes from different studies.

| Study | Study period | No. of patients | Superior pole access (%) | Stone free (%) | Secondary procedures (%) | Complications, major/minor (%) |
|---|---|---|---|---|---|---|
| Ozden et al. [25] | 1997–2008 | 46 | 68 | 80 | 8 | 2/14 |
| El Ghoneimy et al. [26] | 2005–2009 | 17 | 48 | 85.7 | 0 | 5/14 |
| Etemadian et al. [27] | 2006–2011 | 21 | 66.64 | 71.4 | 14.2 | 0/14 |
| Shokeir et al. [28] | 1995–2003 | 34 | 46 | 82 | 35.3 | 13/0 |
| Symons et al. [29] | 1991–2008 | 47 | 48 | 88 | 34 | 2/9 |
| Blackburne et al. [30] | 2002–2015 | 33 | 94.6 | 81.1 | 27 | 3/6 |

planning. A transperitoneal approach is commonly used and pyelolithotomy is easier as the pelvis is anteriorly rotated and can be identified easily [33–35].

## Summary

Urolithiasis with horseshoe kidney is of diverse etiology, requiring a carefully planned, individualized diagnostic and management approach. ESWL is the preferred treatment for the majority of patients with urolithiasis. However, ESWL monotherapy for stones in horseshoe kidneys is likely to provide good fragmentation but stone clearance is suboptimal due to anatomical factors. Excellent stone-free rates can be achieved with ureteroscopy and PCNL in properly selected cases, with the best approach being via the upper pole

See Chapter 18 and Video 18.1 regarding upper pole access.

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# 68

# Pelvic Kidneys

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## Introduction

Renal ectopia signifies an abnormal location of a kidney outside of the orthotopic renal fossa. This is due to abnormal ascent or rotation of the kidney during embryological development. These kidneys may be located in the pelvis, mid-abdomen, or even the thorax. The most common type of renal ectopia is the pelvic kidney, which has an estimated occurrence of 1 in 2100–3000 [1]. Although most patients with pelvic kidneys are asymptomatic, some may have pain due to stones or hydronephrosis [2]. The anatomic location of a pelvic kidney may make treatment of such pathologies difficult, requiring strategic preoperative planning in determining the optimal therapeutic approach. This chapter provides an overview of the development of pelvic kidney, and treatments of associated pathologies excluding neoplastic conditions. In addition, we will discuss the management of patients with stones in transplant grafts, an "acquired pelvic kidney."

## Embryology

During the fourth or fifth week of gestation the ureteric bud interacts with the metanephrogenic blastema. This induces proliferation and differentiation of the blastema into glomeruli and tubules. During the sixth to ninth weeks of gestation the kidneys normally migrate cranially from the pelvis to the ipsilateral renal fossa at the T12–L3 vertebral level. During the ascent, the kidneys undergo a 90° axial rotation from an anterior to ventromedial direction.

Incomplete migration of a kidney leads to an ectopic location. Various factors account for this aberrant process including incomplete development of the ureteric bud or metanephrogenic blastema, genetic defects, teratogens, and vascular abnormalities [3–6]. Renal ectopia also has an increased association with genital defects with an incidence of up to 15% [7]. In females, ectopic kidneys may be associated with bicornuate uterus and hypoplasia or agenesis of the uterus/vagina; in males, the most common genital anomalies associated are hypospadias and cryptorchidism [6, 8, 9]. While most patients with renal ectopia have a normal contralateral kidney, there is an increased incidence of contralateral renal agenesis of up to 10% [6, 10, 11].

Complete failure of ascension results in a pelvic kidney. In this case, a kidney remains in its initial location anterior to the sacrum in the retroperitoneum (Figure 68.1). Due to incomplete rotation, the renal hilum may face anteriorly. The ureter may have a high insertion into the pelvis but usually maintains its orthotopic insertion into the bladder. Arterial vascular supply may be variable, including from the distal aorta, common iliac, or external iliac arteries [4, 6, 12, 13] (Figure 68.2).

## Nephrolithiasis

The evidence that stones are more prevalent in pelvic kidneys is discordant. While a 1971 study by Dretler et al. did not find an increased prevalence, a later study in 1994 by Gleason et al. demonstrated this association [2, 14]. Gleason noted that hydronephrosis was present in 56% of pelvic kidneys. Impaired urinary drainage in such kidneys has been proposed to play a role in stone formation. However, underlying metabolic factors are likely the main driver [15].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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## Shock-wave lithotripsy

Variable success has been reported with using shock-wave lithotripsy (SWL) to treat patients harboring stones in pelvic kidneys. Stone-free rates ranging from 25 to 82% at 3 months after an initial SWL session have been reported [16–19]. The main limitation is the location of the kidney within the bony pelvis and its adjacency to bowel, which may make shock-wave targeting difficult. Various techniques have been used to improve targeting during SWL in such cases. Jenkins et al. used ureteral catheters to mark general stone position for fluoroscopic guidance during SWL [20]. Contrast can also be injected into the collecting system through stents to facilitate targeting.

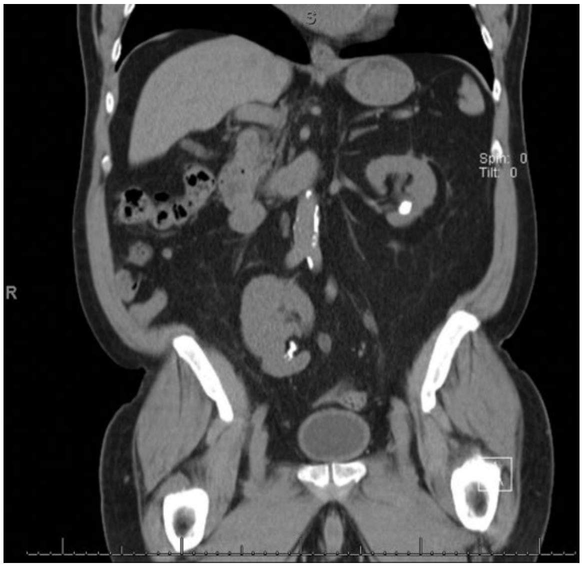

Figure 68.1 Calculus within the right pelvic kidney.

Presence of hydronephrosis may also limit success in these cases [12]. Demirkesen et al. reported significantly lower stone-free rates with SWL in pelvic kidneys (38%) compared to orthotopically located kidneys (78%) [18]. However, Talic et al. have reported a much higher success with SWL in those with stones in pelvic kidneys, 82% [17]. The varying results may be due to patient selection, technique, and the lithotripter utilized.

Proper positioning has been shown to be critical to SWL success in pelvic kidneys [17]. The use of prone positioning for stones located below the iliac crest is recommended to facilitate targeting and limit bony structures from impeding shock waves [20, 21]. If calculi are visible superior to the pelvic brim, a supine position can be used [17].

## Ureteroscopy

Ureteroscopy has become a reliable approach as both a salvage and first-line option to treat patients with stones in pelvic kidneys. This has been enabled by advances in instrumentation including the holmium laser, ureteral access sheaths (UAS), nitinol baskets, and deflectable, flexible ureteroscopes [22, 23]. These advancements have helped overcome the anatomic challenges of the pelvic kidney including ureteral tortuosity and acute angles of access to the ureteropelvic junction (UPJ) and lower pole calyces (Figure 68.3). The use of a ureteral access sheath in particular can help to straighten a tortuous ureter and facilitates access to the renal pelvis [24].

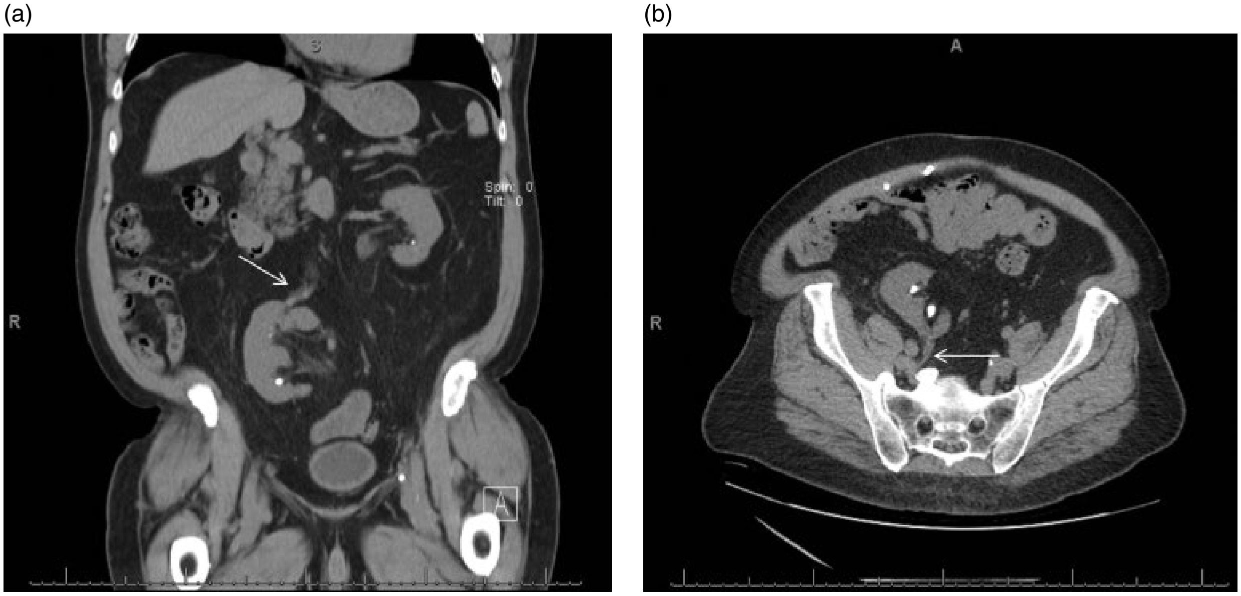

Figure 68.2 Abnormal vasculature of pelvic kidney from (a) coronal and (b) axial views.

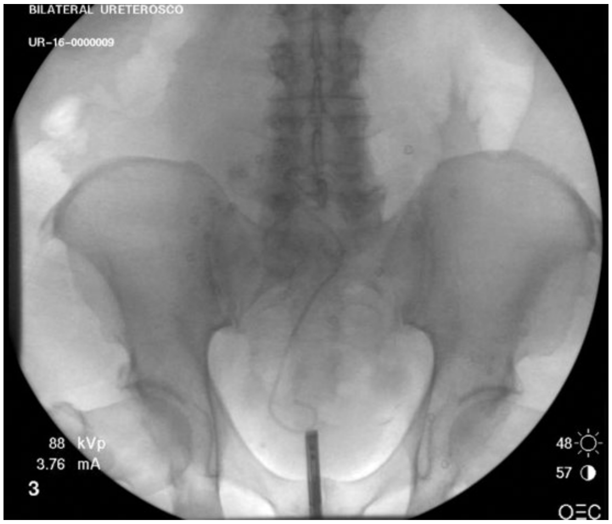

**Figure 68.3** Stent placement demonstrating ureteral tortuosity of pelvic kidney.

Despite the increasing use of ureteroscopy, studies involving its use in anomalous kidneys are scarce. Weizer et al. reported a 75% stone-free rate at 1–3 month follow-up for four pelvic kidney patients who had flexible ureteroscopy performed. In this study, a UAS was used in 50% of the patients [24]. A study by Alkan et al. reported a 100% stone-free rate in three pelvic kidney patients; a UAS was only used in one patient due to failed placement in the other two subjects [25]. Singh et al. achieved 88% stone-free rate in 22 patients with anomalous kidneys for which a UAS was used in all cases [26]. There are two studies, however, which did not utilize a UAS in ureteroscopy and still achieved 75 and 84.6% treatment success rates in populations of four and 26 patients respectively as defined by <2 mm stone burden after ureteroscopy on follow-up [27, 28].

In these studies, position of the stone was a key factor in achieving successful stone-free rates. Singh et al. noted decreased stone-free rates in patients with lower pole stones (60.4%) compared to those with upper, middle, or renal pelvis stones (94.4%) [26]. As with ureteroscopy in orthotopically located kidneys, stone burden may also limit successful treatment in pelvic kidneys. A total stone burden size of >2 cm is associated with higher failure rates [26, 29].

## Laparoscopy-assisted percutaneous nephrolithotomy

Percutaneous nephrolithotomy (PCNL) is an effective approach for treating patients with large stones in pelvic kidneys. With the presence of bowel and other visceral structures adjacent to the pelvic kidney, access often necessitates a different approach for which direct visualization and manipulation with laparoscopy is used to limit injury to these structures.

PCNL in a pelvic kidney was first described by Eshghi et al. in 1985 for treatment of a patient with a staghorn stone [30]. Subsequent reports with this approach noted 100% stone-free rates in 15 and two patients respectively [31, 32]. In the aforementioned cases, a retrograde external ureteral stent was initially placed to guide fluoroscopic access. Patients were placed in a supine Trendelenburg position to assist in bowel displacement. Pneumoperitoneum was established and two ports were placed: 10 mm port through the umbilicus for the camera and a 5 mm assistant port in the lower quadrant contralateral to the pelvic kidney. Others have utilized an additional 10 mm port in the ipsilateral lower quadrant [33]. Under direct visualization, a grasper was used through the 5 mm port to displace the bowel to visualize the pelvic kidney. An antegrade puncture was then performed using an 18G needle under both laparoscopic and fluoroscopic guidance. Subsequent steps mirrored those of a normal PCNL with wire access obtained followed by dilation and sheath placement (Figure 68.4). Methods for urinary diversion at the end of the procedure varied but generally included a double-J stent or a transperitoneal nephrostomy tube [31–33]. If an internalized ureteral stent is place for drainage at the end of the case, some have advocated closure of the nephrotomy with absorbable suture [33].

Various other approaches to PCNL for pelvic kidneys have been described in the literature. Troxel et al. reported an extraperitoneal approach for one patient in which a balloon was used to expand the extraperitoneal pelvic space and push the peritoneal contents cephalad to expose the pelvic kidney. This approach may theoretically reduce the risk of bowel injury [34]. In another case report, Monga et al. performed a posterior approach to a pelvic kidney in a patient by developing a tract just medial to the paraspinal muscles along the quadratus lumborum and psoas major. Stone-free status was achieved; however, the patient developed femoral neuropathy, which was still present 6 months postoperatively. The injury was likely related to trauma involving the dorsal divisions of the lumbar plexus along the psoas muscle incurred during dilation [35]. Thus, we do not endorse this approach. Goel et al. reported a transmesenteric approach to access a pelvic kidney. In this procedure, upon gaining laparoscopic visualization, a tract was established through the mesentery, taking care to avoid the mesenteric vessels. The advantage of this approach is that it limits bowel mobilization. A transmesenteric technique should only be used when the mesenteric vessels can be clearly indentified [36]. Other approaches that have been reported including trans-iliac and trans-sciatic [33, 37]. The latter should only be

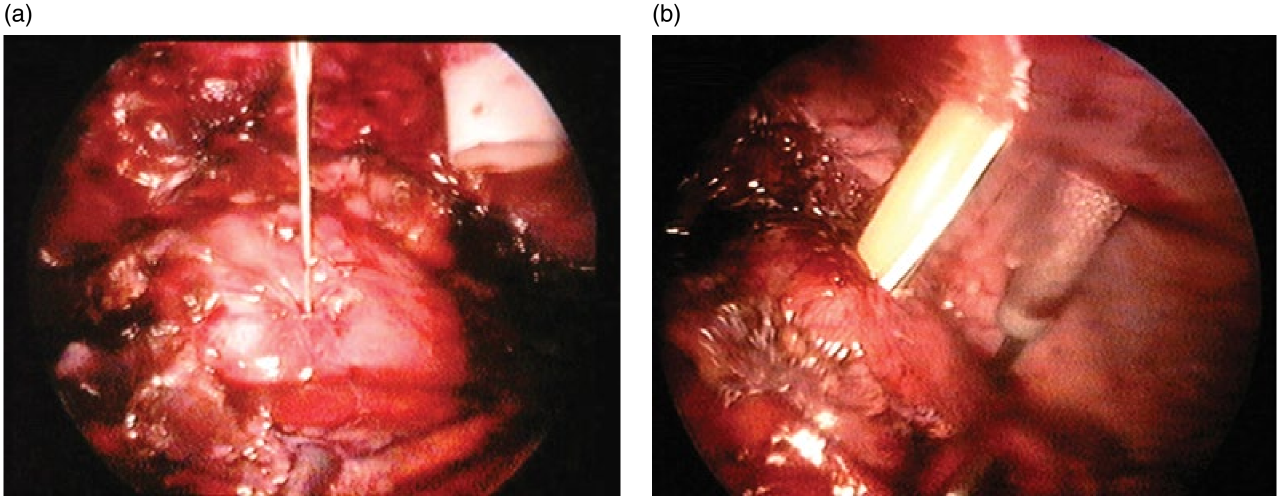

**Figure 68.4** (a) Antegrade puncture and (b) percutaneous access obtained under direct laparoscopic vision for percutaneous nephrolithotomy.

undertaken in cases where there is limited risk of injuring adjacent structures.

Laparoscopy-assisted mini-PCNL, in which a smaller tract and sheath are used, has been performed successfully in pelvic kidney patients. D'souza et al. reported an 88.9% stone-free rate in nine patients who underwent laparoscopy-assisted mini-PCNL. For this approach, after mobilization of the bowel, a 15 Fr tract to the pelvic kidney was established; a rigid mini-nephroscope was subsequently used for laser lithotripsy. Use of a smaller tract could reduce the chances of vascular injury and limit the risk of urine leak [38].

While laparoscopy has been used in a majority of PCNL pelvic kidney series, Desai and Jasani used ultrasound guidance in place of direct laparoscopic visualization. With the patient in a supine oblique position, an ultrasound probe was used to locate the pelvic kidney; pressure was then applied with the probe to displace bowel away from the planned puncture site. Access through an anterior approach in the area of the iliac fossa was then obtained. They were ultimately able to achieve stone-free status in five pelvic kidney patients without any bowel injuries reported. This method would avoid the complexities involved in laparoscopic access. However, this also requires the pelvic kidney to be mobile and displaced toward the abdominal wall for access. The use of ultrasound may also increase the risk of injury to bowel, especially in the setting of collapsed bowel that may not be visible on ultrasound [39]. Thus, this approach should only be considered in highly select cases.

Overall, PCNL for pelvic kidneys with large stone burden (>1.5 cm) has been shown to have a consistently higher success rate (88.9–100%) compared to SWL and flexible ureteroscopy in achieving stone-free status [31, 33, 38, 39]. However, this approach does carry the risk of more serious complications including bowel and nerve injury, bleeding, and intraperitoneal urine leak.

## Laparoscopic pyelolithotomy

Laparoscopy- or robot-assisted pyelolithotomy is a consideration in patients with large volume renal pelvic stones in such kidneys. This should not be undertaken in those with an intrarenal pelvis. These approaches allow for the removal of stones in one piece rather than in fragments. In addition, a flexible nephroscope may be used to facilitate stone evacuation, especially those located in calyces.

Urine leak was a problem encountered in early reported cases of laparoscopy in patients with pelvic kidneys. This was demonstrated in two separate case reports by Harmon et al., and Chang and Dretler published in 1996 [40, 41]. Both cases began with the patient in Trendelenburg position. After pneumoperitoneum, four trocars were placed in the lower abdomen (one in each lower quadrant, one infraumbilical, one midline). After bowel mobilization, the pelvic kidney was located and the pelvis was dissected free. A 2 cm pyelotomy was made after which stone was extracted with laparoscopic forceps. Due to the depth and location of the incision, Harmon et al. were not able to close the pyelotomy; subsequently a double-J stent, perirenal drain, and bladder catheter were left in place. The pyelotomy closed after a long period of bladder catheter drainage. In their report, Chang and Dretler closed their pyelotomy with polydioxanone suture and left a bladder catheter and double-J stent in place. The catheter was removed on postoperative day 1. A subsequent voiding cystourethrogram showed a leak at the pyelotomy site theorized to have been caused by ureteral reflux. The leak closed spontaneously with Foley catheter drainage [40, 41]. Placement of an externalized stent at the beginning of such cases allows one to assess the integrity of the pyelotomy closure as retrograde fluid can be injected to identify leaking sites [42].

The largest series of laparoscopy in patients with pelvic kidneys was reported by Elbahnasy et al. in which 10 of 11 patients were rendered stone-free (90.9%). They used a transmesenteric approach in those with left-sided stones [43].

Bozkurt et al. reported using a retroperitoneoscopic approach for such cases [44]. They inserted three ports in a triangular configuration in the lower pelvic region after pneumoretroperitoneum was established. A potential advantage of this approach is that if a urine leak occurs it would be contained to the retroperitoneum. In addition, this could reduce the risk of bowel-related complications.

The utilization of a robot-assisted approach facilitates closure of the renal pelvis and this is especially true if concomitant pyeloplasty is required. Nayyar et al. reported a robot-assisted laparoscopy that was performed in conjunction with a pyeloplasty. They utilized a transperitoneal approach in which a 1.3 cm renal pelvic stone was removed from a pelvic kidney with a UPJ obstruction. The authors noted that the use of a robotic interface allowed for easier dissection, stone extraction, and pyeloplasty compared to standard laparoscopy [45].

### Nephrolithotomy

A laparoscopic or robotic assisted approach may also be utilized to perform nephrolithtotomy. This may be a consideration in patients harboring stones in large calyceal diverticular cavities. The location of the stone may be identified with fluoroscopy or intraoperative ultrasonography. A nephrotomy is made based on the aforementioned targeting with imaging, the stone(s) removed, and the diverticular cavity fulgurated. Perinephric fat can be inserted into the diverticular cavity. Laparoscopy- and robot-assisted “anatrophic” nephrolithotomy has been reported in patients with large branched/staghorn stones in normally positioned kidneys [46, 47]. A preoperative computed tomography (CT) arteriogram should be considered if this is undertaken in patients with a pelvic kidney to identify the often-variable renal vascular anatomy.

### Open stone surgery

The need for open surgical stone removal in todays practice is rare and this would also hold true for patients with stones in pelvic kidneys [48, 49]. The development and utilization of the previously profiled techniques has dramatically reduced the need for open stone surgery including this patient cohort.

## Ureteropelvic junction obstruction

UPJ obstruction occurs more commonly in ectopic kidneys and is reported to be present in 22–37% of such renal units [2]. Renal malrotation, aberrant vasculature, and a high ureteral insertion may be contributory.

### Endopyelotomy

Endopyelotomy has been used to treat patients with UPJ obstruction since the early 1980s [50]. Although there are a number of reports profiling the effectiveness of endopyelotomy, the results with this approach are not as good or durable as those achieved with pyeloplasty and thus it should be considered mainly for pyeloplasty failure or for those not deemed to be good candidates for the aforementioned procedure [51–53].

The literature regarding endopyelotomy for congenital pelvic kidney, however, is sparse. The data are made up primarily of individual case reports and a few small series that group various forms of anomalous kidneys together (i.e. horseshoe, lumbar, pelvic, cross-fused ectopic). The largest report to date of antegrade endopyelotomy in ectopic kidneys involved nine patients, two of whom had a pelvic kidney. In both patients, a ureteroscopically placed Hunter–Hawkins catheter was used along with laparoscopic assistance to gain percutaneous antegrade access. Both patients demonstrated long-term success on follow up [54]. If antegrade access is already present in the form of a nephrostomy tube, then this can be safely used for subsequent antegrade access without the need for repeat laparoscopic assistance [55]. Laparoscopy-assisted PCNL can be combined with endopyelotomy if stones are present. This technique is not often utilized as laparoscopic repair has better long-term results [56].

While there are a number of reports regarding success with retrograde ureteroscopic endopyelotomy in normally positioned kidneys, we found only one publication in the literature regarding its utilization in a pelvic kidney [57–59]. In this single case report, the patient’s obesity and history of recurrent pyelonephritis discouraged traditional open or laparoscopic repair. A preoperative angiogram is recommended, CT angiogram or magnetic resonance angiogram, if this procedure is contemplated due to variable renal vascular anatomy. This will help guide the direction of incision. Intraluminal ultrasonography can also be used to define vascular relationships with the UPJ [60].

### Open pyeloplasty

Laparoscopy- or robot-assisted pyeloplasty is the preferred treatment approach for patients with UPJ obstruction in a pelvic kidney as recovery is enhanced due to limited invasiveness. However, there are patients for whom this may not be possible due to extensive adhesions or abnormalities of body habitus and thus an open surgical approach would be preferable. A large retrospective review of open pyeloplasty for congenital UPJ obstruction in ectopic pelvic kidneys included 43 patients between 1995 and 2010 at a single institution. All patients underwent open dismembered Anderson–Hynes pyeloplasty. There were no perioperative complications and an overall success rate of 82.6% was reported [61]. In select patients with a severe peripelvic fibrosis and an intrarenal pelvis, ureterocalicostomy should be considered [62, 63].

### Laparoscopic/robotic pyeloplasty

To date there are multiple reports and a small case series demonstrating good results with laparoscopic/robotic pyeloplasty in pelvic kidneys with UPJ obstruction [64–66]. Operative times were similar to patients with orthotopically positioned kidneys. If there is concomitant stone disease in the affected kidney, pyelolithotomy can also be performed [67, 68].

### Pyelovesicostomy

Pyelovesicostomy was first described in 1929 as management for UPJ obstruction in a patient with a pelvic kidney with crossed fusion [69]. Since then, there have been reports of its use in pelvic kidneys and transplant kidneys as well with excellent long-term results [70, 71]. In 2005, Davis and Wolf described their experience with laparoscopic pyelovesicostomy for UPJ obstruction in a patient with a pelvic kidney. The procedure had a short operative time with minimal blood loss and the patient had a durable response at follow up. Downsides to this approach include increased risk of pyelonephritis and bladder pain [72]. Others have subsequently reported success with a laparoscopic approach for this procedure [73]. The utilization of a robot-assisted platform would undoubtedly facilitate the reconstructive portions of this procedure.

## Transplant kidney

### Stone disease

Review of the literature shows that the incidence of stone disease in a transplanted kidney ranges between 0.1 and 6.7% [74]. Renal and ureteral stones in transplanted kidneys can be effectively managed with endourologic techniques. Options for management include the same techniques used in native kidneys: ureteroscopy, SWL, PCNL, and open stone and laparoscopic/robotic surgery with most patients being treated with the first three modalities. When performing ureteroscopy, identifying and accessing the ureter in a retrograde fashion can be difficult and the lateral course of the ureter can make navigation into the kidney difficult. A recent retrospective study investigated outcomes of renal transplant patients treated with ureteroscopy for stone disease and showed that there were no major complications; most patients were able to go home on the same day and 71% were rendered stone-free [75]. Intubation of the transplant ureteral orifice may be challenging and require the use of a curved-tip angiographic catheter and a flexible cystoscope. The safety of utilizing an access sheath has not been determined due to the low numbers of reported cases for this cohort. Stones under 1.5 cm can also be treated with SWL, although its use is limited by the position of the allograft within the bony pelvis that can make stone localization difficult and attenuate shock-wave energy. Furthermore, the course of the transplant ureter may limit passage of stone fragments passage. PCNL is the preferred approach for removing large stones from transplants grafts and excellent results are achievable [76–78]. The utilization of ultrasound- or CT-guided access is frequently required to limit the risk of injuring adjacent structures especially bowel. While McAlpine et al. described their successful experience with outpatient tubeless PCNL in a transplant patient, we do not endorse such an approach in this higher-risk cohort [79].

### Ureteral stricture in transplant grafts

Along with stone disease, urologic complications after renal transplant include urine leak and ureteral stricture. Urine leak from the ureteral reimplantation can be managed with observation if a drain is in place but placement of a nephrostomy tube may be required for management. Some of these patients will develop a ureteral stricture. The incidence of ureteral stricture requiring intervention is reported in a recent large review to be 2.5% [80]. The placement of a ureteral stent at the time of transplantation to limit ureteral complications is undertaken at many transplant centers [81, 82]. While some patients who develop short strictures can be managed with balloon dilation, the results are inconsistent and many require formal reconstruction [83]. The length of available ureter and location of abnormality normally dictates the surgical approach; in a transplant setting, the short ureter limits treatment options.

This may include the utilization of the patient's ipsilateral native ureter for ureteroureterostomy, resection of the strictured segment and reimplantation if there is adequate remaining ureter, pyelovesicostomy, Boari flap, and appendiceal and bowel interposition [70, 71, 80, 84, 85]. Patients who are not thought to be good candidates for reconstruction can be managed with chronic uteteral stenting [86].

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# Management of Stone Disease in Renal Transplant Kidneys

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## Introduction

Over 870 000 individuals suffer from end-stage renal disease (ESRD) in the United States [1]. This number exceeds 2 million worldwide [2]. The majority of individuals being treated for ESRD live in affluent countries with robust healthcare systems and large elderly populations [3].

In 2009 more than US$40 billion was spent treating ESRD in the United States [1]. Despite comprising less than 1% of those covered by Medicare, patients with renal failure account for over 6.7% of the federal program's budget [1]. Between 2009 and 2010 the United Kingdom's National Health Service spent more on chronic kidney disease than on breast, lung, colon, and skin cancer combined [4].

Compared to dialysis patients, renal transplant recipients live longer (35.8 vs. 85.5% 5 year survival rate), and cost the healthcare system nearly three times less [1]. In the United States there are over 400 000 people on dialysis and a little more than 170 000 renal transplant recipients [1]. Globally, the majority of transplants are performed in Western Europe, the United States, and Australia [5].

Despite the survival and cost benefits, many transplant recipients experience urologic complications. A review of 1535 consecutive renal transplants in the United Kingdom found a urologic complication rate of 9.2% [6]. A more recent series reported similar results with 8% of 1670 recipients experiencing a urologic complication [7].

The two most common complications were urine leak and ureteroneocystostomy stenosis. While less common, allograft lithiasis is a potentially devastating postoperative complication. Most cases can be managed endoscopically, but treatment is frequently challenging due to the transplant's ectopic location and associated ureteroneocystostomy. This chapter will review the epidemiology, pathophysiology, clinical presentation, workup, and endourologic management of transplant stones.

## Epidemiology

A review of 2045 renal transplants from a single center found an allograft lithiasis incidence of 0.44% [8]. Mean time to presentation was 3.1 years following transplantation. A similar series of 1525 recipients reported an incidence of 0.46% [9]. A review of 42 096 transplant patients from the United States Renal Data System found a nephrolithiasis-associated hospitalization rate of 0.11% for men and 0.15% for women [10]. Female recipients were noted to be at increased risk of hospitalization for stone-related events compared to women within the general population.

Stones may be passed from the donor to the recipient at the time of transplantation (donor-gifted nephrolithiasis), or develop *de novo* after surgery. Donor-gifted nephrolithiasis is more common following deceased donor transplants as compared to living-donor transplants [11–13]. One explanation for this finding has been the traditionally low rate of imaging done prior to procurement. In a series of deceased donor renal transplants that underwent *ex vivo* ultrasound screening, the incidence of donor-gifted urolithiasis was found to be 0.64% [14].

In contrast, imaging is a fundamental component of the living donor screening process. Institutional variation exists but the following modalities have been utilized: renal ultrasound, computed tomography (CT) angiography, and magnetic resonance angiography. A consequence of this rigorous screening process has been the identification of nephrolithiasis in potential donors. A review of 377 individuals undergoing donor

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evaluation with CT angiography found a 5% prevalence of asymptomatic renal stones [15].

Taking into account the increased utilization of CT to screen potential living donors, Kasiske and colleagues published guidelines in 1996 outlining selection criteria [16]. Nephrolithiasis was considered a relative contraindication to donation given the high risk of stone recurrence. However, the discrepancy between available donors and individuals suffering from ESRD has continued to widen over the past decade [17]. In an effort to address this shortage, some transplant organizations have developed less stringent guidelines to allow for "expanded criteria" deceased and "complex living" donors.

In 2004 more than 100 kidney transplant experts from over 40 countries met in Amsterdam to develop consensus-based guidelines meant to protect potential living donors [18]. Per the Amsterdam Forum, a potential donor with a single stone should undergo a metabolic workup including a 24 hour urine collection. In the absence of hypercalciuria, hyperoxaluria, hyperuricemia, cystinuria, or metabolic acidosis, donation may be considered. Contraindications to donation include infected stones and systemic disorders associated with increased recurrence rates such as inflammatory bowel disease, distal renal tubular acidosis (RTA), and sarcoidosis. The presence of multiple stones or nephrocalcinosis also preclude donation.

## Pathophysiology

A variety of surgical, pharmacologic, and physiologic factors promote *de novo* stone formation following transplantation. Technical factors include vesicoureteral reflux and ureteroneocystostomy stricture. Both complications promote stone formation by increasing the risk of urinary stasis and urinary tract infection (UTI). Foreign bodies such as persistent suture material or a retained ureteral stent also increase the risk of both infectious and noninfectious stones.

Immunosuppressive medications may also play a key role in *de novo* stone formation. Corticosteroids cause bone resorption, which has been associated with increased urinary calcium excretion [19]. Besides being nephrotoxic, calcineurin inhibitors (cyclosporine and tacrolimus) have been shown to induce hypocitraturia and hyperoxaluria [20]. In addition, cyclosporine has been demonstrated to cause hyperuricemia and gout [21].

ESRD is associated with a number of metabolic changes that promote stone formation. These may persist even after renal transplantation. Increased phosphorus levels along with parathyroid hormone resistance result in secondary hyperparathyroidism, which is associated with hypercalcemia, hypercalciuria, and hypocitraturia [22]. Up to 50% of individuals will continue to have persistently elevated parathyroid hormone levels (tertiary hyperparathyroidism) after transplantation [23]. This was confirmed in a series of 15 patients with allograft lithiasis who underwent a metabolic workup [24]. The authors found a 53% incidence of tertiary hyperparathyroidism.

Renal failure results in hyperuricemia because nearly 70% of uric acid is eliminated by the kidneys. Hyperuricemia may not resolve following transplantation for a number of reasons. As previously mentioned, cyclosporine is associated with hyperuricemia. Regardless, up to 55% of recipients not being managed with cyclosporine will have elevated uric acid levels [25]. The cause is not completely understood but graft dysfunction, diuretic use, male gender, diabetes mellitus, and obesity have been implicated [26]. The resulting hyperuricuria is not only a risk factor for uric acid stones but also calcium oxalate urolithiasis by heterogeneous nucleation.

Renal tubular acidosis following renal transplantation is common, with one study finding an incidence of 33% [27]. Type 1 RTA is most common, but type 2 and 4 RTA have also been reported [28]. Poor allograft function, calcineurin inhibitor nephrotoxicity, acute rejection, and ischemic tubular dysfunction have all been reported as causative factors [27]. Other potential etiologies include tertiary hyperparathyroidism, postoperative urinary obstruction, and UTI [29]. Type 1 RTA is associated with hypercalciuria and urinary alkalinization, which promote calcium phosphate stone formation.

## Presentation

Diagnosing an obstructive ureteral stone is relatively straightforward in the general population due to the classic signs and symptoms of renal colic. However, it is notoriously difficult in renal transplant patients due to denervation of the allograft during the harvesting process. Recipients rarely present with renal colic. In fact, more than half of recipients do not have any discomfort at the time of diagnosis [8, 30]. When present, patients usually report mild lower abdominal pain, which is believed to be due to peritoneal irritation from the hydronephrotic allograft. Collecting system dilation may be palpable on physical exam.

Most patients present with less specific signs and symptoms including decreased urine output, gross hematuria, recurrent UTIs, or urosepsis [11, 31, 32]. Acute renal insufficiency may be the only sign in some patients [33]. As a result, recipients with an obstructive stone may be misdiagnosed with acute rejection delaying appropriate treatment [34]. Fortunately, transplant nephrolithiasis does not appear to be associated with graft loss in the majority of those afflicted [35].

Time to presentation and subsequent diagnosis has been reported anywhere from 3 months to 18 years after transplantation [36]. However, a postoperative range of 1–4 years is more commonly cited [9, 11, 24].

## Workup

A high index of suspicion for allograft lithiasis must exist in recipients presenting with vague abdominal discomfort, hematuria, recurrent UTIs, or worsening renal function. Evaluation should begin with a detailed history and physical exam. The presenting complaint should be fully characterized along with a review of the recipient's immunosuppression regimen and other medical comorbidities. On exam the abdomen should be palpated to assess for evidence of allograft obstruction. Men with obstructive voiding symptoms should have a post-void residual performed to ensure adequate bladder emptying.

Laboratory testing should include a urinalysis (with microscopic exam and culture if indicated), complete blood count, and metabolic panel. Imaging should include either an ultrasound or CT. Ultrasonography may visualize a stone or show indirect signs such as hydroureteronephrosis (Figure 69.1). If obstruction is noted without an apparent cause, then a noncontrast CT scan should be obtained. CT should be the initial imaging study in patients presenting with severe signs and symptoms due to its higher sensitivity for urolithiasis and other urologic complications such as urine leak, lymphocele, or stricture (Figure 69.2).

Plain films should not be used as a primary diagnostic modality due to their low sensitivity for urolithiasis and inability to detect other surgical complications. If ultrasound or CT demonstrate an allograft stone, then consideration for obtaining an abdominal X-ray may be warranted to determine if the recipient is a potential candidate for shock-wave lithotripsy (SWL).

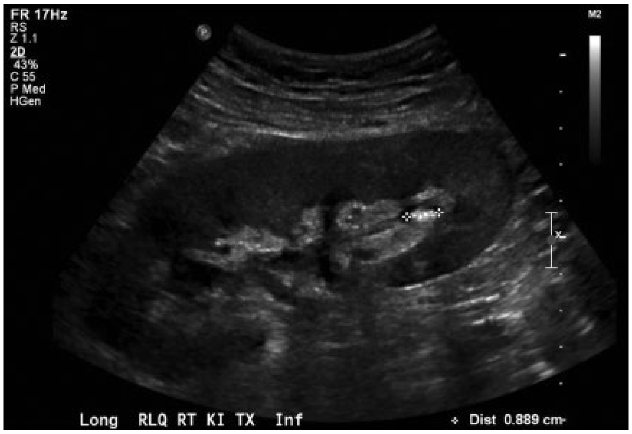

**Figure 69.1** Asymptomatic 8.9 mm lower pole allograft stone detected on annual renal ultrasound. Surveillance was elected. To date the stone has not enlarged or caused symptoms.

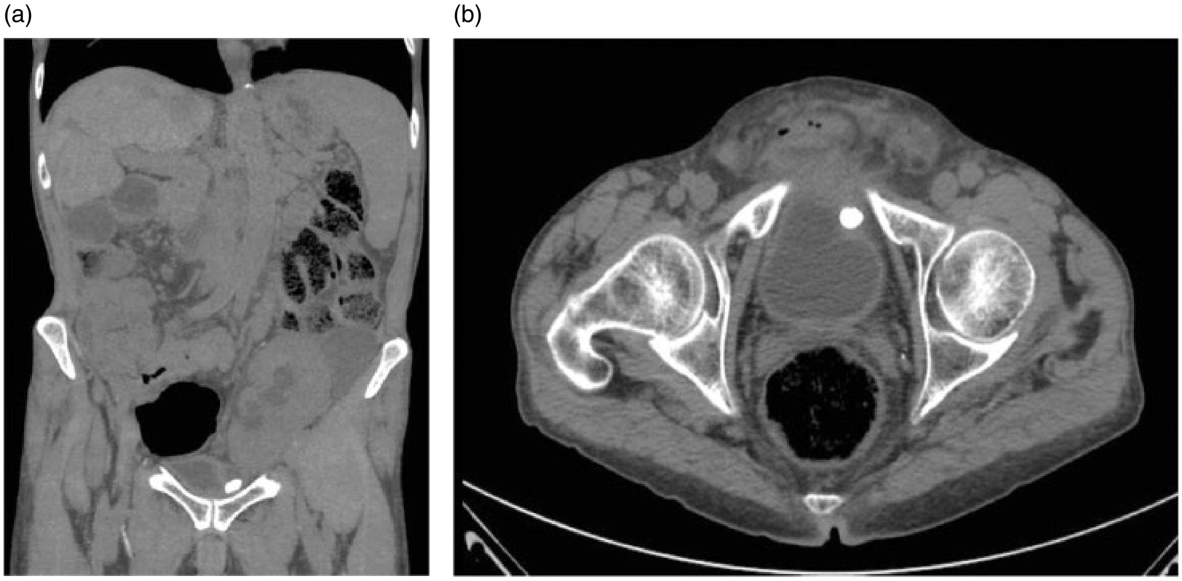

**Figure 69.2** CT images of allograft ureteral calculus measuring 12 × 9 mm at the ureteroneocystostomy site resulting in hydroureteronephrosis. (a) Coronal image. (b) Axial image. The stone was treated with antegrade ureteroscopy.

## Management

### *Ex vivo* ureteroscopy

Nephrolithiasis is no longer an absolute contraindication to kidney donation. Individuals with small stones and no significant metabolic abnormalities may be considered potential donors. Stones identified during the screening process can be treated prior to donation, during transplantation, or in the recipient after recovery. Treatment at the time of transplantation usually involves *ex vivo* flexible ureteroscopy (ExURS), but pyelotomy with flexible cystoscopy and stone extraction has also been described [37].

*Ex vivo* ureteroscopy has several potential advantages. It avoids the morbidity of an extra procedure for the donor prior to procurement, or for the recipient following transplantation. The kidney and ureter can be freely manipulated facilitating endoscopic access to the entire collecting system, which is not possible *in vivo* (Figure 69.3). One potential disadvantage of ExURS is increased cold ischemia time.

Once the kidney has been harvested it is transferred to the back bench and immediately flushed with cold preservation solution. ExURS is performed after the allograft has been prepared for implantation. If required, the ureteral stump is dilated or spatulated to allow passage of the ureteroscope. The allograft remains submerged in slush during the procedure and cold preservation solution is used for irrigation. The nondominant hand is used to manipulate the kidney to bring the stone-bearing calyx into a nondependent position. Small stones are basketed out of the collecting system. Larger stones are fragmented with the holmium laser and then extracted or irrigated out of the collecting system.

Only a few ExURS series have been published. In one series, 17 donors with stones ranging from 1 to 12 mm underwent ExURS with a 7.5 Fr flexible ureteroscope [15]. URS failed to visualize a stone in six cases and one allograft ureter did not accommodate the ureteroscope. ExURS was successful in the remaining 10 cases with five undergoing basket stone extraction, four laser lithotripsy, and one a combination of fragmentation and extraction. There were no stone-related complications. Mean treatment time was not reported.

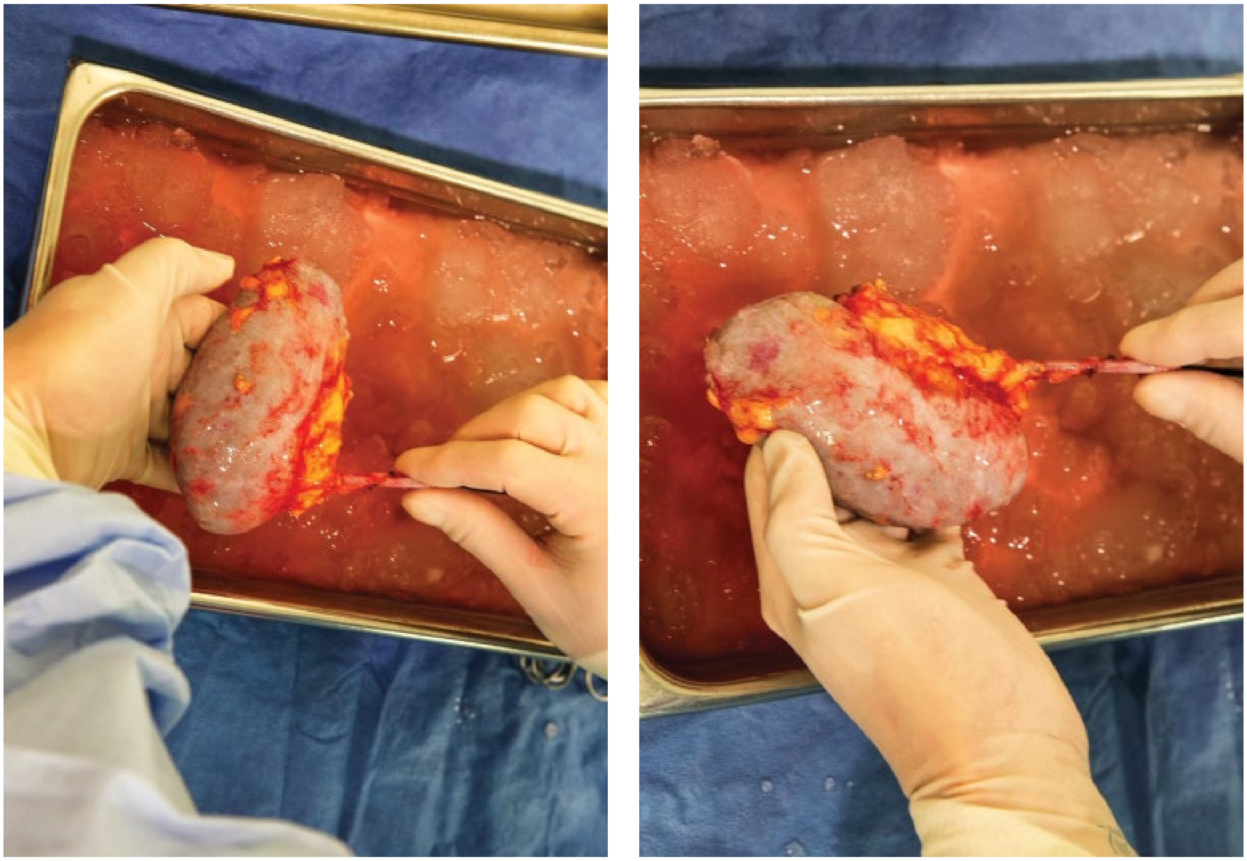

**Figure 69.3** Manipulation of renal allograft on the back bench to facilitate complete inspection of the collecting system during *ex vivo* ureteroscopy.

The largest series to date involved 28 stones in 23 allografts [38]. Mean stone size was 3.9 mm with a range of 3–6 mm. Stones were treated with either a 6.9 Fr semirigid or 9.5 Fr flexible ureteroscope. No stone was visualized in four cases. In the remaining 19 kidneys, 17 were rendered stone-free with basket stone extraction plus or minus laser lithotripsy. There were no intraoperative complications and mean treatment time was 6.2 minutes (range 3–10 minutes).

The most recently published series involved 14 donors with stones ranging from 4 to 10 mm in size [39]. Thirteen allografts were rendered stone-free without any intraoperative complications. Donors and recipients were followed up to 24 months and no graft dysfunction or stone recurrence were noted.

### Urgent decompression

Transplant recipients presenting with acute renal insufficiency or urosepsis from an obstructing stone require urgent urinary decompression with either a nephrostomy tube or ureteral stent. Pearle and colleagues performed a randomized study examining the optimal form of collecting system decompression in nontransplant patients with obstructing ureteral calculi and evidence of infection [40]. In this study of 42 patients, the authors found no clinical difference between the two forms of drainage, but nephrostomy tube placement was associated with a significant cost savings. An equivalent study has not been performed in transplant recipients.

Retrograde ureteral stent placement in transplant patients can be challenging for several reasons. The allograft ureter frequently inserts into the dome of the bladder at an oblique angle making ureteral orifice intubation difficult. In addition, the ureter is often redundant which promotes buckling of the stent during passage.

Ureteral stent placement may be contemplated in recipients who are relatively stable. However, nephrostomy tube decompression should be considered first-line treatment in patients presenting with urosepsis or renal failure with significant electrolyte abnormalities.

### Trial of passage

Transplant patients diagnosed with a ureteral stone may be managed conservatively in highly select cases. Oliguria, renal insufficiency, or evidence of infection are contraindications. Recipients with a history of medical noncompliance or stones greater than 4 mm are poor candidates.

There are no data to support the use of medical expulsive therapy in this setting. Patients should be counseled to watch for decreasing urine output. Close monitoring with weekly serum creatinine measurements and renal ultrasonography should be performed until the stone has passed or until surgical treatment is performed.

### Active surveillance

Intrarenal stones without evidence of obstruction may be managed conservatively provided the stone burden is negligible (generally less than 4 mm) and the patient does not have a history of recurrent UTIs. However, the recipient must be willing to undergo close observation given the risk of stone growth and graft obstruction.

In a study of 300 men with asymptomatic renal calculi followed for more than 3 years, clinical progression was noted in 77% of participants, with 26% undergoing surgical intervention [41]. Stone size was associated with risk of progression. Stones larger than 3 mm were 26% more likely to fail observation. In a similar study of 160 stones in 110 patients, 2% of patients developed painless hydronephrosis prompting surgical intervention [42]. This study highlights the need for radiologic surveillance given the risk of silent obstruction. Very little data exist regarding the safety of active surveillance in the transplant population. In a series from France spanning 30 years, 12 of 31 patients with asymptomatic allograft stones elected to undergo surveillance [13]. Two patients spontaneously passed their stone and the remaining 10 experienced no stone-related events or stone growth.

Spontaneous passage rates have largely been reported in surgical treatment series rather than studies evaluating the feasibility of active surveillance. Challacombe et al. reported a 9.5% passage rate (two of 21 patients) [11]. Similarly, Mamarelis and colleagues reported spontaneous stone passage in two of nine patients [8]. Other studies have reported higher passage rates (38 and 60%, respectively) for stones less than 4 mm in size [43, 44].

Recipients electing to undergo active surveillance must understand that there are little data to support its safety in the transplant population. Additionally, they must comply with close radiologic surveillance (annually at minimum). Metabolic testing with results-directed therapy should also be instituted to decrease the risk of stone progression.

### Surgical treatment

There are no practice guidelines or level 1 data governing treatment of allograft stones. As a result, treatment decisions are generally dictated by stone burden, location, and provider skillset. Surgical options include SWL, ureteroscopic lithotripsy, and percutaneous nephrolithotomy (PCNL). Percutaneous treatment is generally recommended for stones larger than 1.5 cm in diameter, whereas SWL and URS are utilized for smaller stones.

## Shock-wave lithotripsy

SWL has the advantage of being the least invasive treatment option. Factors unique to the transplant population include overlying bowel gas and location adjacent to the bony pelvis, which makes stone localization more difficult. This may account for the high failure and retreatment rates reported by some authors.

In a small series, Verrier et al. reported a 50% (two out of four patients) failure rate [13]. However, one of the patients who failed treatment had a stone larger than 1.5 cm in size. A recent article from Yuan et al. reported successful treatment in four of five patients [45]. In two series, each with seven patients, Klinger et al. and Li et al. reported 100% success treating stones between 0.4 and 1.1 cm [21, 37].

It should be noted that the definition of treatment success has not been uniformly defined across studies. It is common for patients to be considered successfully treated despite requiring multiple SWL sessions to achieve stone-free status. Li et al. reported patients needing anywhere from one to three sessions, and Yuan et al. reported two to four sessions per patient [21, 45]. Eight of 13 subjects required retreatment in a series reported by Challacombe et al. [11]. Roughly 60% of patients treated with SWL will require multiple sessions [46]. In addition to retreatment, adjuvant procedures are often required, which include ureteral stent and nephrostomy tube placement [11].

There have been no studies comparing prone versus supine positioning in SWL for transplant lithiasis. Several studies claim prone positioning allows for better stone visualization on fluoroscopy, which may improve stone-free rates [11, 37].

Following treatment, recipients must be closely monitored for steinstrasse (serial blood work and imaging) given the presence of a solitary, denervated renal unit. There is no consensus on preoperative ureteral stent or nephrostomy tube placement. However, placement should be strongly considered in patients with significant stone burdens (greater than 1 cm). Nephrostomy drainage is usually recommended for recipients with obstruction from stone debris after SWL as retrograde access is unreliable in the transplanted ureter [37].

## Ureteroscopy

Flexible URS has several potential advantages over SWL. It permits finer control over stone fragmentation and has the potential for stone extraction. However, URS is technically more challenging than SWL due to the altered ureteral and renal anatomy.

Retrograde ureteroneocystostomy access is often difficult because the allograft ureter frequently inserts obliquely into the dome of the bladder. Use of a 70° lens, angled access catheters, and the Albarran cystoscope bridge deflector are often required to promote wire passage. Sevinc and colleagues recently described using the semirigid ureteroscope to facilitate identification and access of the allograft ureter [12].

Variations in ureteroscopic treatment options exist in patients with previously placed nephrostomy tubes. The nephrostomy tube may be used to direct a wire down the ureter into the bladder to facilitate retrograde URS. Alternatively, nondilated antegrade URS with or without ureteral access sheath placement can also be performed [47].

Success rates for URS vary, and available studies are limited. In the largest series to date, Basiri et al. reported a success rate of 72% in 13 of 18 patients who underwent URS for either stones or retained stents from 1989 to 2002 [48]. In those treated for calculi, 67% were rendered stone-free. Verrier et al. reported a 67% success rate in three of five patients [13]. More recent studies have reported greater success, perhaps owing to improvements in flexible ureteroscope technology. Yuan et al. utilized flexible retrograde URS successfully in four patients, rendering all stone-free, in calculi up to 1 cm in size [45]. In a cohort of 11 patients from 2006 to 2011, Hyams et al. were able to render 10 recipients stone-free after a single procedure [47]. Five patients in this study had pre-existing nephrostomy tubes that were used for antegrade URS. Lastly, Sevinc and colleagues published a series consisting of five recipients with a mean stone size of 0.9 cm that were rendered stone-free [12].

Complications in patients undergoing URS include hematuria, UTI, pyelocutaneous fistula, ureteral perforation, and stricture [12, 45, 47, 48]. The allograft ureter lacks soft tissue support and is frequently redundant, increasing the risk of perforation during ureteroscope passage and lithotripsy. In one older series, Del Pizzo et al. successfully treated six of seven patients with small distal ureteral stones with semirigid URS [32]. However, one patient suffered a ureteral perforation. Yuan et al. reported ureteral perforation in one of five patients undergoing retrograde flexible URS, requiring an indwelling stent for 2 months [45]. The use of a safety wire with an extra stiff core should be strongly considered, and the bladder should be completely emptied prior to scope passage to minimize the risk of ureteral perforation. In addition, semirigid URS should be avoided in the majority of cases.

## Percutaneous nephrolithotomy

PCNL is the most commonly described allograft lithotripsy modality. It was first reported in 1982 by Fisher and colleagues [49]. Following partial chemolysis, a uric acid stone was extracted with a basket through a percutaneous tract. Three years later Hulbert et al. reported a more traditional PCNL approach with dilation of a percutaneous tract up to 28 Fr to facilitate insertion of an access sheath [50]. At present, PCNL is generally recommended for stones larger than 1.5–2 cm and is thought to have the highest single-procedure stone-free rate [7, 9, 51].

As opposed to traditional PCNL where patients are commonly placed in the prone position and access is obtained through a posterior calyx, percutaneous treatment of allograft stones is performed in the supine position with access through an anterior calyx. Access may be gained under fluoroscopic or ultrasonic guidance. If fluoroscopy is utilized, preoperative imaging is essential to rule out overlying bowel. Many patients will have an existing nephrostomy tube placed by interventional radiology due to obstruction at the time of presentation. However, depending on stone location, patients may require a second puncture to facilitate stone treatment. Once access has been obtained, a sheath is placed using either a balloon dilator or sequential dilators. Tract dilation is oftentimes more difficult due to fibrous encasement of the transplanted kidney. Treatment of the stone then proceeds via a variety of mechanisms: direct extraction, ultrasonic, pneumatic, or holmium laser lithotripsy. A combination of flexible cystoscopy and URS can aid in repositioning as well as treating stones that are difficult to reach with the rigid nephroscope.

In a series of 13 patients treated percutaneously, 77% had complete stone clearance after a single procedure [7]. The remaining three patients underwent second-look nephroscopy on postoperative day 1 for residual stone. In another series, all seven patients who underwent PCNL were rendered stone-free after one procedure [52].

Complications reported after PCNL include bowel perforation, bleeding, urinary or arteriovenous fistula formation, herpes esophagitis, urinoma, and impaired wound healing [11, 45, 52]. Transplant patients are at particularly high risk due to immunosuppression. As a result, many centers avoid PCNL in the perioperative period due to higher immunosuppresive medication requirements [11]. Multiple studies have demonstrated stable renal function over long-term follow-up [7, 45].

As of late, minimally invasive PCNL (mini-PCNL) has been increasingly utilized in both traditional as well as transplant lithiasis. Using a smaller access tract may reduce blood loss by minimizing parenchymal injury and allowing for greater intrarenal maneuverability with less tissue shearing. In the general population mini-PCNL has been associated with decreased blood loss and less postoperative pain despite longer operative times [53]. A recent case report from Croatia used a 12 Fr mini-nephroscope through a 15–16 Fr sheath to successfully treat an allograft renal pelvis stone [46]. The largest series in the transplant literature involved 11 recipients who underwent tract dilation between 14 and 18 Fr [54]. All eleven patients were rendered stone-free after a single procedure. He et al. reported an overall operative time of 53 minutes among seven patients who were successfully treated with mini-PCNL [55]. Only one patient experienced a postoperative complication (recurrent UTIs).

### Open surgery

Thanks to technological advances in minimally invasive stone treatment, open approaches are increasingly rare and are now generally only indicated when all other therapies have failed, or when open repair of another urologic complication (e.g., ureterovesical stricture) is required. Open lithotomy procedures are associated with more pain, longer recovery and increased risk of major complications due to dense adhesions around the grafted kidney and ureter.

## Conclusion

Transplant nephrolithiasis represents a rare but challenging entity for clinicians. The diagnosis is often challenging to establish due to allograft denervation, which can delay treatment resulting in graft injury or loss. However, once the diagnosis is made, treatment is usually successful using traditional minimally invasive therapies such as SWL, URS, and PCNL. Choice of treatment remains largely based upon stone burden and location, and each modality has its own nuances and challenges.

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# 70

# Stones in Urinary Diversions

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## Introduction

Urinary diversion using intestinal segments is a widely employed technique in reconstructive urology for the care of urologic patients with both benign and malignant diseases. Applications include pediatric urology, neurogenic bladders, reconstructive urology, and oncology. A wide range of urinary diversions have been described; however, the ileal conduit and the continent orthotopic neobladder are the two of the most commonly performed urinary diversions at present.

Urinary diversions have posed unique challenges to the urologist. Long-term complications include renal insufficiency, recurrent infections, strictures, metabolic and electrolyte disturbances, secondary malignancies, and calculi. Although modifications and improvements in surgical technique have reduced the risk of complications, postsurgical problems still occur. One such complication is the development of calculi in the diversions. While open surgical management has played an important role in the management of this problem, the advent of endourology and minimally invasive surgical techniques have helped reduce the morbidity from the surgical management of stones in these patients. (See Video 70.1).

## Etiology

The etiology of stone formation in patients with urinary intestinal diversion is multifactorial. These can be classified mainly as idiopathic, metabolic, infectious, or structural. It is well known that patients with urinary diversion have metabolic abnormalities due to the reabsorption of urinary solutes across the intestinal mucosa. Hypercalciuria secondary to hyperchloremic metabolic acidosis is a predisposing factor for calcium phosphate stones. In a study by Terai et al., hypocitraturia was observed in over one-third of patients. An increase in excreted calcium and phosphate coupled with an increase in urine pH created a favorable milieu for infectious calculi [1]. Further, these patients are also often dehydrated, contributing to the process of stone formation.

Patients with urinary diversion are often colonized with urease-producing bacteria. Common uropathogenic organisms cultured include *Proteus*, *Klebsiella*, and *Pseudomonas* [2], which metabolize urea into ammonium and bicarbonate. The alkaline milieu predisposes to infectious stones, including struvite, carbonate apatite, and ammonium acid urate stones.

Other risk factors for stone formation include excessive mucous production by the intestinal mucosa [3], foreign bodies (staples, nonabsorbable sutures, etc.) acting as a nidus for stone formation, urinary stasis in patients who incompletely empty their reservoirs, or obstruction. Irrigation of the reservoir may be helpful in reducing stone formation by clearing bacterial load and mucous deposits [4–6].

## Rates of stone formation

The reported incidence of stones varies depending based on the type of urinary diversion. The incidence of stones is 11–12% in patients with an ileal conduit [7, 8]; 17–43% in patients with a Kock pouch [4, 9, 10]; and 11–19% in patients with an Indiana pouch [10, 11]. Abol-Enein and Ghoneim [12] published their experience with 450 patients having undergone an orthotopic ileal W-shaped neobladder with serous-lined extramural ureteral reimplantation. Their stone incidence rate was 3% [12]. Ferriero et al. reported a rate of neobladder stone formation of 9.2% in 445 consecutive patients who underwent radical cystectomy and a non-absorbable, titanium

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stapled orthotopic neobladder [13]. Overall, the incidence of stone formation in patients with urinary diversion seems to be decreasing, due in part to use of absorbable surgical material, and also the heightened awareness of the metabolic and infectious causes of stone formation [14].

The recurrence rate of stones in patients with urinary diversion is common, with reports suggesting rates as high as 50–63% over 5 years [15, 16]. Recurrent urinary tract infection appears to be a risk factor for stone formation [5, 15]. The rate of recurrence seems to be independent of the treatment technique and patient characteristics [16, 17]. Patients with infectious stones may also have recurrences with other non-infectious type of stones [18].

## Types of stones

Patients with urinary diversion are predisposed to infectious stones due to the frequent colonization of the intestinal segment with urease-producing bacteria. These will hydrolyze urea into the bicarbonate and ammonium. Excess bicarbonate in the urine creates an alkaline urine pH, and leads to the formation of magnesium ammonium phosphate and carbonate apatite stones. Additionally, the hyperchloremic metabolic acidosis state often seen in patients with ileal conduits or colonic reservoirs results in decreased reabsorption of calcium and a decreased production of citrate by the kidneys, favoring calcium stone formation. Calcium oxalate stones are also not infrequently seen in patients with urinary diversion. Hyperoxaluria may be seen in patients when small bowel, especially the terminal ileum, is used for the reconstructive procedure. Resection of the terminal ileum results in an increase in unabsorbed fatty acids and bile salts which undergo saponification by binding with calcium in the bowel. This leads to an increase in unbound oxalate which is absorbed by the large intestine and subsequently excreted in the urine. The resultant hyperoxaluria favors the formation of calcium oxalate stones. In a study by Hertzig et al., the stone composition in 77 patients having undergone a radical cystectomy and ileal conduit was reported. The vast majority (63.5%) were magnesium ammonium phosphate stones, with the remainder being 25% calcium phosphate, 9.6% calcium oxalate monohydrate, and 1.9% calcium oxalate dihydrate [19].

## Surgical management

The surgical approach should take into consideration the location and size of the stone and the anatomy of the diversion to plan the access route. Open surgical extraction has been largely replaced by endoscopic and minimally invasive surgical techniques. Modalities such as extracorporeal shock-wave lithotripsy (ESWL), antegrade and retrograde ureteroscopy, trans-stomal lithotripsy, percutaneous nephrolithotomy, and percutaneous transreservoir lithotomy have been described in the literature.

### Stones in the urinary diversion

Stones in the intestinal diversion may be managed by endoscopic or open techniques. The anatomy of the urinary tract and also the surrounding structures should be outlined with prior radiographic imaging, typically noncontrast computed tomography (CT). Any concomitant strictures should also be delineated and will likely also need to be addressed. Access to the diversion is most easily obtained through the stoma, especially for patients with ileal conduits. In patients with continent reservoirs, care should be taken to avoid traumatizing the continence mechanism. In-and-out access through the continence mechanism should only be used for patients with minimal stone burden, with care to avoid excessive manipulation to prevent postoperative leakage or strictures. A flexible cystoscope can usually be safely passed into most diversions, including an Indiana pouch. Olympus produces a flexible cystoscope that has a suction channel. This can be very helpful as it allows the reservoir to be suction-irrigated, allowing for the clearance of mucus and some debris (see Figure 70.1). In patients with orthotopic reservoirs, access through the urethra with rigid instruments is feasible, although there is a risk of bladder neck contracture. Fragmentation of the stone can be performed with a holmium:YAG laser, ultrasonically, pneumatically/ballistically, or with an electrohydrolic lithotripter. Ultrasonic lithotripters are increasingly being used as they are less harmful to the intestinal mucosa [20].

The use of ESWL in patients with a Kock or Indiana pouch has been reported in a small number of patients. These patients should undergo pouchoscopy to ensure the absence of staples or other foreign material acting as a nidus for stone formation. In addition, basketing of fragments is probably necessary to render these patients stone-free [14, 20, 21].

Percutaneous access has become the technique of choice in patients with a large stone burden in their reservoir. The Amplatz dilator system or balloon dilation, with a large 24–30 Fr working sheath, allows for larger instrumentation use and facilitates stone removal. Access can be directly visualized with a flexible cystoscope placed through the stoma site. Deflection of the endoscope to transilluminate the abdominal wall may help in obtaining the optimal access site. A CT scan to outline

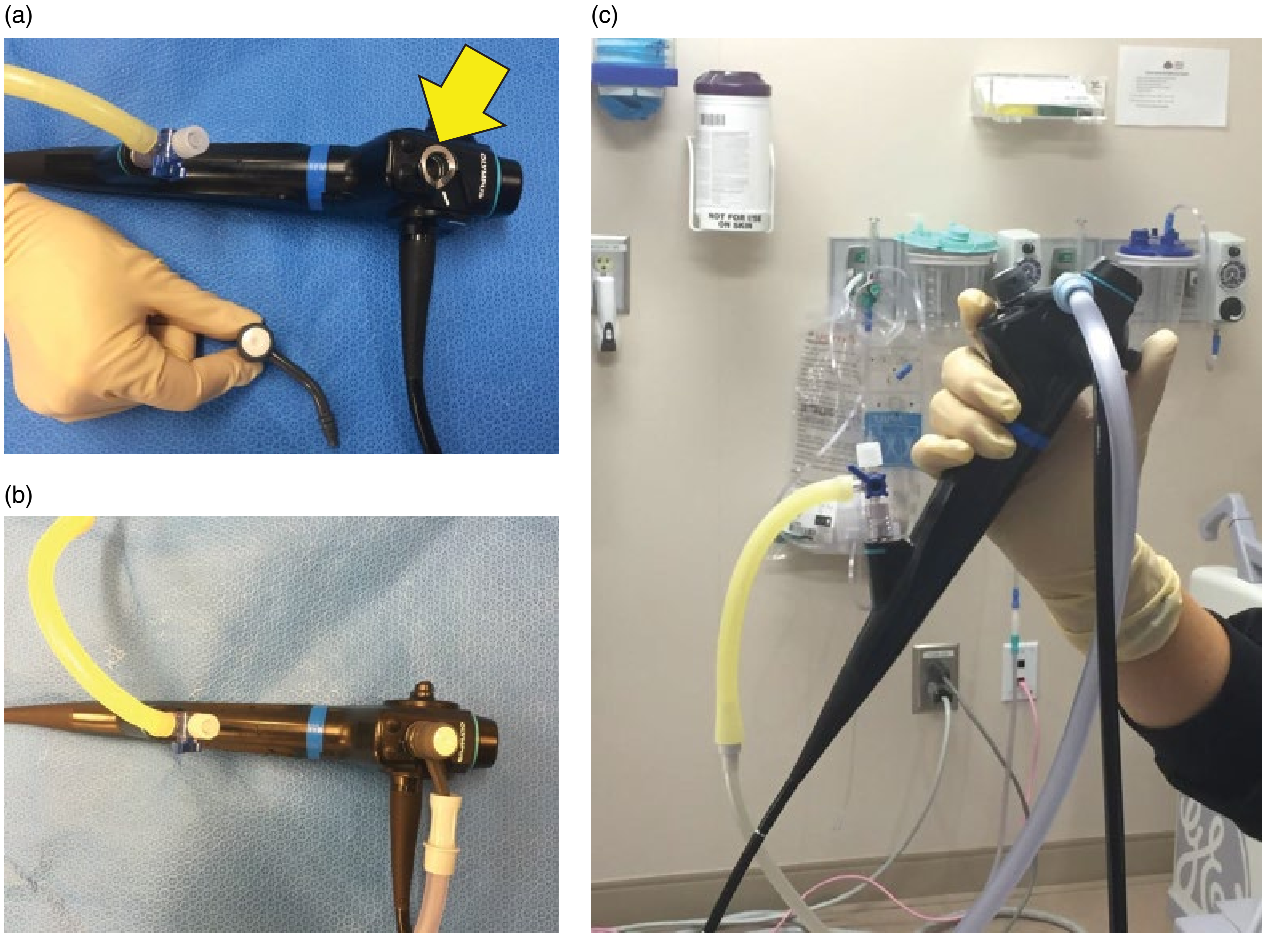

**Figure 70.1** Olympus cystoscope with suction adapter. The adapter fits on the head of the cystoscope and can then be plugged into the usual suction apparatus.

the surrounding anatomy is crucial in these cases to avoid adjacent organ injury. A handheld ultrasound at the time of puncture can also facilitate a safe puncture and avoid adjacent structures such as the bowel. Stones as large as 5 cm have been removed using this technique [22–24]. Breda et al. published the largest known series using exclusively the percutaneous approach in 74 pediatric patients with a reconstructed bladder. Their mean stone size was 2.4 cm (range 1–4.7 cm), and the mean number of stones was 4.6 (range 1–60). Their mean operative time was 96 minutes. The reported stone-free rate was 95% at 2 weeks using a simple abdominal X-ray as imaging. Overall complication rate was 12%, and included infection, difficulty catheterizing the Mitrofanoff channel, and encrustation of the catheter used for drainage [25]. Paez et al. reported their series of percuatenous access in 12 patients with no observed complications. Although stone clearance was achieved in all 12 patients initially, stone recurred in five patients at a median follow-up of 24 months [26].

A combination of endoscopic and laparoscopic instruments may also be used for larger stone burden. After obtaining percutaneous access, stones can be placed in an endocatch bag brought into the reservoir via either the primary access [27] or a secondary access [28]. The endocatch bag is then removed altogether by widening the skin incision, or the stones can fragmented within the bag to reduce intestinal mucosal injury and the loss of small fragments. In their series of eight patients, Lam et al. [27] reported a mean operative time of 123 minutes. The mean stone size was 4.1 cm (range 1.5–7.0 cm), and six of the eight patients had multiple stones. All eight patients were rendered stone-free, and there were no complications. This procedure was done on an outpatient basis, or patients were discharged within 23 hours of surgery.

Open cystolithotomy has fallen out of favor due to efficient and less morbid minimally invasive techniques, and is typically reserved for patients with a very large stone burdens or in centers that lack specialized equipment for a minimally invasive approach. Although there have been no published reports in the literature, pure laparoscopic or robotic cystolithotomy can be considered in experienced hands as an alternative to the open technique [23].

### Stones in the kidney (5 mm or less for expectant treatment) and ureter

Similar to patients without urinary diversion, small symptomatic stones <10 mm may be managed expectantly initially if the pain is well controlled and there is no evidence of infection. The addition of an alpha-blocker to promote stone passage may be considered, although its efficacy in patients with urinary diversion has not been studied. There should be a lower threshold for definitive management of the stone in these patients since a large proportion are colonized by various organisms, and are probably at higher risk of developing an infection. ESWL remains a good initial management option in patients with smaller stones, and avoids the difficulties of obtaining access. The reported success rates of ESWL in patients with urinary diversion range from 25 to 92% [19, 29–32]. Preoperative urine culture should be obtained on all patients prior to treatment, and patients should be treated with appropriate antibiotics when indicated to reduce bacterial colony count. In patients with an orthotopic or continent catheterizable reservoir, pouchoscopy should be considered post-ESWL to ensure that no residual fragments are lodged between the mucosal folds.

Both retrograde and antegrade endoscopic approaches have also been utilized to treat stones in patients with urinary diversions. The main difficulty in this group of patients is finding the neo-ureteric orifices to obtain ureteral access for retrograde access. Difficulty distending the conduit, mucosal folds, and bowel tortuosity can make it challenging to find the neo-ureteral orifices. Hyams et al. published the largest known series of retrograde access in 28 patients with urinary diversion, with a success rate of 90% for orthotopic neobladders, 73% for ileal conduits, and 33% for Indiana pouch patients [33]. Intravenous injection of methylene blue may help to identify the neo-ureteral orifices. Detailed knowledge of the diversion procedure is also critical, although at times that information may not be available depending on when and where the diversion was performed. Knowing the type of ureteral implant (i.e. Bricker, Wallace, etc.), as well as the location of the ureteral implantation (i.e. at the end of the conduit, at the side of conduit) may help in localizing the neo-ureteral orifices. For an antegrade approach, ultrasound-guided access may be used to insert a finder needle and perform a nephrostogram under fluoroscopy to identify the best calyx for the approach [23]. Percutaneous nephrolithotomy remains the standard of care for patients with large stone burden. Once the proper calyx is punctured, dilation of the tract and the formal procedure is then carried out in the same fashion as for patients without a urinary diversion. For smaller stones in the ureter, an antegrade ureteroscopy can be performed with minimal dilation. At our institution we have passed a short 12/14 Fr ureteral access in an antegrade fashion to facilitate the passage of a flexible ureteroscope to treat ureteral stones (see Figure 70.2). The advantage of using the sheath is that it facilitates multiple passes and extraction of the stone fragments.

## Prevention

### General strategies

Due to the very high recurrence rate of stones, preventative measures are of pivotal importance in this group of patients. Patients should be counseled on appropriate dietary measures, including an adequate fluid intake to produce >2 L of urine per day. These patients should have two 24 hour metabolic workups to identify and potentially treat any metabolic abnormalities [34]. Proper emptying of the reservoir should be confirmed. Regular voiding or catheterization schedule should be encouraged to avoid urinary stasis while maintaining a low residual volume. Surgical strategies to prevent stones include using absorbable material and ensuring that nonabsorbable materials are not exposed to urine.

Mucous appears to play a role in the formation of stones in the reservoir, and there may be a benefit at irrigating a reservoir to clear the mucus [3]. Hensle et al. noted a significant decrease in stone formation after instituting a strict irrigation protocol consisting of twice-weekly irrigation of saline (240 mL) and once-weekly gentamicine sulfate solution [6]. Irrigation using 20% urea solution has also been described for refractory cases [5]. Terai et al. noted a 12% risk of stone formation in Japanese patients with an Indiana pouch, compared to 5.4% for US patients. The only difference noted was that patients in the United States were placed on a standard irrigation protocol [4].

### Noninfectious stones

Predisposing metabolic abnormalities need to be identified and corrected. Hypovolemia must be addressed if present. Hyperchloremic metabolic acidosis and the resulting hypocitraturia seen in about one-third of patients can be corrected with oral citrate supplementation. Calcium oxalate stone-formers with enteric hyperoxaluria may benefit from restricting high-oxalate-containing foods combined with higher calcium intakes, which may

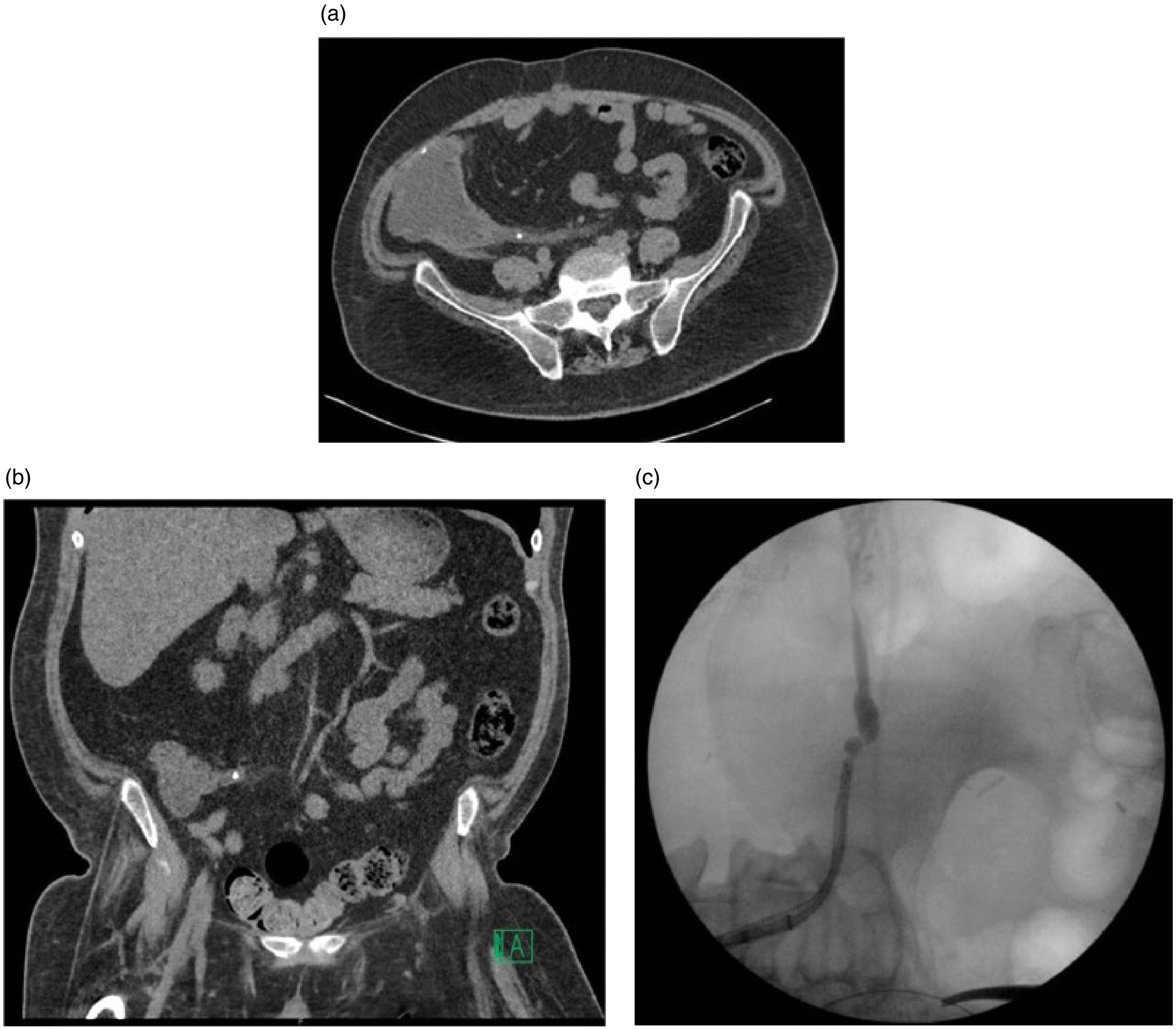

**Figure 70.2** (a, b) Axial and coronal CT images of a patient with an Indiana pouch, found to have a left 4 mm obstructing ureteral stone. (c) Intraoperative fluoroscopy during antegrade ureteroscopy using a 12–14 Fr access sheath.

include supplements, specifically timed with meals. The calcium will bind to oxalate in the gastrointestinal tract, preventing it from being absorbed [34], as indicated.

## Infectious stones

In patients with struvite stones who are colonized or infected with urease-producing organisms, antibiotic therapy is indicated, particularly in the case of recurrent stones. Oral prophylactic measures for struvite stones also include acetohydroxamic acid, an irreversible urease inhibitor. Its extensive side effect profile, particularly phlebitis and other hypercoaguable events, limits its use. Chemodissolution therapy for residual struvite fragments includes hemiacidrin or Suby's G solution. Hemiacidrin reached its pinnacle of publications between 1973 and 1988, with its use described through nephrostomy tubes after pyelolithotomy (open, minimally invasive surgery, or SWL), through ureteral catheters for chronically ill or spinal cord patients, and even as primary therapy through nephrostomy tubes, with complete responses (>75%) reported in most series. Hemiacidrin's shortcomings far outweighed its advantages, and this therapy has declined due to several reasons, namely its cost, intense irrigation protocol (requiring instillation at low renal pelvic pressures), prolonged immobility (requiring deep-vein thrombosis prophylaxis), and hospitalization required to monitor its administration, and the advent of more effective minimally invasive therapy [35]. Hemiacidrin has been shown to be safe and effective in patients with an ileal conduit [36].

## Conclusion

The management of stones in patients with urinary diversion is a common occurrence and something that most endourologists will need to manage. The metabolic, infectious, and structural risk factors to stone formation should be elucidated and corrected to prevent stone formation and recurrence in this high-risk population. Prophylactic measures to reduce stone recurrence rate should be considered in all patients. The advent of endourology and minimally invasive techniques has facilitated stone retrieval in these patients while considerably minimizing morbidity, although unique challenges to these procedures remain.

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# 71

# Management of Stones in Obesity

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## Introduction

Recent data from epidemiological studies suggest that the prevalence of overweight and obese individuals has significantly increased over time from 15 to 35.04% in men and 36.84% in women in the United States [1]. Obesity is a major public healthcare problem, and generally accompanies with comorbid conditions such as hypertension, diabetes mellitus, hyperlipidemia, hypercholestrolemia, and cardiovascular disease. The body mass index (BMI) is an objective measure of obesity and patients with a BMI greater than 40 kg/m$^2$ have an extremely high relative risk of comorbid diseases [2]. Additionally, large population-based studies have shown that obesity and weight gain increase the risk of kidney stone formation caused by alterations of urinary metabolite excretion in adults [3, 4]. In a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES), the prevalence of urolithiasis was 11.2% in obese individuals [5]. Based on prevalence and cost estimation for 2030, obesity and diabetes will independently increase stone prevalence by 0.36% and 0.72%, respectively, and the cost of urolithiasis is projected to increase to an additional US$1.24 billion/year [6]. The management of obese stone formers has become safe and more effective owing to advances in minimally invasive techniques and improvements in anesthesia, but in this group of patients there may be encountered some specific technical challenges that the urologist needs to be aware of to provide optimum care.

In this chapter we discuss obesity and stone risk, covering urine pH, hyperinsulinemia, metabolites, and inhibitors, followed by weight-loss diets and the risks of stone disease after bariatric surgery. We then cover medical therapy in obese stone formers followed by the interventional therapies available: shock-wave lithotripsy, ureterorenoscopy, and percutaneous nephrolithotomy.

## Obesity and stone risk

Studies showed that the most common stone component in obese patients is calcium oxalate and a slightly higher incidence was found of uric acid stones as well [3, 7]. In addition, the authors suggest that obesity is strongly associated with an increased risk of stone episodes. In an effort to elucidate possible urinary changes, a lot of studies have been conducted and several factors have been found to be involved in stone formation in obesity.

### Urine pH

Urinary pH is one of the important factors of stone formation. Li et al. demonstrated that urine pH is inversely related to BMI among obese patients with urolithiasis [8]. They found that the mean urine pH of normal body weight, overweight, and obese groups was 6.25, 6.14, and 6.00, respectively. Hyperinsulinemia, insulin resistance, and gout diathesis may be the factors which cause lower urinary pH in obesity.

### Hyperinsulinemia

Obese patients have a higher incidence of diabetes mellitus which is correlated with hyperinsulinemia or insulin resistance. Insulin is known to stimulate the synthesis of ammonia and sodium–hydrogen exchange in the renal tubule which mediates ammonium excretion in urine. Hyperinsulinemia associated obesity contributes

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to the development of calcium stones by decreasing urinary citrate and increasing urinary excretion of calcium, uric acid, and oxalate [9]. Insulin resistance may be linked to defective ammonium production and the ability to excrete acid, and may cause lowered urine pH. Cameron et al suggested that increased incidence of uric acid stone formation in patients with diabetes may be secondary to production of more acidic urine than in non-stone-bearing counterparts [10].

## Metabolites

High metabolic load is another important factor for urolithiasis in obesity. Powell et al. demonstrated that increased urinary concentrations of sodium, oxalate, uric acid, phosphate, and cystine were found in obese patients compared with non-obese counterparts and these urinary changes mostly appeared in obese women [3]. Taylor and Curhan stated that male obese patients excreted more urinary oxalate, calcium, uric acid, sodium, and phosphate than non-obese patients. Women obese patients also excreted more urinary oxalate, uric acid, sodium, and phosphate than non-obese patients, but increased urinary calcium was seen only in younger women. An inverse relation between BMI and urine pH was seen also in both men and women [11].

Fructose consumption has markedly increased over recent decades owing to widespread use of high-fructose syrup. Taylor and Curhan reported that high levels of fructose intake were associated with increased relative risk of stone formation regardless of BMI, caloric intake, or other risk factors [12]. The mechanisms underlying the relationship between fructose and stone risk are unknown, but may be related to the effect of fructose intake on urine composition. Fructose intake may alter calcium metabolism, particularly in the setting of low magnesium intake. In contrast, Knight et al. demonstrated there was no change in 24 hour urine calcium, oxalate, or uric acid excretion with increasing fructose consumption [13].

The level of physical activity and energy intake may increase risk of stone formation. An observational study reported that among postmenopausal women, increased levels of physical activity and lower energy intake were associated with a significant reduction in the risk of kidney stones, even after taking into account BMI, history of diabetes, and intake of fluid, dietary calcium, sodium, and animal protein [14]. However, a recent study from three large prospective cohorts, the Health Professionals Follow-up Study (HPFS) and Nurses' Health Studies (NHS) I and II, concluded physical activity and total energy intake were not independent risk factors for kidney stones [15].

## Inhibitors

Urinary citrate excretion is determined by acid/base status related to the intracellular pH of renal proximal tubule cells [16]. Acid load promotes proximal tubular reabsorption of citrate and reduced citrate synthesis. Lowered urinary pH is commonly seen in obese patients which leads to hypocitraturia. Magnesium complexes with oxalate, thereby potentially reducing oxalate absorption in the gastrointestinal tract. Consequently, high metabolic load and decreased excretion of inhibitors such as citrate and magnesium facilitate urolithiasis in spite of increased urinary volume [17].

Regarding the negative effects of comorbid disease and urolithiasis on kidney function together with limitations of stone surgery, the medical management of stone disease seems to be the most important goal for preventing further recurrences in morbidly obese patients.

## Weight-loss diets

Weight-loss diets have gained popularity since preventative measures for disease have been shown to reduce healthcare expenses in developed countries. Most dietary fads include low-carbohydrate, high-protein, and/or high-fat diets (e.g. the Atkin's diet, Ducan's diet, South Beach diet, and Sugar Busters diet). These kinds of diet deliver a significant acid load to the kidney, which might increase the risk of stone formation and bone loss. Despite there being no concrete evidence to link stone formation with such diets, addition of alkali therapy may reduce acidosis and hypercalcuria, and normalize citrate metabolism. Taylor et al. concluded that a diet high in fruit and vegetables, and low in animal protein, is associated with reduced risk of stone formation [18].

## Stone disease after bariatric surgery

Use of surgical procedures for obesity (bariatric surgery) has risen over the past two decades. A worldwide survey study performed in 2011 demonstrated that Roux-en-Y gastric bypass (RYGB) for restrictive and malabsorptive surgery made up 46.6% of weight-loss procedures, followed by sleeve gastrectomy (27.8%) and adjustable gastric banding (17.8%) as restrictive surgery [19]. Although such procedures effectively manage obesity-dependent comorbidities, a large controlled study revealed that the patients who underwent RYGB surgery had approximately two times higher risk of nephrolithiasis than obese patients [20]. In patients who have undergone bariatric surgery, fat malabsorption leads to hyperabsorption of oxalate, which is exacerbated by an increased permeability of the gut to oxalate [21].

Patients who have undergone bariatric surgery showed characteristic 24 hour urine parameters including low urine volume, low urinary pH, hypocitraturia, hyperoxaluria, and hyperuricosuria. Nevertheless, the pathophysiology of bariatric surgery-induced hyperoxaluria remains unclear. Potential causes include alteration in intestinal flora (i.e. *Oxalobacter formigenes*), fat malabsorption, or a reduced amount of oxalate secretion [22, 23]. Prevention of stones with dietary limitation of oxalate and sodium and a high intake of fluids is critical, and calcium supplementation with calcium citrate is typically required. Potassium citrate is valuable for treating common metabolic imbalances as it raises urinary pH, enhances the activity of stone inhibitors, reduces the supersaturation of calcium oxalate, and corrects hypokalemia. Both pyridoxine and probiotics have been shown in small studies to reduce hyperoxaluria [24, 25], but further study is necessary to clarify their effects on stone morbidity in the bariatric surgery population.

## Diet and medical therapy

### Dietary modifications and weight loss

Dietary modifications can reduce urinary excretion of stone constituents or increase urinary inhibitors. Dietary changes alone may be sufficient in terms of preventing stone recurrence without the need for drug therapy in low-risk stone formers; however, dietary modifications should always accompany drug therapy in patients at high risk of recurrence. Acidic urine and increased concentrations of sodium, calcium, oxalate, and uric acid may aise the risk of stone disease due to excessive intake of salt, protein, calcium, and a oxalate-rich diet in obese patients. Weight loss and dietary modifications such as increasing fluid and fibre intake, restricted intake of red meat, salt, and oxalate, and mild calcium intake, may alleviate urinary electrolyte changes in some patients [26].

Ekuro et al. found that appropriate dietary modification and tailored medical treatment successfully lowered the recurrence rate of stone disease in obese patients [27]. In general, patients are recommended consuming enough fluid to maintain a urine output of at least 2 L daily. Most beverages can be drunk to increase fluid intake and help prevent stone formation.

### Potassium citrate and urine pH modifications

Potassium citrate acts by providing an alkali load and probably reducing urinary calcium. It increases urinary pH and citrate, thereby increasing urinary inhibitory activity. Potassium citrate can be used in hypocitraturic patients or normocalciuric calcium stone formers regardless of other associated abnormalities. In a randomized trial, potassium citrate was shown to reduce stone recurrence rates by 75% among hypocitraturic stone formers [28]. In patients with gouty diathesis, potassium citrate raises urinary pH and reduces uric-acid-induced calcium oxalate stone formation. It has been shown to be effective in reducing stone recurrence rates for patients with hyperuricosuric calcium oxalate nephrolithiasis and lack of tolerance for allopurinol [29]. Increasing the urine pH above 5.5, preferably between 6.5 and 7.0, plays a key role in the management of gouty diathesis [30]. Potassium citrate should be given at a dose sufficient to maintain urine pH at approximately 6.5. Alkalinizing the urine to a pH higher than 7.0 should be avoided due to increasing risk of calcium phosphate stone formation.

Potassium citrate is prescribed at a starting dose of 10 mEq three times daily, or 20 mEq twice daily. It is prescribed along with a thiazide diuretic or indapamide to reduce the risk of thiazide-induced hypokalemia and hypocitraturia in patients with hypercalciuria. For patients with enteric hyperoxaluria, potassium citrate therapy can raise urine pH and citrate, but the dosages of potassium citrate (up to 120 mEq daily) may be increased higher than used for idiopathic calcium nephrolithiasis.

### Allopurinol

Decreasing the production of uric acid and altering the urinary milieu for the remaining uric acid to be in a dissolved state are two pharmacologic approaches to the management of hyperuricosuric calcium oxalate nephrolithiasis. Allopurinol (300 mg/day) may be used if patients are unable or unwilling to comply with dietary protein restriction. Diluting urine to maintain uric acid at a low concentration and the use of an alkalinizing agent such as potassium citrate (30–60 mEq/day) may promote dissolution of uric acid.

## Interventional therapies

Clinical guidelines of the American Urological Association (AUA) for urolithiasis indicate that spontaneous stone passage is seen in 10–53% for 6–10 mm stones [31]. This shows that patients with a stone size larger than 5 mm may encounter some stone-related complications such as renal colic, urinary obstruction and infection in their lifetime and may require interventional therapies. On the other hand, obesity poses a number of problems in the management of stone disease from diagnosis and imaging through to anesthesia and surgery. Beyond these pitfalls, treatment success of interventional therapy is negatively influenced by obesity as well. Some technical modifications have been outlined by several authors to increase success rates. In this section we emphasize the basic features of these therapies in obese patients.

## Extracorporeal shock-wave lithotripsy

Extracorporeal shock-wave lithotripsy (SWL) has been widely used as the primary treatment modality for most renal and ureteral calculi [32]. Uncorrected coagulopathy, pregnancy, severe skeletal deformity, and morbid obesity are accepted contraindications of this modality. Advantages of SWL for renal and ureteral stones are the avoidance of anesthesia-related complications and the ability to perform the procedure many times without increasing morbidity. On the other hand, exceeding the table's weight limit (135 kg for Dornier HM3) and the short focal length (12–14 cm) of lithotripters restricts the optimal SWL treatment in obese patients [33]. Treatment success for renal stones ≤20 mm was found to be above 90% and was 92.6–97.5% for ureteral stones ≤10 mm in the overall population [32]. However, Delakas et al. suggested that the probability of SWL failure was increased 1.9-fold with a BMI of more than 30 kg/m$^2$ [34]. Munoz et al. found that the success rate of SWL for renal and ureteral stones was 72% in obese patients [35]. Additionally, Ackerman et al. stated that BMI was an independent predictive factor of SWL failure and BMI ≤28 kg/m$^2$ had better treatment results [36]. Recent studies emphasized the importance of skin-to-stone distance (SSD) upon stone clearance measured by the mean of three distances from the renal stone to the skin at 0, 45, and 90° using radiographic calipers or a computational measuring device [25, 37]. Many studies have shown that SWL outcomes worsen when SSD exceeds 10 cm [25, 38–40]. Pareek et al suggested that SSD greater than 10 cm more strongly predicted SWL failure than BMI [41]. Reducing focal length by using an abdominal strap, selecting a lithotripter with a long focal length, and high-energy settings may improve the success rate of SWL [42]. Additionally, Mezentsev states that SWL with the "blast-path" technique in morbidly obese patients enables better treatment success (87%) even if the stone is located a few centimeters from the center of focal area [43]. Treatment of lower calyceal stones is still challenging, as in non-obese patients.

Recently, excessive visceral fat, as measured on non-contrast computed tomography, has been shown to be a useful prognostic tool for SWL outcomes. Juan et al. emphasized that increasing abdominal circumference, visceral fat, subcutaneous fat, and perirenal and pararenal fat are strongly related to decreasing stone-free rates after SWL [44]. Zhou et al. demonstrated that increasing visceral fat was an independent predictor of uric acid stones [45]. Therefore, urinary alkalization should be tailored in obese patients with radiolucent stones and low urinary pH.

Tips and tricks for SWL in obesity are outlined in Box 71.1.

**Box 71.1 Tips and tricks for shock-wave lithotripsy in obese patients.**

Use an abdominal strap to reduce focal length.
Use a long-focal-length lithotripter or high-energy setting.
Use the "blast-path" technique when the stone located a few centimeters from the center of the focal area.

## Ureterorenoscopic treatment

Owing to recent technological advances, retrograde endoscopic lithotripsy for renal and ureteral stones with flexible and semirigid ureterorenoscopy (URS) has become a feasible treatment option. According to the European Association of Urology (EAU)/AUA Guideline Panel on ureteral stones, URS has superior stone-free rates for proximal ureteral stones larger than 1 cm and in all mid-ureteral and distal stones when compared with SWL [46]. Additionally, URS can be safely performed in special circumstances such as pregnancy, ectopic, pelvic, or transplant kidneys, pediatric patients, and patients on anticoagulation medication. Despite SWL being accepted as the first-line treatment modality for renal stones (smaller than 2 cm), it may be precluded by weight limitations of the treatment table and difficulties in focusing on the stone due to impaired radiologic imaging (fluoroscopy or ultrasound) and short focal length [47].

Flexible URS is indicated in renal stones less than 15 mm that do not respond to SWL [48]. Dash et al. stated in a stone-matched comparison (obese vs. non-obese) that URS treatment for renal calculi was effective in obese patients as well as non-obese counterparts without increasing morbidity [49]. Natalin et al. evaluated their URS treatment outcomes of renal and ureteral stones according to BMI, stone size, and location from data of 107 patients [50]. Overall stone-free rates were 91, 97, and 94% in normal, overweight, and morbidly obese patients, respectively. They found no significant difference in terms of stone location (renal/proximal, middle, and distal ureteral stone) and size (cut-off dimension was 1 cm) in all groups. They emphasized that URS treatment is an acceptable modality for all ureteral calculi with a high success rate in obesity and may be preferable to SWL for obese patients [50]. In a multicenter trial, Chew et al. compared URS in patients with normal

BMI values with those considered overweight or obese [51]. No significant difference was found in stone-free rates. Recently, Ishii et al. conducted a systematic review which analyzed the data of 15 studies and 835 patients with a mean BMI of 40.5 kg/m$^2$ [52]. According to cumulative analysis, the initial and final stone-free rates were 76.9 and 82.5%, respectively, with an overall complication rate of 9.3%. The overall stone size was 14.2 mm (range 3–72 mm) with almost a third of the stones in the lower pole. The complication rate for morbidly obese patients (17.6%) was twice that of the obese patients (8.4%), although they were all graded as Clavien I or II. Consequently, they concluded that URS and stone fragmentation are safe and efficient treatment methods in obese patients with a good stone-free rate and a relatively low complication rate.

Generally, additional technical modifications are not recommended when performing URS in obese patients. To prevent further interventions, recent developments in URS treatment such as digital flexible URS, ureteral access sheath, holmium laser lithotripsy, and nitinol stone baskets may be used [53]. Flexible URS may act as a guide for percutaneous renal access in obese patients after failure of a prior attempt. Khan et al. defined a technique in which flexible URS advances to the intended calyx with the patient in a prone split-leg position and exact percutaneous calyceal puncture is performed under direct vision [54].

## Percutaneous nephrolithotomy

Percutaneous nephrolithotomy (PCNL) is recommended for kidney stones larger than 2 cm and staghorn calculi [55]. PCNL is also indicated in cases of SWL failure, stones with concurrent ureteropelvic junction obstruction, stones within calyceal diverticula, and anatomic abnormalities (i.e. horseshoe kidney). The absolute contraindications are active urinary infection and uncontrolled coagulopathy. Studies suggested that the success and complication rates of PCNL in obese patients are comparable with the normal-weight population [56–58].

Pearle et al. found that the stone-free rates of staghorn and non-staghorn stones in obese patients were 84.2 and 90.2%, respectively [56]. Of the patients, 14% had minor or major complications, 8.8% needed blood transfusion, and hospital stay was 4.9 days. They also stated that technical modifications and appropriate instrumentation are necessary for improving stone-free rates in this group of patients. Similarly, El-Assmy et al. reported 4 year PCNL experiences in 1121 patients from their retrospective clinical data [58]. They found the stone-free rate of obese patients were 84.7%. Hematuria requiring blood transfusion (3.2%) and septicemia (2.1%) were the most common major complications in the obese and morbidly obese groups. The complication rate and length of hospital stay were also similar to those in the non-obese group. In conclusion, they stated that PCNL is a feasible and effective procedure in obese and morbidly obese patients as well as in their non-obese counterparts [58]. Kuntz et al. found no difference in stone-free rates, complications, auxiliary procedure rates, or length of stay among patients stratified by BMI, and proved that “tubeless” PCNL could be performed safely in these individuals [59].

The Clinical Research Office of Endourological Society (CROES) PCNL multicenter global study included 3709 PCNL patients. Fuller et al. found equivalent stone-free rates for normal, overweight, and obese cohorts (approximately 80%), but significantly lower stone-free rates for the morbidly obese group (65.6%) [60]. They also concluded the complication rates were not associated with BMI, while patients with high BMI were likely to have comorbid conditions.

Traditionally, PCNL has been performed in the prone position. This position facilitates posterior access to the collecting system through Brödel’s avascular renal plane without causing significant parenchymal bleeding, peritoneal perforation, or visceral injuries. However, prone PCNL often causes respiratory system problems due to restriction of the patient’s chest movement and surgery may not be sustained in this position. The anesthesiologist and the surgeon generally struggle in this situation in morbid obese patients due to compromised cardiopulmonary status and body weight.

Increased knowledge of renal anatomy and clinical experience on PCNL has encouraged urologists to modify prone positioning in an effort to improve results and overcome these limitations. Recent literature has focused on alternatives in patient positioning, widening patient selection, or new techniques (i.e. tubeless PCNL). Gofrit et al. defined lateral decubitus positioning for PCNL in morbidly obese or kyphotic patients [61]. Valdivia et al. first described PCNL in supine position for a patient at high anesthesiologic risk [62]. After pioneering this technique, several authors have reported their experiences [63–68]. The supine position has several advantages such as decreasing anesthetic requirement, preventing respiratory system-related complications, and allowing a simultaneous retrograde ureteroscopic approach. In addition, urologists are more comfortable adopting a sitting position during stone management. Difficulties in filling of the collecting system against gravity, small surgical field for nephroscopic maneuvers, and the challenges of advancing the needle into the upper calyx are some limitations of supine PCNL.

A randomized prospective study was conducted to compare the outcomes of PCNL in supine and prone position. They found the treatment success of supine and prone PCNL were 77 and 80%, respectively [69]. In a comprehensive review, de la Rosette et al. emphasized that prone PCNL seems to be more feasible, with decreased operative times, similar bleeding rates, and slightly better stone-free rates than supine PCNL [70]. In contrast, Manohar et al. reported that the stone-free rate of supine PCNL in high-risk and morbidly obese patients was 95% [65]. Although the supine position seems to have some advantages for obese and morbidly obese patients and patients with staghorn calculi, the prone position has better outcomes over the supine position.

Percutaneous access into the pelvicalyceal system can be more difficult in obese patients. The authors defined some modifications to cope with these difficulties. Grasso et al. reported a technique of passing a flexible ureteroscope to capture the percutaneously inserted guidewire and establish through-and-through access at the beginning of the procedure [71]. Additionally, morbidly obese patients generally have excessive subcutaneous and fatty tissues with which standard PCNL instruments are too short to reach the stone. Segura described a technique for incising the skin and fat. Incision extends down to the muscular fascia and gains the extra length required to reach the stone [72]. Another option is to dilate the tract and place a nephrostomy tube for 1 week to let the tract mature. In some cases, maturation of the tract allows the kidney to fall back posteriorly closer to the skin, allowing the use of standard nephroscopic instrumentation. Flexible nephroscopy also can be performed through the mature tract, reducing the necessity of rigid nephroscopy [47, 56]. Giblin et al. reported the use of a long Amplatz sheath in combination with a 30 Fr gynecological laparoscope with a working length of 27 cm to treat stones in morbidly obese patients [73]. In addition, favoring the shortest tract for percutaneous access and using a longer device such as an Amplatz sheath longer than 17 cm, a longer nephroscope may facilitate the procedure. Moreover, using a ureteroscope through a percutaneous site may be helpful.

Another technical problem specifically encountered in these patients is migration of the Amplatz sheath beneath the skin or muscle fascia (Figure 71.1). Bugeja et al. described a simple technique, making use of a modified 10 mL syringe barrel to facilitate retrieval of a migrated access sheath in obese patients during PCNL [74]. We recommend using two sutures on the Amplatz sheath to prevent it getting stuck under the skin (Figure 71.2). In this situation, these sutures allow pulling it back out of skin manually or using the open jaws of grasping forceps (Figure 71.3). If all those techniques fail, a Foley catheter can be inserted into the sheath (Figure 71.4). Then, pull out the sheath out after inflating the balloon. Surgeons should pay attention to type of nephrostomy tube used in obese patients. Tube displacement tends to occur more often in morbidly obese patients, so balloon-type catheters or re-entry Malecot catheters may be preferable [75]. Tips and tricks for PCNL in obesity were shown in Box 71.2. A video of standard prone PCNL in an obese patient is available (see Video 71.1).

## Conclusion

Epidemiological studies state that obesity increases the risk of urolithiasis. Several pathophysiological mechanisms cause abnormalities in urine composition in obese patients. These include carbohydrate-induced calciuria, increased protein intake, effects of insulin resistance on renal ammonia metabolism and urine pH, the increased prevalence of gout and hyperuricosuria, or some other unidentified abnormality in renal electrolyte transport.

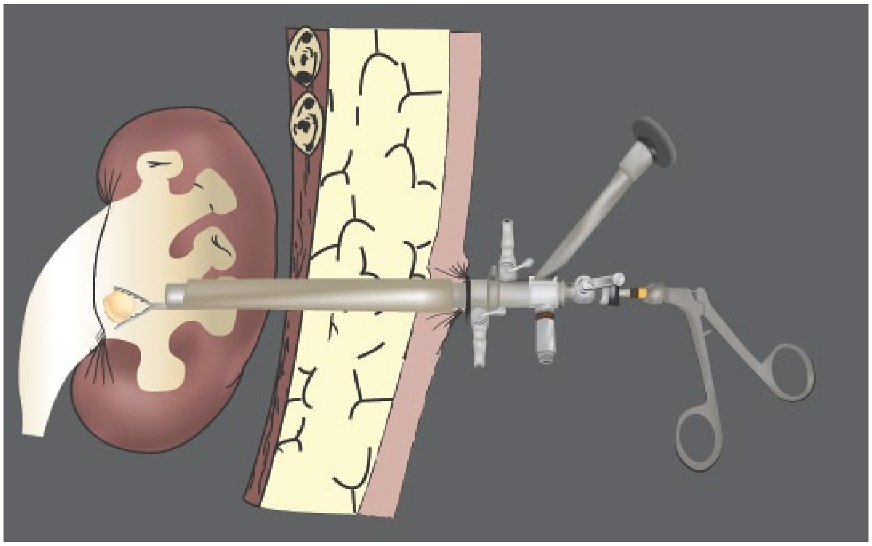

**Figure 71.1** Migration of the Amplatz sheath beneath the skin during PCNL in obese patients.

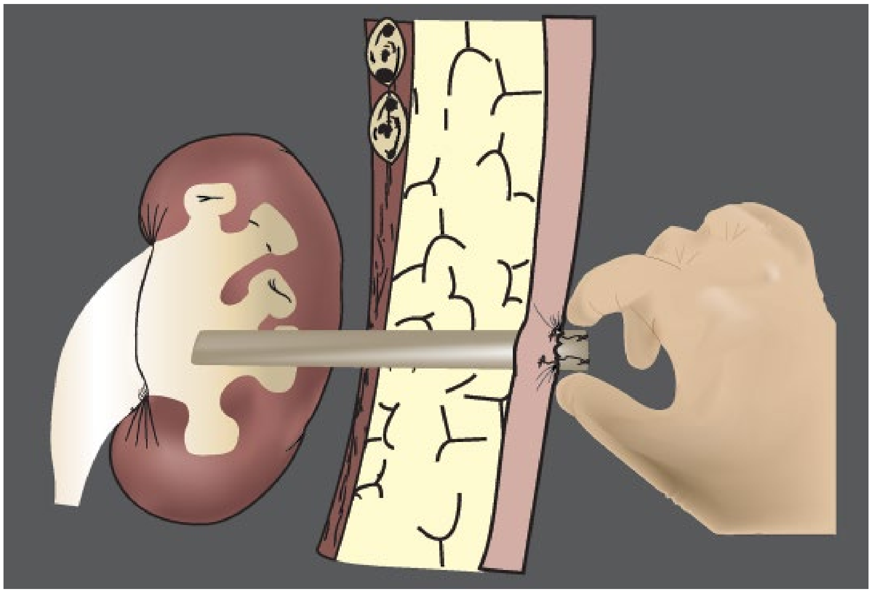

**Figure 71.2** Using two sutures on the Amplatz sheath to prevent it getting stuck under the skin, allowing the surgeon to pull it back out of the skin manually.

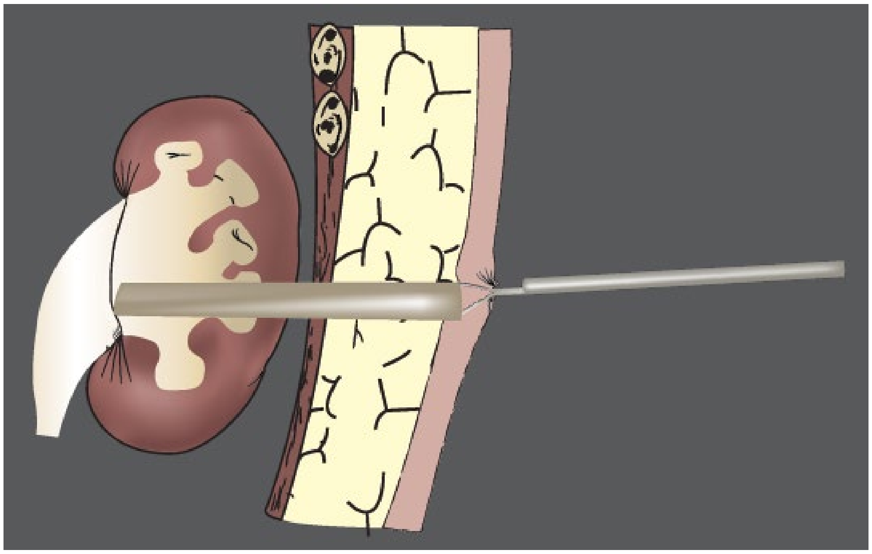

**Figure 71.3** Using the open jaws of grasping forceps to retrieve an Amplatz sheath.

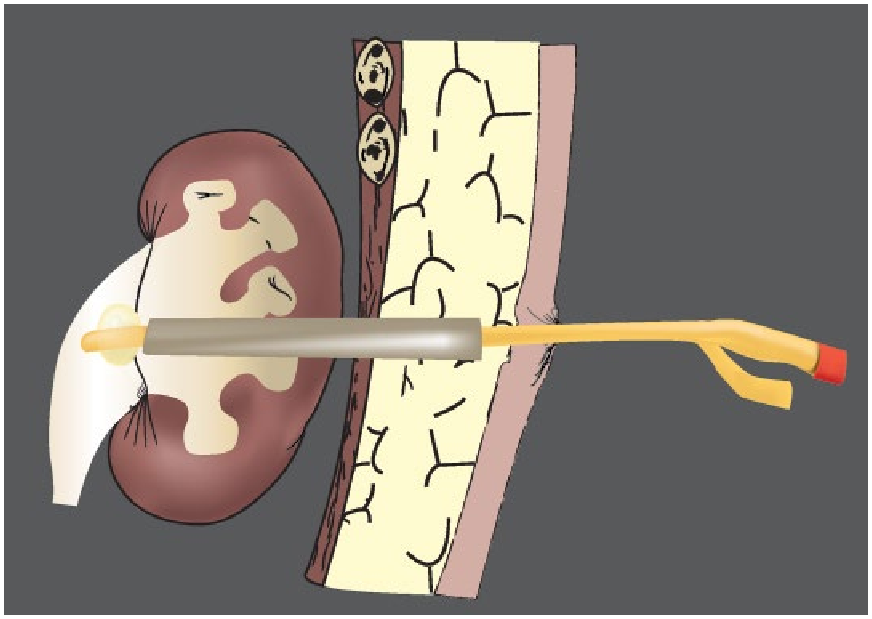

**Figure 71.4** Inserting a Foley catheter into the sheath and trying to pull out it after inflating the balloon.

**Box 71.2 Tips and tricks for percutaneous nephrolithotomy in obese patients.**

Dilate the tract and place a nephrostomy tube for 1 week to let the tract mature.
Use long Amplatz sheaths and nephroscopes.
Favor the shortest possible tract.
Stitch two sutures on the Amplatz sheath.
Balloon-type catheters or re-entry Malecot catheters may be preferable as a nephrostomy tube.
Use supine position in selected patients (to overcome ventilation problems).

Dietary modifications have an important role because metabolic abnormalities are more common in obese stone formers. Medical treatment has been shown to reduce the risk of stone formation. Weight-loss diets and bariatric surgery may cause increased risk of stone disease due to low pH and hyperuricosuria.

Obesity poses a number of problems in the management of stone disease from diagnosis and imaging through to anesthesia and surgery. Comorbidity will be increased and anaesthesia will need special expertise in this group of patients. Extracorporeal SWL has some limitations in morbidly obese patients in terms of exceeding the operating table weight limit and focusing the stone. Several techniques have been described to overcome this limitation in some patients. Flexible URS technology is gaining worldwide acceptance because of high stone clearance rates. PCNL can be modified in obese patients allowing similar outcomes and morbidity to the non-obese patient. To manage obese patients with urolithiasis safely and effectively, the urologist should have enough knowledge about and experience of potential diagnostic and treatment problems, and be aware of the relevant modifications of the standard techniques.

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# Part 3 Cost-effectiveness and Long-term Stenting

## 72

## Cost-effective Strategies for Stone Management

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### Introduction

The economic impact of nephrolithiasis is as important as ever as disease prevalence continues to rise. The most recent National Health and Nutrition Examination Survey (NHANES; 2007–2010) data indicate that kidney stones will affect nearly one in 11 (8.8%) people in the United States, up from 5.2% in 1988–1994 and 3.2% in 1976–1980 [1, 2]. In 2000 it was estimated that spending on treatment of urolithiasis eclipsed US$2 billion, nearly double that spent just 6 years previously ($1.37 billion) [3]. Other estimates suggest an additional cost of urolithiasis treatment of $1.24 billion/year by 2030 if the prevalence of diabetes and obesity continue to rise along with expected population growth [4]. Additionally, as stone disease is most prevalent among working-age individuals, lost work hours contribute a substantial indirect cost [5]. Taken together, these statistics highlight the considerable economic impact of stone disease, for both the individual and society as a whole.

### Assessing and analyzing cost

The reality of limitations on available resources increasingly requires that physicians understand the influence of economics, or, more simply, cost, in terms of how medical care is delivered. Healthcare economics influences the availability of operating room equipment/instruments and disposables, patient access to medication, and in the setting of such limitations physicians must consider not only efficacy but also cost when selecting treatments.

The definition of cost often varies with the perspective of the group that bares the cost, making it anything but consistent to measure. Patient cost refers to out-of-pocket expenses for a given treatment. This can vary significantly by insurance status, which in countries like the United States can be related to employment, with related deductible or co-pays required. Societal cost is another term, one that can have a drastically different meaning depending on the healthcare system. For instance, there is a direct impact on the nation's budget for countries like Canada or the United Kingdom with national healthcare systems, whereas in the United States only the healthcare needs of selected groups are covered by government-funded programs such as Medicaid or Medicare, which ties the healthcare economics to overall budgetary concerns. This is not to mention cost of capital and disposable equipment as well as the level of subsidization, which will undoubtedly vary by country [6]. Common to all countries are indirect economic costs, which are sometimes even harder to quantify. Examples of indirect costs include lost wages secondary to illness and/or treatment.

It is typically much easier to define hospital costs and expenditures; thus, much of the research on healthcare costs are from the hospital's perspective. Despite the fact that hospital costs will undoubtedly vary between centers and countries, many shared concepts exist in this space: the purchase and maintenance costs of capital equipment such as lithotripters, the cost of labor for both physicians and other healthcare workers, medication costs, and services and supplies used during hospitalization.

Not to be overlooked, any discussion involving the financial impact of treatment requires distinguishing the terms "charge" and "cost." Charge includes both the direct cost of an item/service and the indirect cost associated with its supply. Cost most commonly refers to the direct cost to the hospital to provide a service or purchase an item. One big difference is that charge involves a defined profit margin whereas cost does not. The cost-to-charge ratio usually varies between surgical procedures.

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For example, a hospital may choose to collect a larger profit margin from one particular service than another despite a lower actual cost. Overall charge appears on the bill, although its components are often difficult to identify. The most accessible data to researchers are often the hospital billing statement; thus charges are unfortunately frequently used when performing cost analyses. The arbitrary nature of charge data means that it may not consistently relate to actual cost; however, cost data, as previously mentioned, are not without their own inherent flaws.

Lastly, medical decision-making should include outcomes other than cost considerations. Other variables such as stone parameters, patient factors and preferences, available equipment, and surgeon preference may, in many situations, outweigh cost considerations in selecting the best stone treatment option for a given patient.

The remainder of this chapter will discuss cost with respect to diagnosis and treatment of ureteral stones, renal stones, and medical management to prevent stone recurrence.

## Ureteral stones

Treatment of ureteral stones requires consideration of the following factors: diagnosis, determining the need for surgical intervention, and, if surgery is necessary, choosing the optimal surgical treatment. Each decision along the course of treatment has associated cost considerations that impact the overall cost for each treatment strategy.

### Diagnosis

For many years now computed tomography (CT) has been the gold-standard imaging modality for diagnosing ureteral stones. CT scanning has a sensitivity of 98% and a specificity of 95–100% for diagnosing calculi [7, 8] and can also more frequently diagnose the etiology of pain when calculi are not present [7]. In recent years ultrasound (US) has challenged the widespread use of CT due to concerns regarding long-term effects from exposure to ionizing radiation (with CT), CT having a high rate of incidental findings that have the potential to create unnecessary follow-up evaluation, higher cost of CT compared to US, and ease of access to US with more emergency department (ED) physicians obtaining training and certification in point-of-care US. Smith-Bindman et al. performed a multicenter randomized control trial (RCT) to assess the effects of US and CT for suspected nephrolithiasis [9]. Patients who presented to the ED during the daytime (2759) suspected of having nephrolithiasis were randomized to US performed by the ED physician, US performed by a radiologist, or CT. The primary outcome was 30 day incidence of high-risk diagnoses with complications that could be related to missed or delayed diagnosis. The results demonstrated that incidence of high-risk diagnoses with complications did not vary significantly between groups, with the overall rate being low at 0.4%. There were also no significant differences in return ED visits or hospitalizations between the groups. Patients in the US groups were more likely than those in the CT group to undergo additional testing during the initial ED visit (40.7% for ED US, 27% for radiology US, and 5.1% for CT); however, mean total costs for the ED visit was lower by $25 for patients assigned to US than to those assigned to CT ($P < 0.001$). These results suggest that US can be safely used as an initial imaging modality when nephrolithiasis is suspected and leads to a lower overall ED visit cost. This study was not without limitations, especially patient selection prior to randomization. It is also does not address the impact of imaging on subsequent stone treatment or the overall cost of care beyond the ED visit. Thus it is always important to consider clinical context when selecting an imaging study for stones.

### Observation with medical expulsive therapy

In the absence of obstruction and under the correct clinical circumstances, it is reasonable to observe a patient for spontaneous stone passage. Lotan et al. created a decision-tree model in 2002 that showed that if observation did not fail, and no additional financial costs emerged such as ED visits or future surgery, observation was the least costly pathway compared to lithotripsy or ureteroscopy (URS) [10]. However, it is not always easy to predict which patients will pass their stone spontaneously, with studies showing anywhere from 13 to 75% failure of spontaneous passage based on size and location and 17–33% ultimately requiring intervention [11, 12].

The likelihood of spontaneous passage of ureteral calculi depends on ureteral anatomy, stone size, and stone location [11, 13]. Spontaneous passage rates increase the more distal the location of the stone at diagnosis and vary inversely with stone size [13]. Numerous pharmacologic agents have been shown to increase the likelihood of spontaneous passage, thus eliminating the need for surgery or further intervention. These drugs constitute so-called medical expulsive therapy (MET) [14]. The use of MET became widespread based on small RCTs and meta-analyses that demonstrated medication use increased stone passage rates at relatively low cost. However, this conclusion was recently called into question. A large, multicenter placebo-controlled RCT was performed in the United Kingdom in which 1167 patients with ureteral stones ≤10 mm were randomized 1:1:1 to tamsulosin 0.4 mg (alpha-blocker), nifedipine 30 mg (calcium channel blocker), or placebo to determine the proportion of patients who did not require further intervention for stone clearance within 4 weeks of randomization [15]. The study demonstrated that neither tamsulosin nor nifedipine was effective at decreasing the need for further treatment for patients with expectantly managed ureteral stones at 4 weeks, even after adjusting for factors such as stone size and location (Table 72.1). After further extensive sensitivity analyses of the same data it was demonstrated that MET was not cost-effective with either drug, owing to the fact that there was no difference in quality-adjusted life years gained or in cost between the trial groups [16]. Table 72.2 displays these cost data.

Since the primary outcome of the UK multicenter RCT was no need for additional intervention at 4 weeks as opposed to radiographic evidence of stone passage, MET continues to be used to aid passage of distal ureteral stones. Outside of this indication its use has largely fallen out of favor.

## Immediate decompression

If ureteral obstruction is present and infection is suspected/present, immediate decompression of the collecting system is paramount. The two options for decompression include internal ureteral stent placement or percutaneous nephrostomy. Two RCTs have addressed the choice of optimal modality to treat infection in the setting of ureteral obstruction. Pearle et al. randomized 42 patients with suspected infection and obstruction to either ureteral stent or percutaneous nephrostomy, and compared cost and time to clinical improvement [17]. The two modalities were found to be equally effective with respect to the time to normalization of white blood count and/or patient temperature; however, percutaneous nephrostomy was less costly ($1137 vs. $2401, respectively) due to stent placement being performed under general anesthesia. Mokhmalji et al. randomized 40 patients with hydronephrosis due to ureteral calculi both with and without signs of infection to either receive stenting or nephrostomy [18]. The authors concluded that percutaneous nephrostomy was the superior method of decompression due to shorter antibiotic treatment duration (0 vs. 64% requiring antibiotics for longer than 5 days, respectively), reduced time to definitive stone treatment (25 vs. 50% with need for diversion at 2 weeks, respectively), and need for less fluoroscopy (10 vs. 40% with >2 min, respectively). Cost was not evaluated in the later study.

**Table 72.1** Primary outcome results, no need for intervention at 4 weeks.

| | **Odds ratio (95% CI); *P* value** | **Risk difference (95% CI)** |
|---|---|---|
| MET vs. placebo | | |
| Unadjusted | 1.04 (0.77–1.43); 0.76 | 0.8% (−4.1 to 5.7) |
| Adjusted | 1.06 (0.70–1.60); 0.78 | 0.9% (−5.1 to 6.8) |
| Tamsulosin vs. nifedipine | | |
| Unadjusted | 1.07 (0.74–1.53); 0.73 | 1.0% (−4.6 to 6.6) |
| Adjusted | 1.06 (0.73–1.53); 0.77 | 0.8% (−4.5 to 6.1) |
| Tamsulosin vs. placebo | | |
| Unadjusted | 1.08 (0.76–1.56); 0.76 | 1.2% (−4.4 to 6.9) |
| Adjusted | 1.09 (0.67–1.78); 0.73 | 1.3% (−5.7 to 8.3) |
| Nifedipine vs. placebo | | |
| Unadjusted | 1.02 (0.71–1.45); 0.93 | 0.2% (−5.4 to 5.9) |
| Adjusted | 1.03 (0.68–1.56); 0.88 | 0.5% (−5.6 to 6.5) |

CI, confidence interval; MET, medical expulsive therapy.
Unadjusted and adjusted for stone location (lower vs. middle vs. upper ureter), stone size (≤5 vs. >5 mm), and center (random effect).
*Source:* [15]. Reproduced with permission of Elsevier.

In general, percutaneous nephrostomy is highly successful in the setting of hydronephrosis due to the large, dilated collecting system. Failed stent placement due to complete ureteral obstruction, which has been reported to occur in up to 20% of cases, is a definite cost concern in favor of nephrostomy as stent failures will incur the additional cost of salvage [18]; however, currently there are no data comparing costs that take into account failed stent placement.

Presuming equal efficacy for decompression in the acute setting of infection and obstruction, the choice of stent placement versus nephrostomy is commonly based on factors other than cost, such as availability of the interventional radiologist versus the operating room, stone size and/or location, physician, and patient preference.

## Surgical intervention

Surgical intervention must be considered for stones that are unlikely to or have failed to pass based on aforementioned patient and stone characteristics. The mainstays of treatment for ureteral stones are URS and shock-wave lithotripsy (SWL). The 2016 American Urological Association (AUA)/Endourological Society Surgical Management of Stones Guideline [19] states that URS should be offered as first-line therapy for patients with mid or distal ureteral stones who require intervention (those who are not candidates for or who fail MET), as URS is associated with significantly higher stone-free rates in a single procedure than SWL in this setting.

**Table 72.2** Summary of costs.

| | Intervention {*n*, mean [median] (SD)} | | |
|---|---|---|---|
| **Resource** | **Tamsulosin** | **Nifedipine** | **Placebo** |
| Intervention | 383, £4.96 | 383, £6.95 | 384, £0 |
| Analgesics and antibiotics | 383, £4 [£5] (2) | 383, £4 [£5] (2) | 383, £4 [£5] (2) |
| Diagnostic tests[a] | 383, £96 [£120] (40) | 383, £94 [£120] (36) | 383, £98 [£120] (41) |
| Doctor visits | 329, £9 [£0] (30) | 331, £8 [£0] (30) | 325, £6 [£0] (24) |
| Nurse visits | 329, £0.57 [£0] (5) | 330, £0.28 [£0] (2) | 325, £1.14 [£0] (14) |
| Outpatient visits[b] | 377, £73 [£101] (74) | 378, £64 [£101] (67) | 379, £67 [£101] (70) |
| All interventions[c] | 378, £250 [£0] (581) | 379, £267 [£0] (608) | 379, £291 [£0] (632) |
| Excess admission days[d] | 375, £44 [£0] (169) | 377, £62 [£0] (279) | 375, £65 [£0] (298) |
| Total costs[e] | 325, £326 [£228] (494) | 329, £335 [£227] (557) | 323, £367 [£223] (619) |

[a] Includes tests conducted at baseline, 4 weeks and participant-reported tests.
[b] Includes 4 week clinic attendance and participant-reported outpatient visits.
[c] Cost of all interventions as some participants had more than one intervention in a visit.
[d] Consists of duration of admissions reported in the Case Report Form minus the median 1 day admission (urology department) as well as participant admissions.
[e] Estimates based on participants with complete cost data.

*Source:* [16]. Without need for permission by UK Non-commercial government license for public sector information.

Studies comparing URS versus SWL for distal ureteral stones reported the overall success rate for distal ureteral stones to be approximately 92% for URS (2539/2751) compared to 65% for SWL (2260/3488; $P < 0.001$) [20]. SWL is an acceptable alternative for patients who decline URS as it has lesser morbidity and a lower complication rate. The disparity in stone-free rate was greater for mid and distal ureteral stones than proximal ureteral stones, hence the delineation in the guideline.

Costs for URS and SWL differ in great part due to differences in complication rates, stone-free rates, and equipment costs between the two procedures. Furthermore, factors other than cost influence surgical treatment choice, including patient preference, surgeon skill, stone characteristics, and equipment availability. While numerous studies have been performed to assess cost of URS versus SWL, they are plagued by overuse of charge data rather than cost data, lack of uniform inclusion of costs of preoperative evaluation, costs of disposables or other equipment, cost of lost work productivity, and charges associated with complications.

Decision analysis models have been created to eliminate differences across institutions. These models provide theoretical tools for use in comparing the cost of different treatments. Inherent to these models are a series of assumptions about treatment choices, cost, and outcomes. One such model, a decision-tree analysis, was used by Lotan et al. to compare observation, URS, and SWL for the treatment of ureteral stones. The authors went a step further, stratifying patients according to stone location (distal, middle, or proximal ureter). For each location, observation was the least costly strategy, provided the cost of additional treatment and missed work or evaluation (such as ED visits) did not exceed $456 [10]. Comparing the two surgical treatments, SWL was more costly than URS for all ureteral locations by $1750, $1670, or $1440 for patients with distal, middle, and proximal ureteral stones, respectively, principally due to the high cost of purchase and maintenance of a lithotripter. Two-way sensitivity analyses were performed for SWL and URS at different costs and success rates to determine overall cost of treatment according to the model. This analysis enabled the construction of a universally generalizable table, which allows for the identification of the least costly treatment option within a large range of costs ($2000–5000) and success rates (50–95%).

URS continues to be more cost-effective than SWL [21] in managing ureteral stones given high costs of lithotripters compared to ureteroscopes, and the lack of greater efficacy of SWL. Ureteroscope repair costs are balanced out by high annual maintenance costs of the lithotripter.

## Ureteroscope maintenance and repair

Despite evidence in the literature supporting the cost-effectiveness of URS over SWL, maintenance and repair of ureteroscopes can threaten the ability to maintain a URS program. For this reason, numerous studies have assessed the burden of ureteroscope repair on revenue, specifically focusing on frequency of repairs and how accessory tools can affect scope durability.

Tosoian et al. identified maintenance and repair of ureteroscopes as a possible threat to profits and sustainability of the URS program [22]. During the fiscal year of 2013, 190 ureteroscope cases were reviewed during which 20 ureteroscope repairs were required, totaling $115 000 in indirect variable costs. Despite the significant cost of ureteroscope repair, URS cases generated an average profit of $594. The cost of ureteroscope repair per case averaged $605. Furthermore, the study found that for a net loss in revenue, ureteroscope repair would have to exceed $1199 per case.

Carey et al. assessed the rate at which new and previously used ureteroscopes were damaged and required repair [23]. In this study, new ureteroscopes, which at the time included the DUR-8, DUR-8 Elite, and Flex-X 7.5, were used 40–48 times before repair was required. Ureteroscopes that were previously repaired, which included the DUR-8, AUR-7, AUR-9, and 11274AA, required repair after an average of 11.1 cases. The study concluded that disposable costs for refurbished ureteroscopes requiring repair after an average of 11 cases were not as cost-effective when compared to purchasing a new ureteroscope, which can achieve almost triple the number of cases before repair.

In a later review of 501 URS cases at a tertiary care center, an average of 6.9 cases were performed before additional major repairs were needed in already refurbished ureteroscopes. In this study ureteroscopes were sent to an outsourced vendor as opposed to being sent to the original manufacturer [24]. This may account for the reduction in average number of cases before additional major repairs are needed. Nevertheless, costs for refurbished ureteroscopes in this study totaled $129 635.65, which is of concern considering the likelihood of these ureteroscopes frequently needing additional repairs.

Clearly outlined in the studies previously discussed, repair of ureteroscopes is inevitable. However, other research has shown that the durability of ureteroscopes can be maximized with the use of certain accessory instruments during URS and with proper precautions taken during maintenance.

Pietrow and colleagues evaluated the effects that use of ureteral access sheaths, 200 μm holmium laser fibers, and nitinol baskets/graspers have on frequency of ureteroscope repair [25]. A total of 109 URS procedures with four new flexible ureteroscopes were reviewed, in which an average of 27.5 procedures were performed before repair was necessary. Literature prior to the study showed that the average range of cases before necessary repair was 6–15 [26], concluding that the use of specific ureteroscope accessories can prolong durability and decrease necessary repair.

In regards to ureteroscope maintenance, Semins et al. proposed that training house staff in handling ureteroscopes during processing is necessary to minimize unnecessary repair [27]. In their study, a 12 month period where trained nursing staff handled, cleaned, and sterilized ureteroscopes was compared to a prior 12 month period where ureteroscopes were sent to central supply for cleaning and sterilization. Trained nursing staff averaged 28.1 cases before repair was needed. More importantly, no ureteroscope damage could be attributed to cleaning, sterilizing, or storage. For ureteroscopes sent to central supply, an average of 10.8 cases were performed before ureteroscopes needed to be sent out for repair. Reasons for repair included a fractured light cord attachment and fractured eyepiece, damage that may have occurred during processing. These common-sense interventions can be instituted to reduce ureteroscope repair costs.

In 2016, Boston Scientific began advertising the LithoVue, a single-use digital flexible ureteroscope that is intended to eliminate the high costs of ureteroscope reprocessing, sterilization, and repair. A recent study by Proietti et al. compared ureteral and calyceal access, maneuverability, and visualization in the single-use scope and conventional fiber-optic and digital flexible ureteroscopes in cadavers [28]. Subjective review by performing surgeons found the LithoVue to be comparable with regard to visibility and manipulation. If the LithoVue gains popularity in the near future, its expanded use in URS programs could yield more information on cost savings compared to conventional reusable ureteroscopes.

## Post-ureteroscopy imaging

Routine imaging in post-URS patients has been controversial. Although most patients with ureteral obstruction will present with symptoms (flank pain, nausea, vomiting) prompting urological imaging to rule out obstructive pathology, there are a few who can be asymptomatic. In a cohort of 241 patients who underwent URS and had a mean follow-up of 5.4 months with imaging, Weizer et al. identified seven patients who required second URS due to silent obstruction [29]. One patient required permanent hemodialysis making an obvious case for the importance of post-URS imaging to prevent organ loss. Bugg et al. reviewed 77 patients who underwent URS for stone disease and had a mean 7 weeks follow-up with imaging. They found that 96% of patients who did not have preoperative obstruction and no complaints of postoperative pain to have no postoperative obstruction or residual stone disease [30]. A retrospective review of 289 patients who underwent URS with renal US at 1 month follow-up identified 14 patients with asymptomatic hydronephrosis, 21% of whom required further surgery [31].

A recent survey study revealed that only 48% of urologists obtain post-URS imaging. Reasons for not obtaining imaging included cost, radiation exposure, and diagnostic inaccuracy of US [32]. When comparing cost of imaging for all post-URS patients with selective imaging in symptomatic patients, analysis by Sutherland et al. suggests that routine postoperative imaging in all patients imparts a $130 incrementally higher cost per patient compared to selective imaging ($5326 vs. $5196, respectively) [33]. Furthermore, it was projected that medical expenses for patients who do lose a kidney secondary to silent obstruction would still be offset by the cost savings from selective imaging. Assuming a 2% rate of silent obstruction this amounts to $6262 per kidney saved. Table 72.3 shows cost by variable silent obstruction rates and imaging costs [33].

Given the potentially devastating complication of organ loss and greater overall cost of care if this were to transpire, routine post-URS imaging should be considered in all patients.

## Renal stones

In general, the literature regarding cost of treating renal calculi is less robust than that for ureteral calculi. Commonly used treatment modalities for patients with renal calculi are SWL, URS, and percutaneous nephrolithotomy (PCNL).

**Table 72.3** Cost by variable silent obstruction rates and imaging costs.

| | Imaging cost ($) | | Cost difference/ patient ($) | Cost/kidney lost ($)[a] |
|---|---|---|---|---|
| | Routine | Selective | | |
| % Silent obstruction | | | | |
| 0% | 5317 | 5089 | 219 | Not applicable |
| 1% | 5322 | 5149 | 172 | 17 224 |
| 2% | 5326 | 5201 | 125 | 6262 |
| 3% | 5330 | 5252 | 78 | 2608 |
| 4% | 5335 | 5304 | 31 | 781 |
| Imaging cost ($) | | | | |
| $100 | 5162 | 5170 | −8[b] | – |
| $200 | 5264 | 5186 | 78 | – |
| $500 | 5568 | 5234 | 334 | – |
| $800 | 5873 | 5282 | 591 | – |
| $1000 | 6076 | 5314 | 762 | – |

[a] Assuming renal loss in each patient with silent obstruction.
[b] Imaging in all patients is less costly than selective imaging.
*Source:* [33]. Reproduced with permission of Elsevier.

In 2016 the AUA, in conjunction with the Endourological Society, consolidated guidelines for patients with renal stones [34]. The guidelines now stratify patients according to total stone burden and stone location. The recommendation for symptomatic stone(s) in the lower pole ≤10 mm includes SWL or URS, whereas for stone(s) >10 mm SWL should not be offered as first-line therapy. Symptomatic patients with a total non-lower pole renal stone burden ≤20 mm may be offered URS or SWL, as these procedures have acceptable stone-free rates and less morbidity compared to PCNL. Patients with renal stone burden >20 mm should be offered PCNL, and not SWL, as first-line therapy, the rationale being significantly higher stone-free rates for PCNL and the increased need for multiple treatments for SWL in this setting.

### Staghorn stones

PCNL monotherapy is well established as the preferred initial treatment modality for staghorn calculi, due to superior efficiency, efficacy, and cost-effectiveness. One of the first studies to demonstrate cost-effectiveness of PCNL for staghorn calculi was performed by Chandhoke. He developed a "cost-effectiveness index," defined as treatment cost divided by stone-free rate, plus cost of complications multiplied by the complication rate, for different treatments for staghorn calculi. The concept was to demonstrate the average cost of rendering one patient stone free [35]. The model created used complication rates and efficacy from the 1994 AUA Staghorn Calculi Guidelines and charge data from his own institution. He then formulated a decision analysis evaluating PCNL, SWL, and combination therapy (PCNL/SWL). He calculated that PCNL monotherapy was the most cost-effective modality with SWL monotherapy being the least cost-effective. The actual cost-effectiveness index varied by type of secondary treatment used (percutaneous-based vs. URS). Assuming URS as the secondary procedure, cost-effectiveness indices were $36 672 for PCNL monotherapy, $48 095 for combination therapy, and $52 251 for SWL monotherapy.

### Lower pole calyceal stones

New guidelines notwithstanding, optimal management of lower pole renal calyceal calculi continues to be an area of debate. Albala et al., as part of the Lower Pole Stone Study Group, reported the results of a prospective RCT comparing PCNL and SWL for the management of single lower pole stones [36]. They found inferior overall stone-free rates for SWL versus PCNL (37 vs. 95%, respectively), with increasing stone size resulting in more pronounced differences. May and Chandhoke [37] conducted a cost analysis similar to the previously mentioned Chandhoke analysis [36] of staghorn calculi. Despite lower initial success rates, their analysis showed that SWL was more cost-effective than PCNL for treating patients with lower pole stones <2 cm, while PCNL was more cost-effective for stones >2 cm [37].

### Cost factors for PCNL

To better understand the cost component of PCNL, Bagrodia et al. performed a retrospective review of institutional hospital cost data for 179 patients who underwent PCNL [38]. Results of multivariate analysis showed that only stone size was an independent predictor of higher procedural cost. Further analysis by the same authors determined that larger stone burdens tended to increase the need for second-look nephroscopy, which ended up being the main determinant that drove costs higher. Interestingly, factors not predictive of cost were patient age and comorbidities, including obesity.

As PCNL allows for manual removal of all stone material, it has become less acceptable to leave any stone behind. Residual fragments after PCNL, or any stone procedure for that matter, place the patient at risk for future stone events. While the cost of observing versus treating residual fragments after SWL has not been addressed, Raman et al. evaluated the cost-effectiveness of post-PCNL second-look nephroscopy with a decision-tree model [39]. Kaplan–Meier estimates were used to determine the likelihood of a stone-related event. Previously, these authors determined that patients with fragments ≤2 mm had 3 and 5 year survival rates (survival indicating freedom from a stone-related event) of 87 and 65%, respectively, compared to survival rates of 56 and 33%, respectively, for patients with residual fragments >2 mm ($P = 0.04$) [40]. The model demonstrated that for patients with residual fragments ≤4 mm, observation was more cost-effective than second-look flexible nephroscopy, and vice versa for residual fragments >4 mm. Based on these results and the natural history data on residual stones after PCNL, the authors advocate a strategy of second-look nephroscopy for residual fragments >4 mm and observation for ≤2 mm.

### Tubeless PCNL

Tubeless PCNL was first implemented to reduce postoperative pain and shorten convalescence in uncomplicated PCNL procedures. Bellman et al. matched 50 patients by age, gender, and procedure (tubeless vs. standard PCNL), and compared complications, analgesia requirements, length of hospitalization, and cost of treatment between groups [41]. Patients undergoing tubeless PCNL had significantly shorter length of stay (0.6 vs. 4.6 days, $P = 0.0001$) and less morphine sulfate use (11.58 vs. 36.06 mg, $P = 0.001$), both of which contributed to a $2112 cost saving per case (tubeless $1638 vs. standard $3750). Time to return to normal activities was also shorter by nearly 9 days. This result has been replicated in other studies as shown in Table 72.4. The main cost-savings component for tubeless PCNL is shorter hospital stay with associated lesser costs of inpatient care. Since the original description by Bellman et al. tubeless PCNL has been shown to be safe and effective for use in children, simultaneous bilateral procedures, staghorn stones, supracostal access, in obese patients, and in renal units with anatomical anomalies [44]. When a secondary procedure is not needed, tubeless PCNL has a clear cost advantage compared to standard PCNL.

**Table 72.4** Cost data of tubeless versus standard (tubed) PCNL.

| Study | Type of PCNL | Number | Cost (mean ± SD) in US$ |
|---|---|---|---|
| Bellman et al. [41] | Standard | 50 | 3750 |
| | Tubeless with stent | 50 | 1638 |
| Feng et al. [42] | Standard | 10 | 7555 ± 619 |
| | Mini-PCNL | 9 | 6565 ± 300 |
| | Tubeless with stent | 8 | 5562 ± 356 |
| Choi et al. [43] | Standard | 49 | 2846 ± 824 |
| | Totally tubeless | 44 | 2380 ± 549 |

There is a clear need for more prospective studies investigating the cost-effectiveness of PCNL, URS, and SWL for the treatment of renal stones, especially given the expanded use of URS to treat large renal stone burdens and increasing use of tubeless and mini-PCNL. Future research should account for both stone size and stone location for determining relative cost-effectiveness among these treatment modalities.

## Medical evaluation and management

Dietary and medical management aimed at reducing stone recurrence seems desirable given the rising prevalence of stone disease. While dietary modification has been shown to be effective at reducing recurrence and comes at little to no added cost, it does so to a lesser extent than medical therapy, which has been shown to decrease stone recurrence compared to no treatment [45]. When making decisions regarding the need for stone prevention clinicians must weigh the costs of medical therapy along with potential side effects and the effects of lifestyle changes against the idea that not all recurrent stones are symptomatic or require treatment. Numerous authors have investigated the economic consequences of these approaches to better understand these conflicting outcomes.

An early study evaluating medical therapy was performed by Parks and Coe [46]. The authors calculated the cost savings of metabolic evaluation and medical treatment by comparing rates of stone occurrence before and after the initiation of medical therapy. All patients received initial extensive laboratory evaluation and counseling on dietary modifications aimed at minimizing lithogenic risk factors. Select patients were prescribed medications such as allopurinol, potassium citrate, and thiazides based on metabolic background. This approach produced a stone remission rate of 83%. By applying this remission rate, along with estimates of rates of stone passage events, cost of surgical procedures, and need for hospitalization, they estimated that their preventative regimen resulted in an average cost savings of $1162–3162/patient/year. This result is likely an overestimate due to absence of systematic incorporation of dietary measures in the control group, which have been shown to reduce recurrence rates [47–49], until after entry into the stone clinic. It is important to point out there was no true control group in this study, and pretreatment stone incident rates were based on patient recall, which is subject to bias.

Disease aggressiveness certainly plays a role in the decision to initiate dietary and/or medical therapy. Lotan et al. performed a cost analysis (decision-tree modeling) to compare the costs of six different treatment strategies: dietary measures only (conservative), empiric drug therapy (empiric), or directed drug treatment based on simple (SMEM) or comprehensive (CMEM) metabolic evaluation with either all patients undergoing drug treatment (SMEM or CMEM) or only selected patients with diagnosed metabolic abnormalities receiving drugs (modified SMEM and modified CMEM) [50]. The model accounted for accrual of cost for evaluation, drugs, emergency treatment, and surgical treatment for recurrent stones.

Conservative therapy was the most cost-effective strategy for first-time stone formers, resulting in a recurrence rate of one stone episode every 14 years. Conservative therapy was also the least costly approach for recurrent stone formers, but it was associated with an excessively high recurrence rate of 0.3 stones/patient/year. As expected, each of the four drug treatment strategies were all more costly than dietary measures alone ($885–1187 vs. $258/year for the conservative approach), but the benefit was that drug treatment further reduced recurrence rates by 60–86% compared to conservative therapy. Modified SMEM was slightly more costly and marginally more effective than empiric therapy. Modified CMEM had little or no improvement in efficacy over modified or empiric SMEM with equivalent or greater cost. This data can be seen in Table 72.5 [50].

**Table 72.5** Model outcomes by treatment strategy.

| Strategy | Stone formation rate (stones/patient/year) | Model cost ($/year) |
|---|---|---|
| First-time stone formers | | |
| Conservative | 0.070 | 133 |
| Empiric | 0.013 | 966 |
| Modified SMEM | 0.011 | 1085 |
| SMEM | 0.028 | 835 |
| Modified CMEM | 0.009 | 1170 |
| CMEM | 0.015 | 1087 |
| Recurrent stone formers | | |
| Conservative | 0.300 | 258 |
| Empiric | 0.057 | 990 |
| Modified SMEM | 0.048 | 1104 |
| SMEM | 0.120 | 885 |
| Modified CMEM | 0.041 | 1187 |
| CMEM | 0.065 | 1114 |

CMEM, comprehensive metabolic evaluation; SMEM, simple metabolic evaluation. For details about the treatments, see text.
*Source:* [50]. Reproduced with permission of Elsevier.

Significant improvements in recurrence rates (by up to 60%) were observed with treatment strategies in which all patients received medication, regardless of metabolic abnormalities, compared to strategies where only patients with a 24 hour urine abnormality were prescribed drugs. Moreover, since CMEM significantly increased the cost of treatment without added efficacy, the results recommend modified SMEM in which all patients received either drug treatment or empiric therapy. Interestingly, since the least costly approach (conservative therapy) was associated with an disappointingly high recurrence rate, this model demonstrated the benefit of treating every recurrent stone former with medication despite the relatively high drug costs, due to the associated significant reduction in rate of recurrence.

Decision-tree analysis has also been used to evaluate the cost-effectiveness of medical evaluation and treatment strategies across healthcare systems. Lotan et al. created a model using data derived from a published international cost survey to determine the most cost-effective strategy for countries for which data was available [6, 51]. Treatment arms were limited to conservative therapy, empiric treatment, and comprehensive metabolic evaluation with targeted medical therapy for patients with a metabolic abnormality. For first time stone formers, conservative (dietary) therapy alone was the most cost-effective strategy in all 10 countries. The most cost-effective strategy for recurrent stone formers in all countries except the UK was conservative therapy, followed by empiric therapy and then directed therapy. Empiric therapy was the least costly strategy in the UK that enjoyed a low cost of drug therapy (at the time estimated at only $29/patient/year). Similarly, in other countries with relatively low medication costs, like Switzerland and Turkey, there was a marginal cost difference between conservative and empiric therapy; however, empiric therapy produced a significant improvement in efficacy. Two-way sensitivity analysis demonstrated that more than one stone episode per year would be necessary to render empiric therapy cost superior to conservative therapy in all analyzed countries except Switzerland and the United Kingdom. In countries with high drug costs, like the United States, conservative therapy naturally offered an even greater cost advantage. Use of metabolic evaluation to direct medical therapy was not cost-effective in any of the countries studied since the model had little difference in efficacy between empiric and targeted medical therapy.

International cost analyses make it clear that differences in medication costs and surgery across healthcare systems, predominantly based on subsidization, drive differences in the cost-effectiveness of medical management treatment schemes. Drug therapy is favored when medication costs are low. A conservative approach is favored when medication costs are higher, due to relatively less frequent need for surgical treatment of stone recurrences and fixed reimbursement for surgical procedures.

## Conclusion

Delivering high-quality, cost-effective healthcare is more important now than ever before. For stone disease, cost can be scrutinized at every step of care, from diagnosis to decisions about observation versus treatment and subsequent need for medical prevention. While cost-effectiveness is certainly important when considering care in the abstract sense, medical and surgical treatment decisions should always be made with best interests and safety of the patient in mind. This may result in a treatment selected to maximize stone clearance compared to another outcome and in the process result in higher cost. Going forward, new comprehensive cost analyses and cost-effectiveness studies will help clinicians further refine and improve stone treatment.

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# 73

# Long-term Stenting of the Ureter

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## Introduction

Ureteral stents are widely used in urologic clinical practice. The efficacy of ureteral stents in the management of various urologic conditions causing upper urinary tract obstruction has been extensively proven and their contribution to urology remains enormous. Ureteral stents are available in various shapes and made of various materials. Ureteral stents can be divided into polymeric stents (PSs) and metal mesh stents (MSs). PSs are usually composed of polyurethane and silicon-based polymeric biomaterial. A unique category of PSs is the biodegradable stents which are composed of biomaterials such as poly-L-lactide-co-glycolide (PLGA) or L-lactide-glycolic acid copolymer. MSs are based on metal alloys such as MP35N (a nonmagnetic nickel–cobalt–chromium–molybdenum alloy), nickel-cobalt, or stainless steel. Stent designs depend on their use and composition. The most commonly used PS design is the double-pigtail (double-J) design, which is characterized by coil-shaped stent ends. MSs are either MSs identical to those used in coronary vessels or double-J stents composed of metal wire (Resonance, Cook Urological) [1].

Regardless of the stent design and composition, the use of ureteral stents is associated with several complications, which limit their use and necessitates the escalation of research towards the introduction of the "ideal" ureteral stent. The properties of the ideal stent include the ability to hold its position (memory) over time (durometry), easy manipulation of its shape (elasticity), and excellent tensile strength while having elongation capacity. Moreover, placement of the ideal ureteral stent should not be associated with degradation of its structure and function (biodurability) or influence the urothelium (biocompatibility). The ideal stent should be radiopaque and therefore visualized by fluoroscopy [1, 2]. Patient comfort and resistance to bacterial colonization could also be considered important properties of the ideal stent. The ideal stent is currently not available and the problems related to ureteral stenting remain an issue, especially in cases requiring long-term stenting to maintain ureteral patency.

## Indications for ureteral stents

The insertion of stents in the ureter serves several purposes: relief of ureteral obstruction, promotion of ureteral healing, and prevention of possible complications. Postoperative nephrostomies are usually avoided by the use of ureteral stents. The stent acts as a scaffold for the growth of epithelium, promotes ureteral healing by aligning the ureteric wall, and reduces extravasation around the ureter (less inflammation) [3, 4].

The use of ureteral stents for the management of stone disease provides obstruction/hydronephrosis relief, and reduction of colic and infection incidents. Double-pigtail PSs are inserted in lithiasis patients for temporary management of stone-related obstruction [5]. An absolute indication for the management of stone cases by ureteral stenting is the concomitant presence of ureterolithiasis and active infection [6]. The routine use of double-pigtail PSs after shock-wave lithotripsy (SWL) and ureteroscopy (URS) remains questionable [7, 8]. Transplantation-related ureteral strictures are an indication for PS insertion [9–11]. Partial ureteral lacerations are successfully managed by double-pigtail stent placement [12], as are ureteropelvic junction obstructions (UPJOs); this provides relief of flank pain and healing of the repaired site after pyeloplasty and endopyelotomy [4, 11]. PSs are

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also inserted intraoperatively in reconstruction of the ureter to, as mentioned above, provide alignment of the area of the anastomosis and act as scaffold around the ureter, which may eventually facilitate the healing process. Moreover, the presence of a ureteral stent minimizes urine extravasation and reduces ureteral wall edema [4]. Ureteral stents make a significant contribution to the treatment of ureteral fistulas: 85% of such cases are efficiently healed with the use of a PS [12].

Malignant ureteral obstruction remains a challenging field for PSs. Despite the use of PSs as an alternative to nephrostomy tubes in the above cases, extrinsic malignant ureteral obstruction managed by PSs is associated with high failure rates [13, 14]. Two ipsilateral pigtail ureteral stents were proposed as a method to address cases of single stent failure, with various success rates. A double-lumen double-pigtail stent has also been introduced and evaluated with promising results in a pig model [5, 15].

MSs have been used for the management of extrinsic malignant ureteral obstruction in cases where PSs have failed. The reported success rates were high and the method proved to be useful [2]. The use of MSs has expanded in benign cases of ureteroileal anastomotic strictures and UPJO, with promising success rates. In fact, long follow-up of the former indicates that MSs are an alternative to challenging reintervention procedures performed for ureteroileal anastomotic strictures and UPJO [2, 15, 16].

## Complications of ureteral stents

Long-term urinary drainage by ureteral stent insertion is limited by several complications. These complications are related to the design and material of the stent. Major problems of stent use include infection, patient discomfort, encrustation, migration, and hyperplastic reaction.

### Stent syndrome

The “stent syndrome” represents the most common double-pigtail PS-related complication and is characterized by irritative voiding symptoms, flank pain, suprapubic discomfort, and occasional hematuria [4, 5]. Urinary system symptoms may be present in up to 80% of patients with stented ureters. Bladder pain (80%) and incontinence (60%) are important problems for these patients [17]. Insertion technique and stent characteristics are unrelated to these symptoms, while selection of the appropriate stent length is related to reduced morbidity [4, 18, 19]. Voiding symptoms, such as urgency and dysuria, attributed to irritation of the bladder floor by the stent, were significantly more frequent in patients with longer stents [20]. Nevertheless, flank pain was not reduced by the stent length as this symptom is related to vesicoureteric reflux [22]. Softer or tapered lumenless tails have been also proposed for symptoms reduction [21, 22]. Recently, the concept of replacing the distal coil of the double-pigtail PS stent with a 0.3 Fr suture was evaluated. The suture is left in the bladder and facilitates removal. Moreover, the presence of less foreign material in the bladder was theorized to result in reduced lower urinary tract symptoms. A prospective study on 79 patients showed that this design significantly reduced urinary symptom score and pain score [23].

### Stent migration

Several factors affect stent migration including stent length, material, and diameter [24, 25]. Migration of the PSs is associated with stent design. Double-pigtail stents are less prone to migration in comparison to single-pigtail stents. PSs usually migrate towards the kidney rather than towards the bladder [26]. Proximal stent migration is less common with an incidence of 1–4.2%; the management of these cases could represent a greater challenge in comparison to the distal migration [27–29]. When the distal end is below the pelvic brim it could be managed with the use of URS, a stone basket, or a Fogarty catheter with success rates reaching 90% [30]. A percutaneous approach might be more successful than the retrograde retrieval in special circumstances including cases of proximal migration above the pelvic brim, migration above a stricture, or a recent ureteral repair [31]. Covered MSs have been associated with rates of migration up to 81.2% [32].

### Encrustation

Encrustation is a major problem encountered in long-term ureteral stenting with both PSs and MSs. The risk of encrustation is associated with both the stent biomaterial and the patient’s history. Stent encrustation in urolithiasis patients occurs in 9.2% of stents removed in under 6 weeks, 47.5% of stents removed between 6 and 12 weeks, and 76.3% of stents removed after more than 12 weeks [28]. Kawahar et al. observed that stents smaller than 6 Fr were significantly more likely to encrust than those 7 Fr or larger [33]. Other risk factors for stent encrustation include urinary tract infection or urosepsis, history of stone disease, pregnancy, urinary diversions, metabolic or congenital abnormalities, and chronic renal failure [34–36]. Encrustation is always related to biofilm formation despite the absence of evident urinary infection. Biofilm is formed by adhesion of microorganisms on the stent surface and gradual development of a thin film of extracellular matrix around them [37]. Biofilms and urease-producing organisms on a stent surface induce elevation of urinary pH and precipitation of salts such as calcium hydroxyapatite and magnesium ammonium phosphate. The latter process eventually results in struvite and calcium phosphate accumulation [38]. The subsequent encrustation and infection of stents may be responsible for pain, hematuria, and sepsis [39]. The phenomenon of encrustation makes routine exchange of PSs necessary for the prevention of related complications. "Stone formers" are difficult to manage because the exchange intervals are unpredictable [4]. Many algorithms have been proposed for the classification and management of encrusted stents. The suggested management modalities include URS, percutaneous nephrolithotomy, extracorporeal SWL, and cystolitholapaxy [40–42].

Encrustation of MSs is associated with the aperistaltic segment of the stented ureter in conjunction with ureteral peristalsis and urinary stasis, resulting in encrustation of the areas of the MS uncovered by urothelium [43]. An encrustation-resistant MS needs to be made of a biomaterial resistant to bacterial infection and subsequent biofilm formation. In addition, it should be easily covered by endothelial cells and become incorporated into the ureteral wall [44, 45].

### Urothelial hyperplasia

Urothelial hyperplasia is a significant complication of MS insertion in the ureter. Ureteral patency can be compromised by the development of hyperplastic tissue protruding through the stent struts. The hyperplastic tissue is responsible for restenosis of the stented ureter. An experimental study in a porcine model by Desgrandchamps et al. revealed that only one of eight stents was patent 35 days after insertion [45]. It appears that hyperplasia can be prevented by avoiding overextension of the strictured area of the ureter, followed by careful stent implantation. It should be noted that urothelial hyperplasia regresses within 4–6 weeks of MS insertion, resulting in ureteral lumen narrowing [46–50]. Flueckiger et al. suggested that the initial effect (first 1–2 weeks) of the inserted MS in the ureter is reactive swelling of the ureter and not hyperplasia of the urothelium leading to constriction of the ureteral lumen [51]. A characteristic trumpet-like morphologic configuration of the ureter located on the upper extremity of the stent has been described, but is not related to ureteral patency risk [27, 50].

## Polymeric stents

PSs are the most commonly used ureteral stents. A variety of synthetic polymeric compounds has been used for the manufacture of PSs. These materials are based on polyurethane or silicone, such as Silitek (Surgitek, Medical Engineering Corporation, Racine, WI, USA), C-Flex (Cook Urological, Spencer, IN, USA), and Percuflex (Boston Scientific, Natick, MA, USA) [52, 53]. Silitek is a block copolymer based on silicon, while C-Flex is a proprietary silicone with styrene/ethylene/butylene block copolymer. Percuflex is composed of an olephinic block copolymer. In contrast, Tecoflex (Thermedics, Woburn, MA, USA) is a proprietary aliphatic thermoplastic and is not based on silicone or polyurethane. Polyurethane is a relatively cheap material and has the advantage of high versatility, but its biocompatibility is considered poor and it is related to significantly more urothelial ulceration and erosion [54]. The gold standard of biocompatibility is silicone [55]. Although all the polymeric materials described above are susceptible to encrustation, Siliteck, C-Flex, and Tecoflex are less frequently affected by this complication. Moreover, polyurethane, Silitek, and Percuflex provide high tensile strength [53].

### Double-pigtail polymeric stents

The efficiency of retrograde ureteral stenting in obstruction of extrinsic and intrinsic etiology has been reported by Yossepowitch et al. [56]. Extrinsic obstruction was associated with a higher degree of hydronephrosis and the site of obstruction was located more distally. Ureteral stents achieved successful alleviation of the obstruction in 94% and 73% of patients with intrinsic and extrinsic obstruction, respectively. Intrinsic obstruction cases were successfully managed at 3 month follow-up, while extrinsic ureteral obstruction was successfully relieved in only 54.6% of the stents after the same time period. Other investigators reported a success rate for retrograde stenting of intrinsic ureteral obstruction of 88%. The mean follow-up was 25.5 months [57]. The experience gained by the same investigators with the management of extrinsic ureteral obstruction by retrograde stenting revealed success rates of 81, 85, and 100% for malignant, retroperitoneal fibrotic, and benign-etiology obstruction, respectively. Average follow-up was 16 months (range 0.7–98 months) [58].

A large experience with 2431 patients (2685 ureters) who were treated by double-pigtail stent insertion has been recently published [59]. The majority of the indications for ureteral stent insertion were URS or percutaneous lithotripsy, SWL, and open lithotomy. Iatrogenic ureteral injury, extrinsic ureteral obstruction, UPJO, and ureterocysteoneostomy were also managed by double-pigtail stent insertion. Several complications were observed: pain, gross hematuria, bladder irritation, high fever, encrustation, stent migration, and stenosis (or recurrence of stenosis). The mean follow-up period was 31 ± 1.9 days (range 1–123 days). As a result, the insertion of double-J stents for endoscopic and open procedures for upper urinary tract diseases can be considered as a safe and efficient method, at least for up to 4 months.

The long-term outcome of double-pigtail ureteral stenting for the management of extrinsic ureteral obstruction was evaluated by Rosevear et al. in a study including experience accumulated over 9 years [58]. In total, 54 patients (87 ureters) with malignant, retroperitoneal fibrosis, or benign tumors were successfully treated in 81, 85, and 100% of cases, respectively. The mean follow-up period was 16 months (range 0.7–27 months) and mean interval between stent exchanges was 3.6 months. The average interval to stent failure was 4.8 months (range 0.7–27 months).

Quality of life is an important issue for patients with ureteral stents as the stent-related complications may have a significant impact. Joshi et al. investigated the effect of ureteral stents on quality of life and associated urinary symptoms. Storage symptoms, bladder pain, and hematuria were the most common symptoms observed, and at least one symptom was encountered in 80% of patients. In addition, the available questionnaires did not elucidate the entire range of symptomatology [60].

A coil-reinforced polymeric double-pigtail stent has been recently introduced for the treatment of malignant ureteral obstruction. The Silhouette stent (Applied Medical, Rancho Santa Margarita, CA, USA) has been introduced due to the high failure rate of common polymeric ureteral stents [5]. The stent proved to be more resistant to extrinsic compression than the also newly introduced double-J all-metal Resonance [60].

A unique double-pigtail stent is the Zebra (Neo Medical, Bruckmühl, Germany). It is a Teflon-coated lumenless double-pigtail stent, which facilitates passage of residual stone fragments through the ureter. Comparison of Zebra to standard PSs in two stone-forming patients who underwent SWL revealed no ureteral damage, and after 4 and 5 weeks there was no encrustation on the Zebra stent, while the standard PSs were covered by considerable encrustation [61]. Moreover, the material fatigue evaluation of the Zebra stent in an experimental model simulating the movement of the ureter estimated that the stent would not break even if it was left indwelling for 9 months [62].

#### Ipsilateral and dual-lumen double-pigtail polymeric stents

The use of two ipsilateral double-pigtail PSs for the management of extrinsic ureteral obstruction resistant to a single stent insertion was proposed more than a decade ago [63]. This stent configuration has been referred to in the literature as "tandem ureteral stents" (TUS). The first report included five patients who were treated for ureteral obstruction due to ureteral orifice stricture, retroperitoneal fibrosis, and middle-ureter stricture. These patients were managed successfully by the insertion of two ipsilateral 7 Fr ureteral stents, which were exchanged at 3 month intervals until the patients were managed surgically [63]. In a subsequent report, malignant ureteral obstruction in seven patients was managed by the insertion of two ipsilateral stents [64]. Previous insertion of a single double-pigtail stent had been unsuccessful in the management of the obstruction. Three patients died within 3 months of insertion of the two ipsilateral stents, while the remaining four had a mean follow-up of 16 months (38 months maximum). Stents were exchanged every 4–6 months to avoid long-term complications. Recently, Elsamra et al. published the largest series in TUS. TUS insertion or exchange was performed in 187 cases. The latter cases included 39 renal units with malignant ureteral obstruction and 36 units with benign ureteral obstruction. Stent failure was noted in 12.8% of patients with malignant ureteral obstruction and none in the benign ureteral obstruction cases. The investigators proposed that TUS are highly successful in both benign and malignant causes of obstruction [65]

A novel dual-lumen double-pigtail stent composed of two adhered ureteral stents has been evaluated in a porcine model. The stent provides better flow in comparison to a single ureteral stent. The main advantage of this stent is that its insertion requires only one guidewire, whereas insertion of two ipsilateral stents requires two guidewires, making the procedure more cumbersome, Clinical experience with this interesting stent has not been reported since its experimental evaluation [15].

#### Coil-reinforced double-pigtail polymeric ureteral stent, the Silhouette stent

The coil-reinforced double-pigtail PS Silhouette stent is a new metal stent that has been tested *in vitro* studies. These showed that the stent can resist higher compressional forces than the Resonance stent and is less prone to kinking than other stents, and hence has a lower rate of failure [66, 67]. Nevertheless, clinical data are not currently available to evaluate the efficacy of this PS.

### Biodegradable polymeric stents

Biodegradable polymeric materials and stents have been present in urology for over a decade. Their main advantage is that they do not need to be removed. The additional procedure for the extraction of the inserted stent is not necessary, the complications of this procedure are avoided, and the period of discomfort for the patient is shortened [5, 53].

In a porcine model, a PLGA ureteral stent inserted after experimental Acucise™ balloon incision endopyelotomy was shown to provide similar drainage to a standard PS (Applied Medical) in pigs, but its biocompatibility was not favorable compared to a standard stent since the musculature of the incised ureteral segments revealed inferior healing [68].

A biosolvable ureteral stent (TUDS, Boston Scientific) was evaluated in terms of biodegradation and biocompatibility in a porcine model. The stent is designed to maintain ureteral patency for 48 hours, after which it softens and eventually degrades. Histologic results were similar for both a standard hydrogel-coated stent and TUDS [69]. The clinical assessment of the TUDS stent showed safe and efficient drainage. Dissolution took place in 90% of the stents after an average of 8 days. Satisfaction was reported by 89% of the patients treated by TUDS [70].

Tajla et al. evaluated a horn-shaped helical PGLA stent that was used for the postoperative management of antegrade endopyelotomy (cold-knife technique) performed for UPJO [71]. *In vitro* studies estimated the degradation time for the stent to be 2–2.5 months. Percutaneous nephrostomy or stent removal procedures were not deemed necessary for the treated patient. The stent contributed to the reduction of vesicoureteral reflux and postoperative renal infection due to its function as a partial catheter.

Uriprene is a biodegradable copolymer composed of L-glycolic acid, polyethylene glycol, and barium sulfate which has been recently considered for use in PSs. *In vivo* studies in porcine models of uriprene stents showed promising preliminary results. These stents resulted in lower inflammatory response compared to conventional PSs and successfully degraded after 4 weeks [72–74].

Newer biodegradable substances are also under investigation. Novel substances include the tocopherol acetate and the magnesium yttrium biodegradable alloy which seem to possess antibacterial characteristics and have been tested *in vitro* [75–77]. Another biodegradable stent comprising polysaccharides of natural origin was recently described by Barros et al. [78]. These stents contained different blends of gellan gum, gelatin, and alginate and were tested in in artificial urine. The stent degraded between 2 weeks and 2 months with the ability to control degradation rate by altering the ratio of biodegradable materials. The ability to resist bacterial adherence was evaluated and compared to a plastic biostable stent as a control. The comparison showed that there was no difference in bacterial adherence between the described biodegradable stent and the control. In addition, no encrustation was observed within the tested time frame [78]. Considering the above, the field of biodegradable stents seems to be promising for stents that could be used for long-term stenting of the ureter without significant complications. In addition, the need for removal of the stent may be diminished.

## Drug-eluting and drug-coated polymeric stents

Polymeric ureteral stents that are coated with pharmaceutical substances or release drugs from their surface to the surrounding tissue have been introduced and clinically tested. Triclosan is a broad-spectrum antibacterial and antifungal agent that has been reported to inhibit the growth of common bacterial uropathogens *in vitro*, and is thus considered useful for the reduction of urinary tract infection and subsequent encrustation of an indwelling stent [79]. A significant decrease in *Proteus mirabilis* growth and survival was observed in a rabbit experimental model when a triclosan-eluting ureteral stent was inserted in the urinary system (bladder) [80]. In eight patients significantly fewer antibiotics were administered, and there was a slightly higher number of positive urine cultures, but significantly fewer symptomatic infections with long-term use of the triclosan-eluting stent. Bacterial resistance to triclosan was not noted during the 3 month follow-up period [81]. Mendez-Probst et al. evaluted triclosan-eluting stent in a randomized prospective study. They compared the triclosan-eluting stent with a non-eluting stent (control). The triclosan-eluting stent group didn't receive any antibiotics and the control group received 3 days of prophylactic levofloxacin. The results showed no significant differences in the infection rate or encrustation. Nonetheless, triclosan-eluting stents showed to significantly decrease ureteral-stent-related symptoms [82].

Ketorolac-eluting stent was evaluated for its short-term efficacy in a double-blind randomized multi-institutional clinical trial [83]. The 276 patients included were divided into two groups (triclosan stent and conventional stent). There were no significant differences in primary and secondary intervention rates between the two groups. Fewer patients with the ketorolac-eluting stents used pain medication in comparison to the control group.

A heparin-coated double-pigtail ureteral stent was introduced in an attempt to minimize microbial adhesion, biofilm formation, and subsequent encrustation of long-term indwelling stents in the urinary tract. In five patients, a heparin-coated ureteral stent was inserted in one ureter and a conventional double-pigtail stent in the other for a month [84]. The thickness of the encrustations observed by electron microscopy on the heparin-coated stents was significantly less compared to that on the conventional ureteral stents. Moreover, the encrustation on the heparin-coated stents was less uniform and more compact. Two heparin-coated stents were left indwelling in long term (10 and 12 months) and on removal showed no evidence of encrustation and an unchanged heparin layer.

## Metal mesh stents

### Self- and balloon-expandable metal mesh stents

MSs used in the ureter can be divided into four general groups: self-expandable, balloon-expandable, covered, and thermo-expandable shape-memory stents. Covered MSs were introduced in an attempt to minimize tissue ingrowth, which eventually compromises ureteral patency [27]. MSs implanted in the ureter for the management of various malignant and benign diseases are the Wallstent (Microvasive, Natick, MA, USA), Memokath 051 (PNN Medical, Kvistgaard, Denmark), self-expanding polytetrafluoroethylene-covered nitinol stent (Hemobahn Endoprosthesis, W.L. Gore and Associates, Flagstaff, AZ, USA), and the recently introduced all-metal double-pigtail Resonance stent.

The Wallstent is composed of braided biomedical cobalt-based alloy monofilaments and is the most extensively used self-expandable endoprosthesis in the ureter [1]. Inserted in the ureter it appears to represent a safe and effective method for the palliative treatment of malignant ureteral strictures. Benign and malignant ureteral strictures in patients not suitable for surgical treatment were treated with the Wallstent by Pollak et al. [85] One of six stented ureters were patent after 11 months. In two patients, three stents were implanted for the palliative management of malignant disease and were patent up until death (3–5 months after implantation). Ingrowth of hyperplastic and granulation tissue was responsible for the occlusion of all stents inserted for benign strictures, while tumor ingrowth and granulation tissue were observed in malignant cases. Wallstent endoprosthesis proved to be ineffective for long-term drainage in patients with benign ureteroenteric strictures. The mid-term clinical outcome of the Wallstent self-expandable stent implantation for the management of malignant ureteral obstruction was evaluated in 40 patients with 54 malignant ureteral obstructions [49]. Patency was confirmed in 51 of the stented ureters during the mean follow-up period of 10.5 months (range 1–44 months). Almost half of the ureters (49%) required additional procedures to maintain patency. Adequate drainage preventing hydronephrosis was observed in the majority of the cases and major complications were not encountered.

Malignant ureteral strictures due to gynecologic cancer were managed in 14 patients with self-expandable MSs in a report by Barbalias et al., and ureteral obstruction was relieved in all cases [50]. The mean follow-up time was 15 months (range 9–24 months). Tumor ingrowth requiring additional coaxial stent placement and borderline tumor overgrowth was observed in one case each. Urothelial hyperplasia was noted in all stented ureters and additional retrograde insertion of a double-pigtail stent was deemed necessary for a 1 month period. On the proximal edge of the stent, a mild ureteral narrowing was noted (trumpet-like configuration), which did not impact ureteral patency. The trumpet-like configuration was a constant finding during the follow-up period. The authors concluded that the implantation of self-expandable MSs is a safe and effective method for by-passing gynecologic malignant ureteral obstruction.

The combination of self-expandable MSs with coaxial double-pigtail stents was proposed by Hekimoglu et al. [39]. Ten ureters (10 patients) with malignant obstruction were treated with this combination. The double-pigtail stents were removed in seven patients 2 and 3 months after the implantation. Six patients developed hydronephrosis and double-pigtail stents were reinserted. PS exchange was performed at 3 month intervals. The MS lumen was compromised by hyperplastic tissue and encrustation. Nevertheless, this combination was adequate to achieved internal urinary drainage.

Several authors have reported promising results with the management of ureteroileal anastomotic strictures by MS insertion [2, 5, 86–93]. In these reports between one and 18 patients were treated, while the number of treated ureteroileal strictures ranged between one and 24. The mean follow-up period ranged from 6 to 22 months. Stricture recurrence was observed by the majority of the authors. Our group reported long-term results in 18 patients with ureteroileal anastomotic strictures who were managed with MS placement [2]. Mean follow-up was 21 months (range 7–50 months). The technical success rate of stricture crossing and stenting was 100%. Immediate poststenting patency rate was 70.8% (17 of 24 cases), while primary patency rates at 1 and 4 years were 37.8 and 22.7%, respectively. Fifteen stented ureters required secondary interventions. Secondary patency rates were 64.8 and 56.7% at 1 and 4 years, respectively. Periodic exchange of external–internal double-pigtail catheters until the end of the follow-up period was performed in six ureteroileal conduits. Definitive treatment for the ureteroileal strictures was achieved by MSs in more than half of the cases. The remaining cases were managed by regular exchange of double-J catheters in retrograde fashion. Surgical revisions of ureteroileal anastomotic strictures are challenging, while MS implantation provides efficient drainage while preserving the quality of life.

Barbalias et al. have proposed the use of self-expandable MSs for the management of UPJO [16]. MSs were placed in four patients who had previously undergone open pyeloplasty and in whom recurrence of UPJO was diagnosed. The mean follow-up period was 16 months (range 9–24 months). The placement procedure was successful in all cases and patency was confirmed in all four patients. Ingrowth of fibrotic tissue through the stent led to additional coaxial overlapping MS insertion in one patient 2 months after initial stent placement. The results were promising and the authors suggested the performance of more extensive clinical trials in order to validate this application of MSs.

Balloon-expandable stents have not been extensively used in the ureter. Barbalias et al. treated six patients with malignant disease with self-expanding stents and six with balloon-expandable stents [46]. Additional interventions were deemed necessary in three cases due to urothelial hyperplasia, tumor ingrowth, and local recurrence of primary cancer invading the upper end of the ureter. Mean follow-up was 9 months (range 8–16 months).

The Memokath 051 represents a unique type of MS. It is a thermoexpandable shape-memory stent composed of nickel and titanium alloy. It has a tight spiral structure, which prevents urothelial growth [94]. The Memokath 051 softens below 10 °C and regains its shape when reheated to 50 °C. The thermal shape memory feature makes the removal of the stent possible. Kulkarni and Bellamy have used the endoprosthesis for the management of ureteral obstruction of both benign and malignant etiology [95]. Long-term results for the management of malignant and recurrent benign strictures are available: 18 malignant and 10 recurrent benign cases were treated with the Memokath 051 and followed up for a mean of 19.3 months (range 3–35 months). At the end of the follow-up period, 15 stents (13 patients) provided adequate drainage, while eight patients carrying 13 functioning stents had died. Infection and migration were not observed. In general, the Memokath 051 proved to be advantageous over conventional double-J catheters. Moreover, the potential for removal of the stent due its thermal memory was a significant advantage over conventional MSs. This removal capability was not a feature of any other MS until the introduction of the Resonance double-pigtail MS.

Such favorable results with the Memokath 051 were not reported by Klarskov et al., who used it to treat 37 stenosed ureters (33 patients) attributed to both malignant and benign conditions [96]. The mean follow-up period was 14 months (range 3–30 months). Migration towards the bladder was observed in 10 stents and 12 stents malfunctioned, giving a total of 22 nonfunctioning MSs. Encrustation resulted in occlusion of four stents at intervals after stent insertion ranging between 1 and 10 months. In other studies, a need for stent reinsertion or manipulation was reported in 20–25% of patients. Long-term complications of the Memokath 051 were noted to be encrustation in 3–5% and stent migration in 15–18% [97, 98].

Li et al. evaluated a titanium–nickel alloy-based self-expandable stent in benign ureteral strictures over a long mean follow-up period of 92 months (range 12–131 months) [99]. Encountered complications included hyperplastic reaction, infection, and encrustation with stone formation. The investigators concluded that MSs could adequately manage selected cases of ureteral strictures.

Recently, we reported our 10 year experience with metal mesh stenting for the management of malignant ureteral obstruction [100]. Ninety patients (119 ureters) with ureteral obstruction from various pelvic and metastatic tumors were treated with several different types and brands of MSs in an attempt to provide long-term urinary drainage without requiring nephrostomy tubes, and followed up for a mean of 15 months (8–38 months). Hyperplastic reaction and/or tumor ingrowth resulting in tissue protruding through the stent struts and obstructing the stent lumen were the most common problems and were addressed by repeat balloon dilations. Those cases resistant to balloon dilation were managed by insertion of a double-pigtail stent coaxially, which ensured ureteral patency. With primary and secondary patency rates of 51.2 and 62.1% it was concluded that metal mesh stenting of the ureter should be carefully considered for long-term urinary drainage.

## Covered metal mesh stents

Covered MSs were introduced as a solution to the urothelial hyperplasia compromising the patency of conventional MSs. The high migration rate (81.2%) of covered MSs, which could induce renal colic, represented a major problem in clinical application and minimized further use of these stents in the urinary tract. The inability of covered MSs to anchor into the ureteral wall was associated with the coating material and the enhanced ureteral peristalsis [27]. Migration was managed by cystoscopic removal of the migrated covered stents and the coaxial insertion of bare stents.

Recently, an S-shaped covered MS was introduced and underwent comparative evaluation to bare MSs in the canine ureter. The shape of the stent was responsible for the anchoring into the ureteral wall. The stent was covered with polytetrafluoroethylene (PTFE) for prevention of lumen occlusion due to hyperplastic reaction. Both migration and the hyperplastic ureteral obstruction were avoided [101]. In an attempt to reduce urothelial hyperplasia, a study group recently evaluated the additive effects of placing a PS together with a MS in the management of obstructive uropathy in animal model. The PS is inserted through the MS in order to maintain the patency of the latter stent. The one group underwent covered MS and PS placement. The other group received the same MS without a PS. Although there was no significant difference in the development of urothelial hyperplasia, the group with the combination of PS and MS showed a significantly lower degree of obstruction severity due to hyperplasia [102].

Allium (Allium Medical Solutions Ltd, Caesarea, Israel) and the UVENTA (Taewoong Medical Co. Ltd, Gyeonggi-do, South Korea) stents,which are specially designed for the urinary tract-covered MSs, have been recently introduced [103, 104]. The Allium stent is composed of nitinol and is covered with PTFE to avoid tissue ingrowth inside its lumen and early encrustation. It has an intravesical anchor to prevent migration. Moskovitz et al. inserted the Allium stent in 49 cases with a history of malignant disease [103]. Perioperative complications were not observed. Over a mean follow-up time of 21 months (range 1–63 months) stent migration occurred in 14.2% and only one case of stent occlusion was noted. Other investigators evaluated the Allium stent in 12 benign cases of ureteral obstruction and achieved patency in all cases without intraoperative complications [105].

The UVENTA stent has a PTFE-membrane-covered metal mesh to avoid tissue ingrowth and hence prevent hyperplasia related obstruction. The design of the stent also aim to prevent any migration [43]. Kim et al. [104] published their experience with the use of UVENTA stent in 18 patients with malignant ureteral obstruction. During a mean follow up of 7.3 months no obstruction of the stents occurred. In addition, hyperplastic reactions, migration or encrustation were not observed. Chung et al. evaluated UVENTA over a 10 month follow-up period and reported a primary patency rate of 64.8% and a secondary patency rate of 81.7%. Stent failure was predominantly a result of tumor progression at an adjacent ureteral segment. Stent migration was not reported [106]. Another study evaluated the efficacy of the UVENTA in comparison to Memokath 051 [107]. It showed that UVENTA had a higher clinical success rate over the Memokath 051 in benign and malignant obstructions. A multicenter study compared the efficacy of UVENTA with PS insertion for the management of 42 malignant ureteral obstructions. The study showed that the UVENTA was superior to the PSs in terms of technical success and patency [108].

### Double-pigtail metal stents (Resonance)

The Resonance stent was recently introduced as an all-metal double-pigtail stent. It is composed of MP35N alloy in a tight spiral structure. Ureteral obstruction, due to either malignant or benign conditions, can be managed with Resonance [109–112]. Borin et al. were the first to report a case of Resonance stent insertion and successful management of ureteral obstruction due to retroperitoneal fibrosis from metastatic breast cancer [109]. The obstruction had not been controlled by the previous insertion of two 6 Fr double-pigtail PSs. The ureter was patent over a 4 month follow-up period. Resonance stent insertion was used to manage malignant ureteral obstruction without bulky pelvic disease in 15 patients (17 ureters) who were followed up for between 1 week and 8 months [110]. In three patients, the initial stent was exchanged after 6 months, and after 12 months in one patient. Long-term drainage of the obstructed ureters was reported to be efficient and encrustation was minimal. Stents were patent and functioning in four patients who were still alive at the end of the follow-up period. The Resonance stents were not removed in seven patients who died during the follow-up period. Nagele et al. treated 14 patients (18 ureters) with ureteral obstruction of either benign ($n$ = 5) or malignant etiology ($n$ = 13) [111]. Mean follow-up was 8.6 months. Encrustation was evident on two stents. Seven stents were removed due to persistent hematuria, severe dysuria, pain, and inadequate drainage. In an attempt to ensure patient comfort, an appropriate stent length should be selected. In addition, satisfactory drainage under circumstances of extrinsic ureteral obstruction was confirmed by an experimental study. Nevertheless, less overall flow than with a standard PS was noted for the Resonance stent [113].

Our group assessed in a porcine model the effect of SWL or radiotherapy on ureters with an indwelling Resonance stent. The histologic deterioration of pig ureters stented with Resonance was not significant compared to control ureters (standard stents) after SWL or radiotherapy, and ureteral temperature was not detected to be significantly higher for the Resonance ureters [114, 115].

The clinical efficiency of Resonance was evaluated by our group in a clinical trial including 50 patients with malignant or benign ureteral obstructions [112]. All cases of extrinsic obstruction due to malignant factors were managed adequately (25 patients), while patency was observed in 44% of the benign intrinsic obstruction cases (25 patients). The benign case group included patients with lithiasis, ureteroileal obstruction, iatrogenic strictures, or an occluded ureteral MS and who were contraindicated for any surgical or endoscopic procedures due to comorbidities. Further clinical trials are deemed necessary to clarify the indications for the insertion of the Resonance stent. Average overall follow-up was 8.5 months (range 4–14 months), and the mean follow-up for malignant and benign cases was 11 months and 6.8 months, respectively. The removed Resonance stents underwent laboratory investigation to identify the presence of encrustation and the type of deposits. Encrustation was evident in 20% of the extracted stents. The most common location of enscrustation was the edges of the stent. Even stents without evident encrustation were observed to have deposits on scanning electron microscopy (Figures 73.1 and 73.2). Calcium oxalate was the most frequent encrustation deposit.

The clinical application of the Resonance stent in ureteroenteric strictures was reported to be unsuccessful by Garg et al., who inserted it for the management of 10 strictures in 10 patients with ileal conduits [116]. Distant migration was observed in nine cases in a mean of

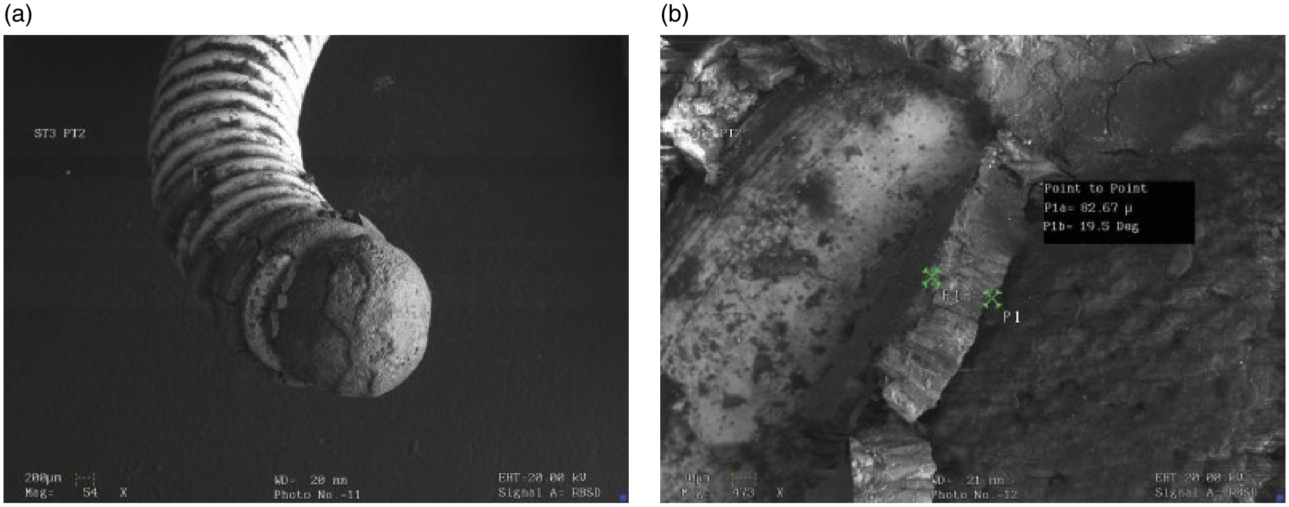

**Figure 73.1** (a) Scanning electron microscopy image obtained from the lower extremity of a Resonance stent that was indwelling for 9 months. Note the encrustation layer, which was barely visible macroscopically. (b) Same Resonance stent at higher magnification. The crystals of the encrustation deposits are visible.

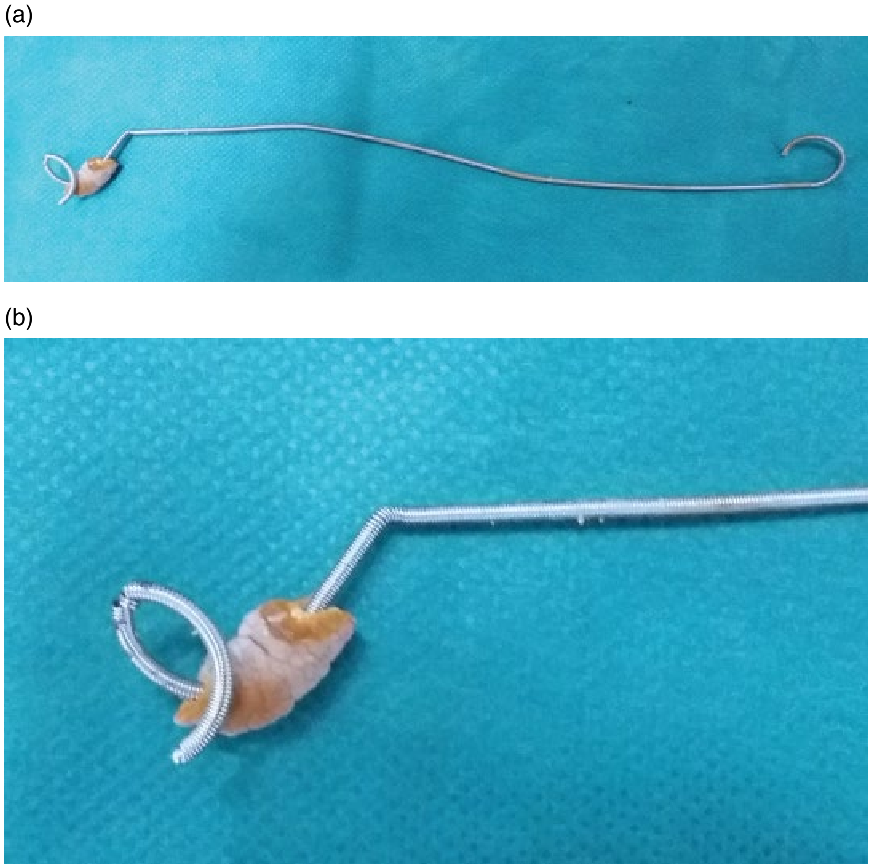

**Figure 73.2** (a) A heavily encrusted Resonance stent with an indwelling time of 12 months. At the exchange of the stent, a large stone burden on the distal coil of the stent was noted. Removal of the stent was impossible and the patient was treated with laser lithotripsy of the stone. Some visible encrustation sites are also present on the stent. (b) The distal coil of the stent with a portion of the initial stone burden on it. Notice that the spiral coil of the stent has been damaged during the laser lithotripsy.

21 days (range 3–60 days). Lopez-Huertas et al. managed 13 patients with benign upper urinary tract ureteral obstructions with the Resonance stent (15 stents) [117]. The majority of the stents provided adequate drainage and 12 patients were efficiently managed. The stents were removed in three patients who showed voiding symptoms such as hematuria. The remaining patients had their stents exchanged after a mean follow-up of 11.6 months. The investigators also conducted a cost-effectiveness analysis and reported a significant cost reduction in favor of the Resonance stent. More recently, Kadlec et al. published their 5-year experience with the Resonance stent [118]. A total of 139 metallic stents were placed in 47 patients, including 27 (57%) with malignant and 20 (43%) with a benign etiology ureteral obstruction. A failure rate of 28% was reported due to pain, stent migration, progressive renal insufficiency, encrustation, recurrent urinary tract infection, progressive hydronephrosis, hematuria, or lower urinary tract symptoms. The failure rates were similar for malignant and benign cases. Nonetheless, Resonance stents were successful in managing benign and malignant ureteral obstruction in the majority of the patients in their series, and a subset of patients in each group continued to do well for more than 3 years' overall follow-up [118]. See Video 73.1 .

### Drug-eluting metal mesh stents

Interventional cardiology has gained significant experience with drug-eluting MSs (DESs). In fact, the DESs represent the most commonly used stents in this specialty. The concept of DESs is to minimize or even eliminate the reaction of the coronary tissue to the stent, which is responsible for platelet adhesion (activation of coagulation cascade) and neointimal hyperplasia [119]. The use of DESs in the ureter is currently limited to experimental animal studies, which have demonstrated reduction of ureteral tissue hyperplasia. Our group has investigated the effect of the paclitaxel-eluting stent in porcine ureters (10 pigs in total). A DES was inserted in one ureter and a bare MS in the other ureter of each animal. Over a follow-up period of 21 days, the majority of MSs were occluded and the remaining MSs were stenosed by hyperplastic reaction, while all the DESs were patent [119]. Later, we evaluated zotarolimus-eluting MSs (Endeavor; Medtronics, Minneapolis, MN, USA) in porcine and rabbit models. Three weeks after placement we observed less hyperplastic reaction in the DESs in comparison to the bare MSs, which were used as the control in the contralateral ureter of the same animals [120] (Figure 73.3). The effectiveness of DESs in these animal models is promising for their clinical application.

## Outcome of long-term ureteral stenting

The long-term use of ureteral stents currently represents a challenge for biomaterial science, pharmacology, and urologic research [1]. The frequent exchange of double-pigtail PSs is accepted clinical practice, with complications addressed by pharmaceutical therapy or additional interventions, and these stents should not be expected to be in place for longer than a few months. Clinical experience with biodegradable PSs remains limited and further refinement is necessary for the wide acceptance of these stents [1]. The development of newer biodegradable materials could lead to the introduction of new biodegradable stents. Drug-eluting and drug-coated PSs are rapidly evolving and their first clinical application appears promising. Moreover, the potential of the latter stent type could be increased with the countless pharmaceutical substances that could be used on their surfaces.

MSs are a completely different category of stent and are used significantly less frequently in urologic practice. Nevertheless, experience has accumulated over the years. Long-term results have proved to be poor despite the initial promising outcome [1, 99]. Thus, patients

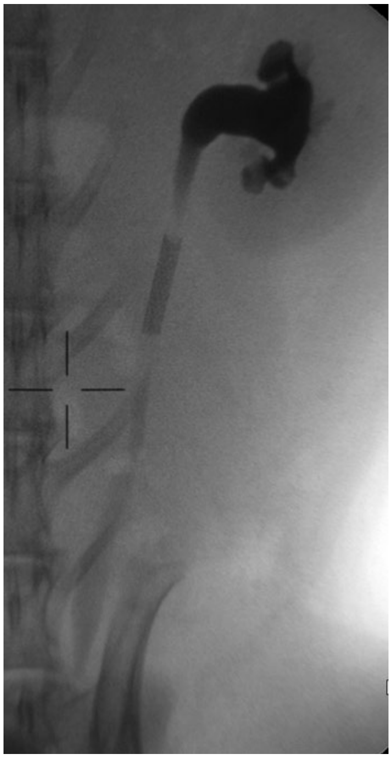

**Figure 73.3** Fluoroscopic image of a zotarolimus metal stent a week after its insertion in a rabbit ureter. Note the trumpet-like configuration on the ureter segment located at the upper extremity of the stent. The configuration did not influence the patency of the stent. Note the lack of hyperplastic reaction in the lumen of the stent.

should be carefully selected for stenting with an MS. The first MS with a double-pigtail design provides adequate drainage in cases of PS failure and has shown excellent results in long-term management of malignant ureteral obstruction. In contrast, benign cases have been associated with unfavorable results. Further clinical investigations will elucidate the true efficacy and indications for these stent [111]. DESs are the next step in the evolution of metal stenting in the ureter. These stents have a tremendous impact in interventional cardiology. Their use to overcome the difficulties encountered during metal stenting is expected. Available experimental reports are rare but still promising regarding the possible outcome in clinical trials.

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# Smith's Textbook of Endourology

# Smith's Textbook of Endourology

Fourth Edition

**VOLUME 2**

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# Foreword

"Endourology" was the 1978 branding brainchild of Elwin Fraley, Arthur Smith, and Paul Lange.[1] Most felt that the Minnesota cold had finally gone beyond their woolen headgear to create a "brain freeze" of monumental proportions. Fast forward nearly 40 years and, today, endourology has become urology. Diagnostically, from the urethral meatus to the uppermost renal calyx, the entire urogenital tract can be revealed in great detail using both endoscopic and sophisticated imaging technologies. Therapeutically, urologists of talent, innovation, and persistence have supplanted standard incisional access with an endoscopic, image-guided, or combined approach.

If you are reading this Foreword then you are reading a book that contains every aspect of urology and how it is benefited by a minimally invasive (i.e. percutaneous, ureteroscopic, laparoscopic, robotic) or noninvasive image-guided (i.e. shock-wave lithotripsy, focal therapy) approach. The authors are an international *Who's Who* of experts in endourology. The content ranges from basic to futuristic endourology. In 166 chapters, the latest advances in antegrade and retrograde endoscopic nephrostomy, laparoendoscopic single-site surgery, and robotic procedures as well the newest image-guided therapies are clearly detailed and illustrated both in photographs and often by instructional video demonstrations.

A wise mentor[2] once advised me: "You are only as good as tomorrow." That single sentence should haunt each of us as we arise every morning to provide relief to those who suffer. To that end, we must seek methods to relieve suffering rather than cause it, to heal without harming, to cure without substituting one malady for another. Endourology empowers each of us to provide all individuals seeking our care with a kinder, gentler solution to their urological problems. In the first part of the twentieth century, Sir William Osler opined: "Diseases that harm require treatments that harm less."[3] A century later, his dictum has been largely realized in the practice of endourology.

My heartfelt congratulations go out to Drs Smith, Badlani, Kavoussi, Preminger, and Rastinehad, who have provided a comprehensive guide of immense value to me, to you, and to all of our patients. Read *Smith's Textbook of Endourology* well, apply its principles earnestly, and, if opportunity presents, seek to further innovate and build on its contents. The text is not an end in and of itself; rather, it is another paver in the surgical journey in which each of us plays a role — using techniques borne of today's technology to proceed to further reduce the burden of the "surgical" cure we are obligated to apply.

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## Notes

[1] Smith AD, Lange PH, and Fraley EE. Letter to the Editor: applications of percutaneous nephrostomy. New challenges and opportunities in endo-urology. *J Urol* 1979;121:382.

[2] Arthur D. Smith.

[3] Attributed to Sir William Osler (1849–1919).

# Preface

The cover of this textbook synthesizes the concepts of endourology. In order to perform endoscopic surgery one needs access to the organ and various forms of energy to facilitate access, control bleeding, and obliterate tissues. These goals can only be accomplished with appropriate devices. Fortunately, evolving technology allows the manufacture of improved devices. It is essential for endourologists to keep abreast of these advances. The fourth edition of this book accomplishes this with an update of the existing chapters by the original authors or complete revision by new authors.

In 1978 the concept of endourology was launched. It was defined as closed, controlled manipulation within the urinary tract. The word "closed" was used to indicate either a minimal incision or no incision at all and the control was achieved either endoscopically or by noninvasive imaging. Until then, residents had been taught that the only way to have good exposure was through a large incision. Now the ultimate goal is good exposure with no incision at all. This is achieved by utilizing a combination of endoscopy and the new modalities of imaging. There are now relatively few accepted open urological procedures and this has had the gratifying result of a dramatic decrease in the morbidity of our patients undergoing treatment.

In this era of fewer working hours for residents, the amount of time that the residents spend in the operating room has decreased dramatically and the necessary skills have to be taught using a combination of additional educational modalities. In addition to books and journals, there are an abundance of videos on surgical techniques, animal laboratories, teaching models, and virtual reality simulators. Fortunately, endourologic techniques are uniquely suited to these modalities and the student can become quite adept by using them before being instructed in the operating room.

As the technology has evolved, courses have been organized by the Endourology Society to train not only the residents and fellows, but also the practicing urologist so that their "learning curve" can be accelerated, and they can then use these techniques with the required expertise. In addition, the Endourology Society has developed the *Journal of Endourology* and the *Journal of Endourology Case Reports* to update urologists on the latest technology. The *Journal of Endourology* allows the members access the *Journal of Videourology* which features videos of new and established techniques on the computer or tablet.

This textbook consists of two volumes. Volume 1 is on stones of the upper tract. Volume 2 is on robotic and laparoscopic surgery and image-guided diagnostic and therapeutic techniques together with minimally invasive therapy of the lower urinary tract. Volume 1 consists of five sections. Section 1 discusses the basic principles. Section 2 is devoted to percutaneous renal surgery. Section 3 discusses the intricacies of ureteroscopy. Section 4 is on shock-wave lithotripsy. We are cognizant of the fact that there is no single modality for the treatment of stones and hence Section 5 describes the management of the patient with various stone-related problems in a composite format.

Volume 2 covers robotic and laparoscopic surgery. At present, there is very little difference between the techniques and that which there is is primarily related to technical experience, availability of the robot, and financial considerations. Sections 6 and 7 discuss image-guided diagnostics and therapeutics. This is an important addition to our *Textbook of Endourology*, as it is an essential component of the armamentarium of the practicing urologist, particularly as we move into the era of "no incision." If the procedures described in this section are not performed by urologists, then they will be taken over by radiologists. This in turn will result in the loss of continuity of care of our patients.

I would like to thank each of the contributors for the many hours they have devoted to writing, illustrating, and creating videos for their chapters. Hopefully, they will be as delighted with the results as the editors and publishers of this textbook. I am also deeply indebted to my co-editors, who have reviewed, edited, and re-reviewed chapters countless times. Thanks to their families as well, as the time spent on the book could have been devoted to them. The staff at Wiley Blackwell and the project manager Mirjana Misina have been highly professional and encouraging. When one deals with a large organization, it is reassuring to know that as a book bounces from one stage to the next there has been a "continuity of care throughout the operation." They are a great team and we appreciate all the help we received from them.

Finally, I would like to thank my wife, Kay, who inspired me to edit this fourth edition and has repeatedly helped me with this and countless other projects throughout my academic career. If I am regarded as the "father" of endourology, she is unquestionably the "mother" who has helped to nurture this field of urology.

June 2018 *Arthur D. Smith*

# About the Companion Website

This book is accompanied by a companion website:

**www.wiley.com/go/smith/textbookofendourology**

The website includes:

- Over 100 videos showing procedures as described in the book
- PowerPoints of all figures from the book for downloading

All videos are referenced in the text where you see this icon: 👁

# SECTION 6

# Laparoscopy and Robotic Surgery

# Part 1 General Principles

## 74

## New Surgical Robotics

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### Single-site robots

Robotic technology was first reported to have been incorporated with single-site surgery in 2011 using the da Vinci Single-Site© surgical platform (Intuitive Surgical, Sunnyvale, CA, USA), which aimed to improve the technical limitations of laparoscopic single-site surgery including external clashes, poor visualization of critical structures, and surgeon fatigue [1]. In 2015 a systematic review showed that the da Vinci surgical platform had proven to be a valuable asset in single-site surgery, owing to the combination of robot use and dedicated single incision; the main reported limitation was the lack of an EndoWrist [2].

The da Vinci single port (SP) is Intuitive Surgical's new surgical platform for single-incision surgery, and gained US Food and Drug Administration approval in early 2014. It is composed of a three-dimensional (3D) high-definition (HD) camera and three fully articulated instruments, all in a 25 mm port. The fully wristed EndoWrist SP instruments have two more degrees of freedom than the da Vinci Single-Site instruments. The surgeon controls the instruments and the endoscope while seated at the da Vinci Surgical System console. Intuitive Surgical plans not to release it onto the market until it has been made fully compatible with the latest da Vinci Xi robot. This will require product refinements, supply chain optimization, and additional regulatory clearances [3]. The system is designed for urologic minimally invasive procedures that are already performed via a single incision. Major urologic procedures have been successfully completed using the da Vinci SP without conversions [4].

A second single-port system is called Single Port Orifice Robotic Technology (SPORT™; Titan Medical, Toronto, ON, Canada; see Figures 74.1 and 74.2). The system utilizes a 25 mm single-access port which contains a 3D HD vision system and interactive multi-articulating instruments, and a highly ergonomic surgeon workstation that provides the surgeon with an interface to the robotic platform, as well as a 3D endoscopic view inside the patient's body cavity during minimal invasive surgical procedures. It is expected to be commercially available in late 2019. The first targets of the SPORT system are gynecologic, gastrointestinal, and urologic procedures [5].

In December 2015 the building of the first SPORT Surgical Systems to include both the work station and the patient cart was announced. These will undergo extensive testing as a part of engineering verification (EV). These two EV systems will be tested to measure performance in relation to design specifications and to measure compliance with regulatory guidelines. These EV systems were precursors of the systems that were made ready in early 2016 for the first in-human trials. The multi-articulating, interactive, snake-like instruments are designed to couple with removable and sterile single-patient-use robotic tools that provide first-use quality in every case and eliminate the need for instrument reprocessing. The use of reposable (re-usable for a specific number of uses) robotic instruments and single-patient-use tools allows more use cases for each robotic instrument, thus reducing the per-case cost. The robotic platform is also designed to include a mast, a boom, and wheels for optimal configurability for a variety of surgical indications and the ability to be maneuvered around the operating room and surgical centers where applicable [5].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

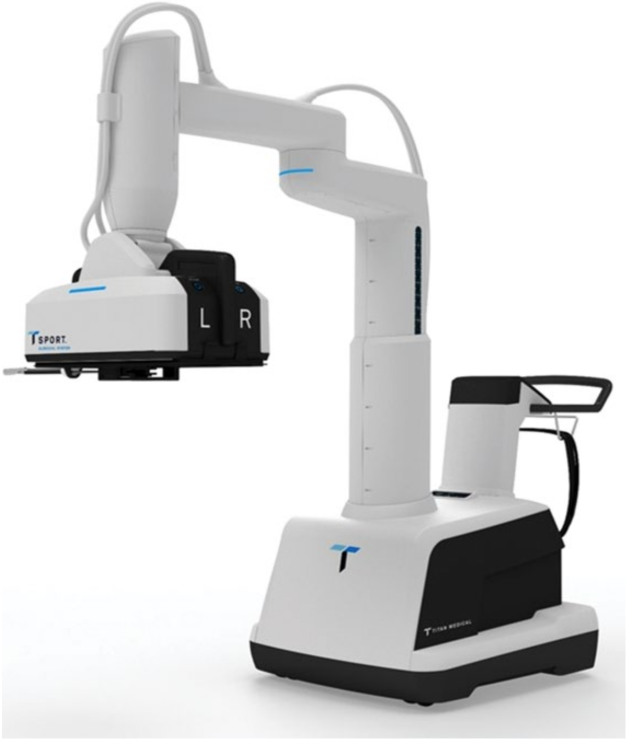

**Figure 74.1** The patient cart of the SPORT system. *Source:* Titan Medical, Inc., Canada. Reproduced with permission of Titan Medical, Inc.

Another single-port robot is the SurgiBot (TransEnterix, Morrisville, NC, USA; Figures 74.3 and 74.4). It enhances laparoscopic surgery through robotic assistance, while allowing the surgeon to remain in the sterile field, at the patient's side. It is composed of an integrated 3D HD camera for HD images with depth perception and delivers up to three articulating instruments through a single incision. One of its main advantages is that it has minimal reliance on surgical assistants and staff [6].

The Avicenna roboflex flexible uretroscopy robot (Elmed, Turkey) consists of a console and a manipulator. The hand piece of the scope is locked to the robotic arm. The surgeon at the console can control two joysticks to manipulate the rotation, deflection, and in-and-out movements of the endoscope. A central wheel enables fine tuning of deflection inside the collection system. The surgeon can rotate robotically 440°. This minimizes the torsion risk of the endoscope. Laser fiber can be remotely moved in and out which is very helpful for providing a suitable distance between the stone and the tip of the laser fiber. Software prevents firing of the laser shot when the laser tip is very close to the endoscope to prevent damage. The integrated water pump can also be adjusted remotely. In this way it is possible to treat a stone with a minimal flow rate and to provide low-pressure lithotripsy [7]. A human trail on 81 patients showed efficacy, safety, and a significant improvement in ergonomics [8].

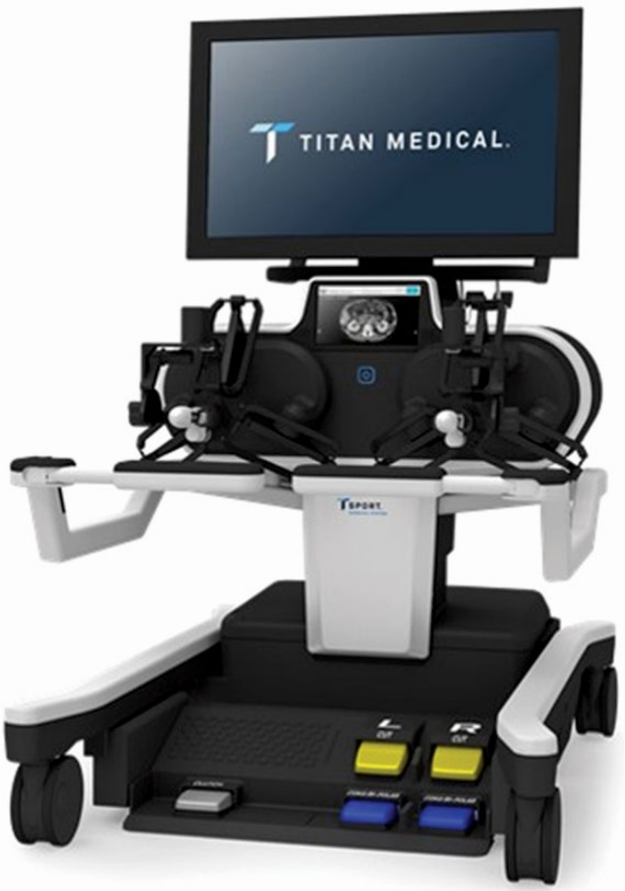

**Figure 74.2** The surgeon console of the SPORT system. *Source:* Titan Medical, Inc., Canada. Reproduced with permission of Titan Medical, Inc.

The last robot reaching the market soon and utilizing a single port (natural orifice transluminal endoscopic surgery, or NOTES) is the Flex (Medrobotics Corp., Raynham, MA, USA). It utilizes a highly articulated multilinked scope that can be steered along nonlinear, circuitous paths in a way that is not possible with traditional, straight scopes. The maneuverability of the scope is derived from its numerous mechanical linkages with concentric mechanisms. This enables surgeons to perform minimally invasive procedures in places that were previously difficult or impossible to reach [9]. Surgeons can operate through a single access site and direct the scope to the surgical target. Once positioned, the scope can become rigid, forming a stable surgical platform from which the surgeon can pass two flexible surgical instruments. The system includes on-board HD visualization to give surgeons a clear view of the navigation path and surgical site [9].

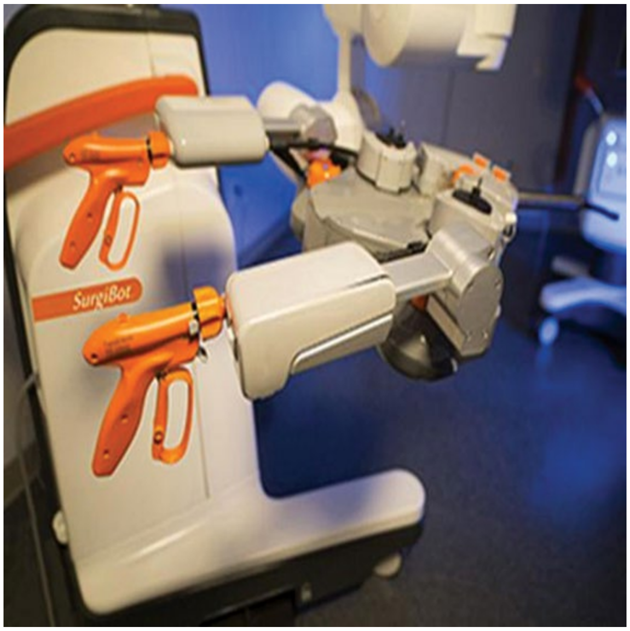

**Figure 74.3** The SurgiBot hand piece. *Source:* TransEnterix, USA. Reproduced with permission of TransEnterix, USA.

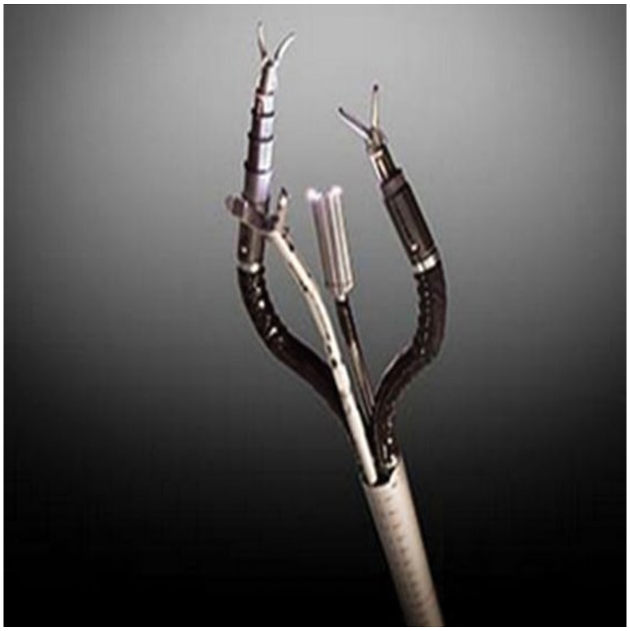

**Figure 74.4** The SurgiBot patient-side single port. *Source:* TransEnterix, USA. Reproduced with permission of TransEnterix, USA.

Approval was achieved in Europe in 2014, and aim for a first limited commercial launch on selected European markets [10].

## Multiple-site robots

Figure 74.5 shows the ALF-X system, developed by Sofar S.p.A. (Trezzano Rosa, Milan, Italy) and currently owned by TransEnterix. It is a multiport remotely operated robotic system that utilizes a remote control station and robotic arms. Three system features include haptic feedback, an eye-tracking system, and reusable endoscopic instruments. Haptic feedback allows the surgeon to "feel" the force employed through the instruments and the natural resistance of the tissues. The eye-tracking system allows accurate movement of the 3D endoscope. The first targets of the system were gynecology, urology, and thoracic surgery procedures. The ALF-X gained CE market approval in 2011 [11].

ALF-X has a comprehensive set of multipurpose tools that can be sterilized, which allows a significant cost reduction in the field of robotic surgery and makes it more accessible. Another feature is that there is no need to dock the robotic arm to a trocar, which decreases the operative time and facilitates easy patient repositioning intraoperatively. The console handpiece is similar to that for laparoscopic instruments which facilitates easy familiarization and a shorter learning curve.

The system can handle up to four arms and each manipulating arm is carried by its own patient side cart. The tools are introduced through standard 5 mm laparoscopy ports, making it possible to maneuver both laparoscopic and robotic instruments simultaneously. Since the beginning of clinical trials in 2013, a few studies have shown safety and feasibility in the treatment of various gynecological conditions [12–14].

The second multiport system is Surgenius (Surgica Robotica S.p.A., Trieste, Italy). The system consists of six degrees of freedom (DOF) arms, equipped with six DOF tip-force sensors, providing haptic feedback to the operator. The robotic arms can be positioned freely around the surgical bed, as they are independent of each other. They can be equipped with Surgica Robotica's high-dexterity instruments, which allow great precision and wide maneuverability. The surgical system can be configured with the number of robotic arms that is necessary for the intervention, from one single arm to as many arms as can fit around the surgical bed. Surgenius gained CE market approval in 2012 [15].

The Bitrack system by Rob Surgical Systems S.L. (Catalonia, Spain) was designed to cover current limitations in laparoscopic surgery, like for example a system's lack of flexibility and modularity, and the set-up time. The prototype for the robot was finished in early 2015 and moved into the clinical validation phase to gain approval for the European and US markets. Rob Surgical Systems expects to obtain European approval in 2018 [16, 17].

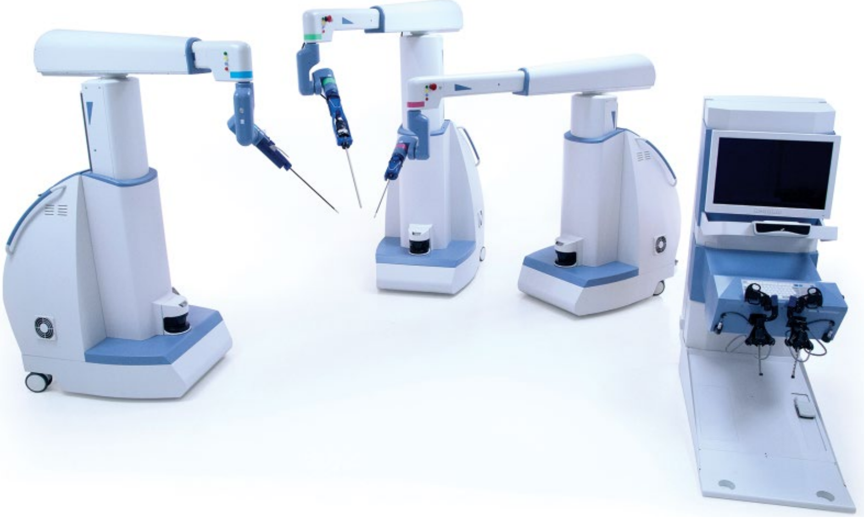

**Figure 74.5** The ALF-X. *Source:* TransEnterix, USA. Reproduced with permission of TransEnterix, USA.

The Chinese surgical robotic system Micro Hand S was invented at Tianjin University. It has three main technical advantages. The first is multi-DOF wire transmission, making instruments for minimally invasive surgery with the benefits of no coupled motion, fixation, skid resistance, and anti-looseness more conducive to maintaining accuracy. Second is a reconfigurable layout and implementation of a "slave hand," making the robot "arms" lighter and more adaptable to the needs of the operation. The third is homogeneous control model building technology for hand–eye–instrument motion consistency in the 3D visual environment. The first clinical trials were done in March 2014 and showed the safety and effectiveness of the Micro Hand S in performing robot-assisted minimally invasive surgery [18].

The NeuroArm is a magnetic resonance imaging (MRI)-compatible image-guided computer-assisted device specifically designed for neurosurgery. In 2008 it made history when the robotic system was used to operate on a human patient at the Faculty of Medicine, University of Calgary, Canada. This landmark operation was the first time a robot was used to perform image-guided neurosurgery [19].

End-effectors are equipped with 3D force sensors, providing a sense of touch. The surgeon, seated at the workstation, controls the robot using force feedback hand controllers. The workstation recreates the sight and sensation of microsurgery by displaying the surgical site and 3D MRI displays, with superimposed tools. NeuroArm enables remote manipulation of surgical tools from a control room adjacent to the surgical suite. It was designed to function within the environment of 1.5 and 3.0 tesla intraoperative MRI systems. As NeuroArm is MR-compatible, and stereotaxy can be performed inside the bore of the magnet with near-real-time image guidance. NeuroArm possesses the dexterity to perform microsurgery outside of the MRI system [19].

The DLR Institute of Robotics and Mechatronics in Germany has developed MIRO, a second generation of robot arms for surgical applications. With a low weight of 10 kg and dimensions similar to those of the human arm, the MIRO robot can assist the surgeon directly at the operating table where space is tight. The scope of applications of this robot arm ranges from guiding a laser unit for the precise separation of bone tissue in orthopedics to setting holes for bone screws, robot-assisted endoscope guidance, and minimally invasive surgery. Arms can be mounted directly to the operating table [20].

The DLR also developed a system called MicroSurge, which includes a master console with a 3D display and two haptic devices as well as a teleoperator consisting of three MIRO robot arms. Usually two MIRO arms carry surgical instruments equipped with miniaturized force/torque sensors to capture reaction forces with manipulated tissue. The third MIRO arm can (automatically) guide a stereo video laparoscope. The stereo video stream as well as the measured forces are displayed to the surgeon at the master console. Therefore the surgeon is not limited to seeing but can also experience force feedback from the input devices [21].

The system is designed to be able to perform complex procedures, e.g. beating-heart operations, where the tools and camera are moved synchronously with the heart, to give the surgeon the impression that the heart stands still. The virtual stopping of the heart and lung reduces the trauma to the patient [10].

AVRA Surgical Robotics is developing a surgical robotic system of modular construction which offers a portable lightweight and maneuverable robotic solution not available in any current available systems. The basic AVRA Surgical Robotics System (ASRS) employs four robotic arms with a weight/payload ratio that is unavailable in the current surgical robotics market [22]. This ratio allows robotic applications for a vast range of minimally invasive operations as well as robotic application for potential use in traditional open surgical procedures. ASRS's intelligence is incorporated within the arms and joints. The system can be configured with four or fewer arms and as such can be used, for example, in a single-arm construct with applications such as in-joint orthopedics.

The ASRS arms can be mounted on a patient-side cart, placed next to the operating table, or directly mounted to the operating table as well as attached to an overhead structure. The ASRS surgeon console merges the high-resolution view of the surgical field, the data, information management, and action of the robotic system with the biomedical and IT environment in the operating theater. This console will provide a newly developed human–machine interface (HMI) for the maneuvering of both instruments and the camera head.

## Conclusion

Robot-assisted surgery is a rapidly growing field, helped by continually evolving technology and its use in a wide variety of surgical settings. The near future is packed with a promising number of surgical robotic systems which can give better outcomes. Product costs are expected to go down as more competitors offering distinct technologies enter the market.

The first challenge for the near future will be to adapt the conventional forms of treatment to integrated, computer-assisted alternatives. This requires new training plans for medical staff, and changes in the layout of hospitals to accommodate the new requirements. Without a team that can exploit these opportunities to the fullest, gains from the use of this technology will remain small.

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# 75

# Training and Credentialing Laparoscopic and Robotic Surgery

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## Surgical training today: a complex scenario

"See one, do one, teach one" has been the mantra of surgical training for decades. Unfortunately, when we ask *where* are we going to see, do, and teach, the answer is often still "the patient." In its early days, laparoscopy was considered too challenging and surgeons asked "why work through a keyhole when you can just walk through the door?" [1]. Indeed, operating through a keyhole adds even more complexity to surgery: fulcrum effect, decreased haptic feedback, and loss of depth perception, to name a few [2]. Despite these challenges, the early 1990s saw rapid acceptance of laparoscopy driven by patient demands: reading and hearing about faster recovery, less pain, and less scarring. The field was caught by surprise and device companies started to provide training courses led by the early adopters. A weekend course was often considered enough by many surgeons to try this new technology at their home institutions. There was no standardized curriculum established and training was performed mainly on porcine models.

The desire to overcome some of the challenges in laparoscopy and an interest in remote surgery to perform operations in underserved or dangerous venues led to research in robotically assisted surgery. These efforts were funded by Defense Advanced Research Projects Agency (DARPA; Arlington, VA, USA) and the National Aeronautics and Space Administration (NASA; Washington DC, USA) [3–5]. This new technology provided the surgeon with stereoscopic vision to reinstate depth perception, hardware compensation of the fulcrum effect via console design, and tremor control and scaled motion to improve the accuracy of instrument movement well beyond what a normal set of hands was capable of. Yet robot-assisted surgery came with its own learning curve in addition to the basics, such as console management, robotic instrument knowledge, docking of the machine, and emergency undocking in case of life-threatening complications. At the same time, complete knowledge of surgical anatomy, procedural skills, and basic surgical principles still had to be properly mastered before dealing with the new technology. Moreover, modern surgery with its complex scenarios has raised the importance of so-called "nontechnical skills" [6] (situational awareness, communication, teamwork, leadership, stress management) in order to safely perform a surgical procedure, in spite of technological advancements.

Whenever we approach mastering something new, scaffolding [7, 8] facilitates acquisition of the required skills. This principle is equally valid whenever we are learning to ride a bicycle or to perform a new surgical intervention. Despite the famous phrase "to err is human," limiting errors and facilitating the correct technique becomes critical in the surgical field, as patients cannot continue to be the training platform.

Simulation has the goal of approaching the same situation multiple times, in order to understand it, apply different strategies to solve it, assess the pros and cons, select a preferred approach, and improve on it in a safe environment. It is widely used in several nonmedical fields to test new products and procedures, improve performance, predict future outcomes, and certify the acquisition of skills. In surgery, shortened hospital stays, shortened residency hours, and the rate at which new procedures and new technologies are introduced translate into a reduced number of operative cases for learners to participate in for any given procedure [9–11].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
© 2019 John Wiley & Sons Ltd. Published 2019 by John Wiley & Sons Ltd.
Companion website: www.wiley.com/go/smith/textbookofendourology

Moreover, *in situ* skills assessment is challenging and the results of residency training are barely measured or considered in view of becoming a full surgeon. Although the use of simulation could potentially fill these gaps, its application is not yet as standardized or widespread as one would imagine. Indeed, it is used to varying degrees from country to country and even from institution to institution, leading to significant differences in technical and nontechnical skills between young practitioners in the same field.

The American College of Surgeons' Accredited Educational Institutes (ACS-AEI) program was started in 2005 with the aim of providing guidelines and standards for simulation centers inside and outside the United States. The results turned out to be outstanding, and there are currently 94 accredited centers worldwide [12]. Despite the significant inroads, many sim-centers still prefer not to adopt a standardized training model, continuing to create their own model instead.

In Europe simulation is not typically considered a critical part of the urology residency curriculum. In the last decade some countries have adopted standardized training protocols to provide learners with a unified model to follow, preparing them for medical practice. This happened in the Netherlands with the 40 hours program and in the United Kingdom with the "Guidelines for training" [13] written under the auspices of the British Association of Urological Surgeons (BAUS). In Europe, simulation centers are still not common and few universities offer residents a chance to use pelvic trainers or simulators in general. Recognition of the need for deliberate, repeated simulation training and the lack of proper tools has led hands-on training (HoT) sessions to become more and more popular all over Europe. HoTs provide tutoring on dedicated models during congresses and educational events. These sessions use standardized training kits with predefined exercises and learning objectives. The European Urology Residents Education Program (EUREP) [14], flagship training event of the European Association of Urology (EAU), introduced the HoT format into its schedule in 2006 and today attracts hundreds of final-year residents from all over Europe, exposing learners from many countries to a unified training protocol [15].

The Urological Society of Australia and New Zealand (USANZ) streamlined the training regimen with the nSET Program, which includes training activities through the six residency years up to independent clinical practice, including the achievement of primary operator skills for laparoscopic surgery. Technical skills training is still not common practice in Africa, South America, and Asia, where structured technical skills teaching is limited to few training centers and dedicated courses.

Robotic surgery training is not yet formally considered as a part of urological education worldwide and few residents have a chance to perform robot-assisted surgery as first operators before the end of their learning path.

## History of surgical training: a growing field

Although ancient texts, such as the *Sushruta Samhita* from India, laid down in Sanskrit around 500 CE (original date unknown, but thought to go back to 1000 BCE), mention the use of various models to practice surgical skills for speed and accuracy, we will focus on recent history to follow our current model for medical education. Surgical residency as we know it today in the United States began in the early 1900s at Johns Hopkins University in Baltimore, MD, under the guidance of William Halstead. During those formative years, we have evidence that dog labs were used to teach both procedural as well as team-based skills. We also tend to point at flight simulators to make a case for the use of simulation in medicine. Surprisingly, that path began later, in 1929, with the Link Trainer (Figure 75.1) [16], which was instrumental in training young pilots how to land on aircraft carriers.

These early trainers can be compared to the basic skills trainers we see today, such as FLS, BLUS, and E-BLUS (see below) [17–19]. The growth of the Link Trainer into today's full flight simulators and regimented training programs could not have happened without a significant investment by the US Department of Defense (DoD) to develop the science and technology that underlies them.

We can recognize multiple phases in the progression of simulation in healthcare. The initial driver was the promise of objective assessment. In theory, by using virtual reality (VR) for training and assessment, we could measure everything that was represented in the mathematical models. Thus we could look at variables such as time and distance, but also collisions, penetrations, and path lengths, and even the use of energy, radiation, and blood loss. The believers were so excited about the possibilities that the mantra was "build it and they will come." For the first VR simulators to be developed a number of technologies had to evolve. Many of them were supported by the DoD, such as graphics processors, head mounted displays, and haptic interfaces. As these technologies came into existence, by many accounts Dr Richard Satava, a laparoscopic surgeon who at the time was at DARPA, began funding projects in the late 1990s to see if "flight simulators for surgery" were within reach

**Figure 75.1** The Link Trainer.

[20]. Some of these early efforts resulted in a sinus surgery platform [21, 22] and a vascular anastomosis trainer, among others [23, 24].

The second wave came only a few years after that, with the tagline "validate it and they will come." Early validation studies provided much-needed proof of the scientific and educational merits of surgical simulation. The key study which set the standard that many followed was that by Seymour et al. [25]. By that time a number of companies in the United States and abroad had launched commercial products into the market. That opened up the door for the next phase in development: an integrated curriculum, where simulation was one component of the whole. Validation studies gave the new technology legitimacy, while the integrated curriculum concept paved the way for today's comprehensive view: backwards design, predefined learning objectives, assessment tools, part task trainers, human patient simulators, and full procedural VR simulators.

In the last few years the DoD has refocused on medical simulation with significant investment in infrastructure: funding the development of open-standards-based building blocks to support the big picture and exponentially accelerate development. To formalize even more the birth of this new field of medical education and to push its development and widespread, ACS-AEI accredited in 2014 a research fellowship program in education and simulation technologies, to be delivered by selected centers.

## From FLS to the concept of modular hands-on training

When a new surgical intervention has to be learned, there are many topics that need to be addressed. Given a learner's previous experience, some of those may be skipped, some may just need refreshing, and others may require in-depth study and practice. Figure 75.2 provides a picture of the many elements that go into learning a surgical procedure. The concept is based on two principles: first and foremost a focus on patient management; second, bringing all contributors to safely performing a new procedure under one umbrella. This allows the learners to assess what they already are comfortable with, review where they have gaps, and finally layer in the new and difficult components specific to the procedure. The complexity of the procedural training template in Figure 75.2 demonstrates how difficult it is to move from basic clinical knowledge in medicine combined with basic technical skills to complete procedures and finally take on the responsibility of independent patient management. The true value of having a standardized template is to allow academic surgeons from all over the world to collaborate and contribute to this vast endeavor in developing training materials for all procedures [9, 26, 27].

To acquire the technical skills portion of a new procedure, we can often use some of the existing simulators. One of the first simulators to be validated with sufficient

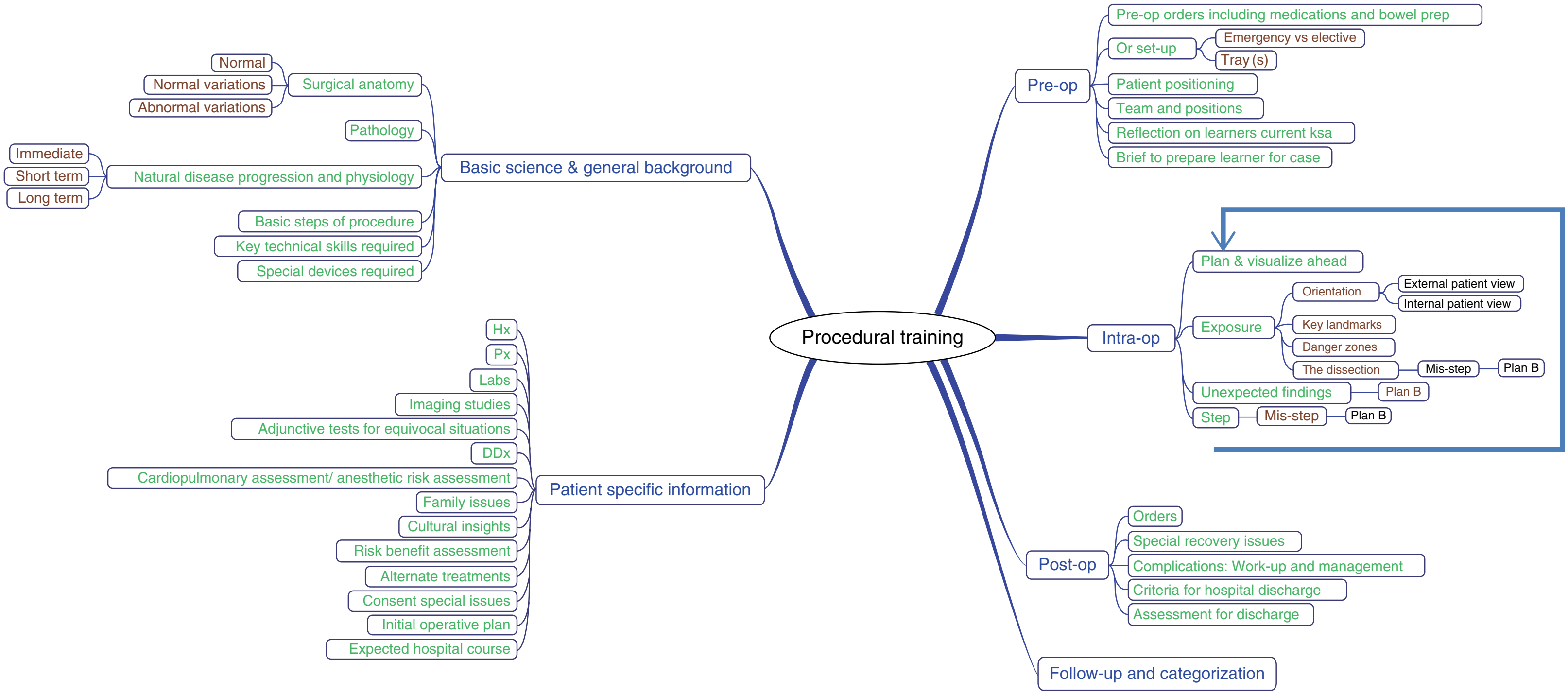

Procedural training
Basic science & general background
Surgical anatomy
Normal
Normal variations
Abnormal variations
Pathology
Natural disease progression and physiology
Immediate
Short term
Long term
Basic steps of procedure
Key technical skills required
Special devices required
Patient specific information
Hx
Px
Labs
Imaging studies
Adjunctive tests for equivocal situations
DDx
Cardiopulmonary assessment/ anesthetic risk assessment
Family issues
Cultural insights
Risk benefit assessment
Alternate treatments
Consent special issues
Initial operative plan
Expected hospital course
Pre-op
Pre-op orders including medications and bowel prep
Or set-up
Emergency vs elective
Tray (s)
Patient positioning
Team and positions
Reflection on learners current ksa
Brief to prepare learner for case
Intra-op
Plan & visualize ahead
Exposure
Orientation
External patient view
Internal patient view
Key landmarks
Danger zones
The dissection
Mis-step
Plan B
Unexpected findings
Plan B
Step
Mis-step
Plan B
Post-op
Orders
Special recovery issues
Complications: Work-up and management
Criteria for hospital discharge
Assessment for discharge
Follow-up and categorization

**Figure 75.2** Procedural training template. *Source:* CREST, University of Washington, USA. Reproduced with permission of CREST.

rigor in order to be used for a high-stakes exam was Fundamentals of Laparoscopic Surgery (FLS). It was first proposed at McGill University by Dr Gerry Fried [17], then developed under the auspices of SAGES, and validated in collaboration with the ACS [28]. FLS tasks were thought to reproduce the basic movements used in laparoscopy and were so well planned to be easily adapted to basic skills teaching in other laparoscopic specialties, such as gynecology and urology. FLS was developed to target basic maneuvers and not full procedures. In the United States FLS has been used as a starting point for the creation of the Basic Laparoscopic Urological Skills (BLUS) curriculum. Despite a study [18] showing validity, the BLUS exam is not mandated and is used only by choice at select residency programs. The EAU started to build upon the FLS experience in 2011, when the European Basic Laparoscopic Urological Skills (E-BLUS) [19] exam was given for the first time. E-BLUS is today the only technical skills certification to be mandated by an international urological society. It is made up of four tasks: peg transfer, circle cut, needle guidance, and intracorporeal knot tying (Figure 75.3). Depending on faculty's preference, basic training protocols often include the use of a camera navigation trainer [29] for a 30° laparoscope, although this exercise is not included in the examination. Initially intended as a stand-alone certification program, E-BLUS is rapidly evolving into the first step of a comprehensive pathway, guiding the novice from basic skills to full procedures and mastery.

Modular hands-on training, as depicted in Figure 75.4, suggests approaching technical skills training in three distinct steps: basic (simple skills), intermediate (complex tasks), and advanced (full procedures) [30, 31]. This general concept, in this case applied to laparoscopy, prescribes a logical progression for novices, a learning path to prepare them for mentored cases with patients.

*Basic skills* target fundamental building blocks: simple maneuvers like camera handling, grasping, traction/countertraction, cutting, and single-knot tying, which form the basis of any surgical technique. These are common to different laparoscopic specialties and that's why FLS, originally designed for general surgeons, was so easily adopted by urologists. Given the proven validity of trainers like FLS and E-BLUS, a novice should never learn basic skills on a patient.

*Intermediate training* is much more specialty-specific and focuses on the "complex tasks:" the most challenging steps of full procedures. Indeed, mastering basic skills, as well as practicing complex tasks on bench models, prepares the trainee to approach full procedural, or *advanced training*. At this stage the trainee has to link all the concepts learned along the way in order to perform the whole procedure (making errors, and learning how to recover) in a safe, simulated environment, before working on a real patient. While progressing from basic skills to full procedures, focus shifts to different aspects of surgical education, from technical skills to decision making and patient management, necessitating very different types of simulators.

While laparoscopic basic skills are already well documented and standardized, complex tasks for intermediate training are not yet fully defined and incorporated into validated curricula. Moreover, these are much more challenging to simulate. A first comprehensive curricular implementation exists as a joint effort between the ACS and the Association of Program Directors in Surgery (APDS) as the ACS/APDS Surgery Resident Skills

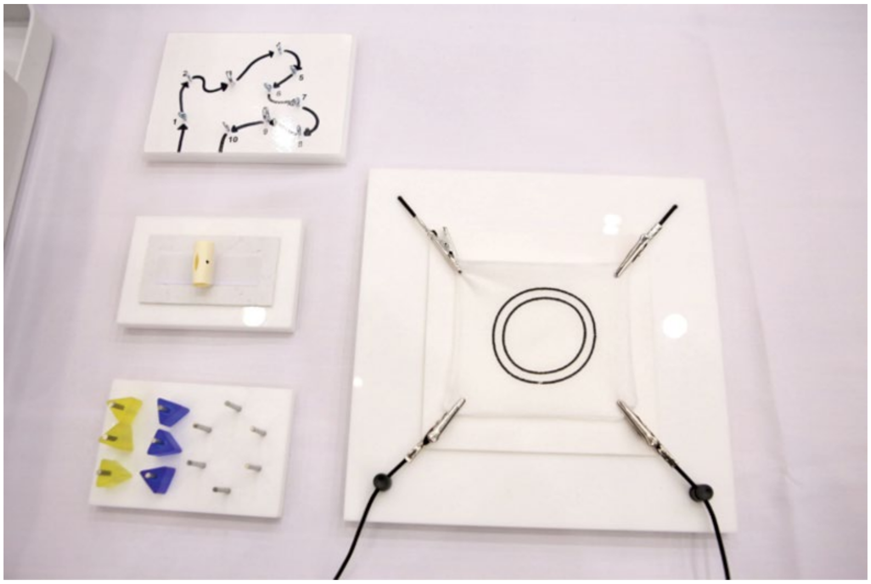


**Figure 75.3** The E-BLUS tasks.

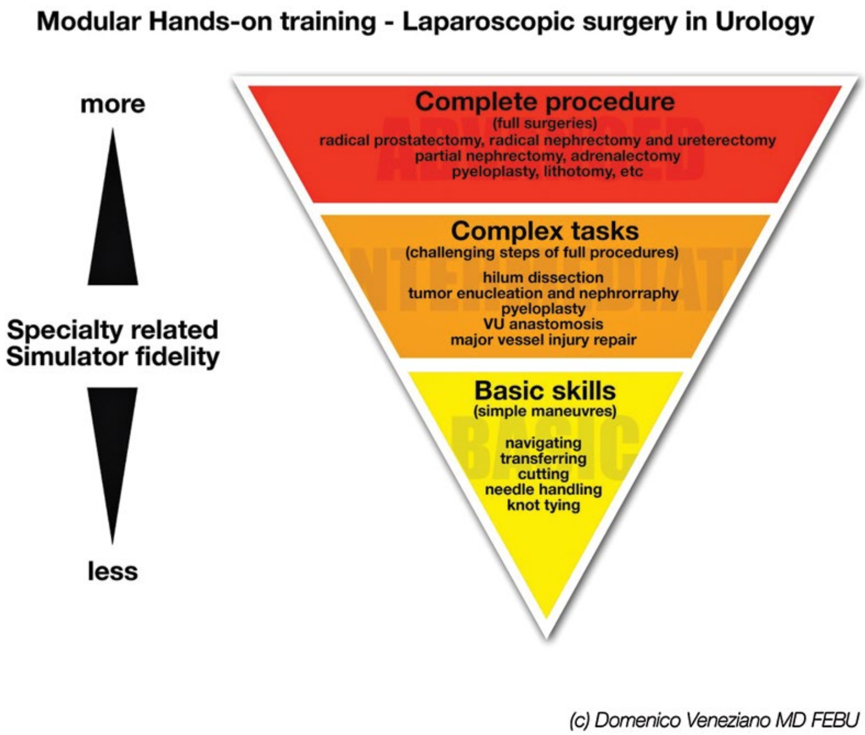

Modular Hands-on training - Laparoscopic surgery in Urology
more
Specialty related
Simulator fidelity
less
Complete procedure
(full surgeries)
radical prostatectomy, radical nephrectomy and ureterectomy
partial nephrectomy, adrenalectomy
pyeloplasty, lithotomy, etc
ADVANCED
Complex tasks
(challenging steps of full procedures)
hilum dissection
tumor enucleation and nephrorraphy
pyeloplasty
VU anastomosis
major vessel injury repair
INTERMEDIATE
Basic skills
(simple maneuvres)
navigating
transferring
cutting
needle handling
knot tying
BASIC
(c) Domenico Veneziano MD FEBU

**Figure 75.4** Modular hands-on training. *Source:* infographics by D. Veneziano MD.

Curriculum Phases I, II, and III, going from basic steps and tasks to procedures and team-based training [32–35]. Laparoscopic complex tasks according to the American Urological Association (AUA) and the EAU are summarized in Table 75.1. In either case, both American and European Urological societies agree that mastering complex tasks is critical before continuing on to perform complete procedures.

If laparoscopy made control of the instruments more difficult, putting a surgical robot in between surgeon and the instruments created new challenges, still being studied. Regarding basic skills, robotic consoles are explicitly developed to make instrument control much easier, eliminating fulcrum effect and lack of depth perception. On the other hand, becoming proficient on the console itself requires practice. Just like the cockpit of a car, it has few but important controls that need to be internalized so that the operator can focus on the procedure itself. Moreover, robot-assisted surgery requires continuous collaboration between console operator and bedside assistant, necessitating nontechnical skills training. Following on the footsteps of basic laparoscopy curricula, several training models [36] have been suggested for robotic surgery in urology. The first paper about the fundamentals of robotic surgery (FRS) was dated 2014 [37] and describes the process followed to design a basic training curriculum which could address the needs of multiple specialties and their societies. FRS includes cognitive content with pre-, intra- and postoperative activities, psychomotor skills, and team training exercises. To support the FRS curriculum, a physical training dome has been designed in order to place FLS tasks into a tridimensional environment. To maximize repeatability and standardization, the FRS dome with its predefined tasks was also reproduced on virtual platforms. In 2015, Fundamental Inanimate Robotic Skills Tasks (FIRST), a second training model for basic robotic skills, was validated [38]. The study enrolled 96 participants and scored performance in relation to completion time and errors performed on four FLS-inspired inanimate tasks. The most relevant experience in Europe regarding

**Table 75.1** Complex tasks according to AUA and EAU.

| AUA Laparoscopic, Robotic and New Surgical Technology (LRNST) | ESU/European School of Urology and section of Uro-Technology (ESUT) training research group |
|---|---|
| Pyeloplasty | Horizontal anastomosis (as per pyeloplasty) |
| Y-V plasty | Vertical anastomosis (as per vesicourethral) |
| Vesicourethral anastomosis | Hilar dissection |
| Control of aortic and inferior vena cava injury | Major vessel injury repair |
| | Tumor enucleation and suture of renal parenchyma |

robotic training was documented in 2015 [39] under the auspices of European Robotic Urology Section (ERUS). The article describes a fellowship curriculum to be carried out at an ERUS-accredited center, which is able to guide attendants in 6 months from VR training platforms up to the successful completion of a robot-assisted radical prostatectomy.

After the completion of a full training curriculum, mentored procedures on the patient can be supervised in robotic surgery thanks to the use of the dual console, which allows the tutor to eventually step into the procedure and help the operator, if needed.

Both in laparoscopy and in robot-assisted surgery, following a step-by-step path will shorten the learning curve, lead to faster mastery of a new surgical procedure, and increase patient safety.

## The science of curriculum development

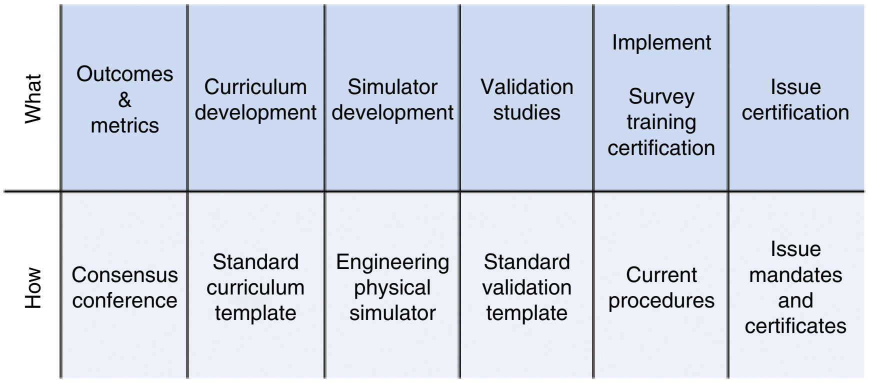
The creation of a comprehensive curriculum requires a rigorous process, beginning with deep insight into the intervention. The process links training outcomes to learning objectives and the validation process to the educational intent [25, 40]. The focus has to be on the curriculum, which in many cases will require a simulator to practice on.

There are three distinct roles in developing curricula: the clinician, the educator, and the developer; it is key that those roles are kept separate. The clinician is the source of all insight into the intervention, the disease, management of the patient, and the underlying basic science. The educator helps with the educational design and creation of valid assessment instruments. Finally the developer addresses content development, which may include simulators. Although the participants may want to play multiple roles in the process, we should resist that and keep these efforts distinct to ensure the best outcome.

One effective template to follow in order to avoid missing any important step is the one described by Richard Satava, named full life-cycle curriculum development [41] (Figure 75.5). The template describes a well-defined process, which begins and ends at the same point (full life cycle): the outcomes. The primer *ACS Principles and Practice for Simulation and Surgical Education Research* [42] provides many tips on how to approach the process.

Desired training outcomes and metrics need to be defined at the beginning, in order to guide the design process. These should be defined by the training program coordinator, in the case of an institution-specific course, or by an expert committee if proposed by a professional society. The initial framing opens the way to collect all the data required to develop the curriculum. It starts with a thorough literature review and development of an Anatomic Bill of Material, indicating all structures involved in the procedure. The analysis of best practices will separate choreography from safety considerations. A well-executed cognitive task analysis (CTA) [42, 43] allows us to document the series of decisions behind every single maneuver for a surgical procedure and the set of cues that need to be recognized to make those decisions [44–47]. It is usually completed by interviewing one or more experts while viewing a video of the procedure. Once completed, the CTA documents all steps of the procedure and, if appropriate, all phases of patient management in detail. It is the primary document used for all curriculum development work, didactic content, physical trainers, and assessment instruments.

The CTA frames the educational requirements, which can be translated into simulation requirements. Based on these, simulators on the market are reviewed. If none meet the requirements, a development team is tasked to address those needs and create one or more dedicated simulators. Afterwards, the simulators are verified and validated along with the associated curriculum. In case validity is shown and no major modification is required, the curriculum can be implemented into training courses.



| | | | | | | |
|---|---|---|---|---|---|---|
| What | Outcomes & metrics | Curriculum development | Simulator development | Validation studies | Implement<br>Survey training certification | Issue certification |
| How | Consensus conference | Standard curriculum template | Engineering physical simulator | Standard validation template | Current procedures | Issue mandates and certificates |

**Figure 75.5** Full life-cycle curriculum development template. *Source:* Richard Satava. Reproduced with permission of Richard Satava.

Multiple rigorous validation studies organized by professional societies can lead to the simulation being considered for credentialing. This could lead to certification that the learning objectives defined at the beginning of the development process have been reached [48, 49].

## Available and future simulation technologies

Learning objectives and desired training methods determine what kind of training is required and which simulators can be used. As identified in the full life-cycle curriculum development template (Figure 75.5), simulator selection/development always comes *after* "outcomes and metrics" and "curriculum development." Before considering the development of a new simulator, which can require considerable investment, one should review existing ones. Over the last decade the range of commercially available simulators for training healthcare professionals has grown exponentially. Training tools available for laparoscopic and robotic surgery range from physical and virtual to hybrid.

In the context of simulation, a concept that needs to be carefully examined and understood is that of fidelity. Although "simulation" is considered a reproduction of reality, it is an approximation of the tasks with some degree of fidelity. A *high-fidelity* surgical simulator aims to replicate the actual surgical setting, mimicking every detail from anatomy and physiology to tissue behavior. On the other hand, a *low-fidelity* trainer has the goal of focusing just on some specific detail, putting the rest aside. Thus, a cadaver could be considered an "organic simulator" that is closest to the surgical concept of high fidelity, while FLS/E-BLUS tasks, with their pegs and gauzes, are synthetic low-fidelity trainers. High-fidelity simulators, due to their complexity, are usually more expensive and require more time to be prepared for a training session, whereas low-fidelity ones are often more transportable, cheaper, and easier to arrange. Some exercises may be reproduced on both types of simulator; some others may not. Fidelity also needs to be seen in the context of the targeted learning objectives, which may change the definition of fidelity itself. Despite the level of fidelity, assessment capabilities also need to be considered, ranging from expert observation to embedded sensors or software-based assessment.

### Physical simulators

For laparoscopic training, the most common simulators today are physical. The first laparoscopic box-trainers were built in the 1990s and they are still produced in many different shapes (Figure 75.6). The concept is always the same, with a trocar-retaining upper wall and a base to host different exercises. A great variety of tasks have been developed, with FLS-related ones being the most common. Apart from the FRS dome, still not commercially available, and the FIRST tasks, validated basic skills physical simulators are not available in the robotic training field. These low-fidelity trainers lack embedded assessment instruments, but rely on time to completion and counting of errors to assess performance. Some more sophisticated trainers have been recently made available by the Center for Research in Simulation and Education Technologies (CREST; University of Washington, Seattle, WA, USA). These simulators target the intermediate training level as they reproduce parts of full procedures. These include the Major Vessel Injury (MVI) repair model [50] and the Pyeloplasty model [51, 52] (Figure 75.7), which can be used for both laparoscopic and robotic training. These models, in contrast to to many other physical models, have embedded assessment markers to objectively measure surgical skill. The MVI model, connected to a synthetic-blood bag, allows for objective measurement of blood loss, focusing on a clinically relevant measure. The Pyeloplasty model uses Black Light Assessment of Surgical Technique (BLAST) technology to objectively assess the alignment of the ureteropelvic junction. Similar tasks can also be performed, even without embedded assessment, on actual perfused

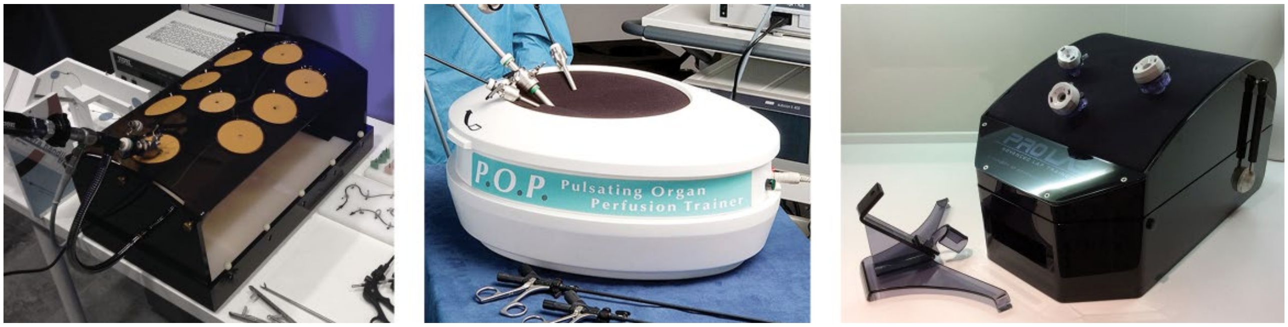


**Figure 75.6** Three laparoscopic box trainers: (from left to right) Szabo Berci, Pulsatile Organ Perfusion, Optimist (POP), and Pro Lab.

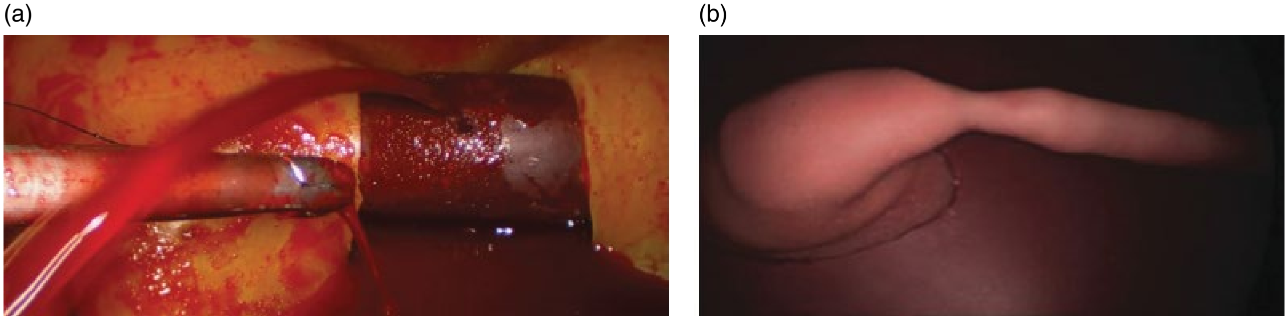


**Figure 75.7** Two Intermediate training tasks: (a) MVI repair model and (b) Pyeloplasty model by CREST. *Source:* CREST, University of Washington, USA. Reproduced with permission of CREST.

animal organs inside dedicated boxes like the Pulsatile Organ Perfusion, Optimist (POP) trainer (Innsbruck, Austria), and the Pro Lab (INTECH, Reggio Calabria, Italy), shown in Figure 75.6. When it comes to advanced, full procedural training, cadavers are often considered the gold standard of surgical simulators, although they present significant pitfalls. Indeed, they are not able to provide objective feedback about performance, as relevant damage could be caused without ever knowing it. This shortcoming of cadavers used as simulators has already been addressed in the automotive safety field and lead to the creation in 1976 of Hybrid III [53], the first modern crash-test dummy. Dummies have the ability to record an incredible amount of data, allowing a deeper understanding of what is happening to the driver during an automobile collison. Laboratory animals are often used for advanced training, although their anatomy is not a good analogue for the corresponding human one. Meanwhile, next-generation physical simulators are being instrumented to support real-time, objective assessment. Some attempts have already been made to create accurate synthetic anatomic structures representing the surgical space inside simple training boxes, to support repeatable *advanced* training without the use of organic or animal models. An example is the Radical Nephrectomy model by INTECH (www.intechsimulation.com), silicon-based and assembled over a 3D-printed structure. Mostly made of reusable parts, it was designed to fit inside a laparoscopic box-trainer. Finally, the US DoD has funded a major initiative for the development of an Advanced Modular Manikin(TM) open source, open standards platform that allows both technical and non-technical skills to be trained on a hybrid, full patient simulator being developed by CREST(Award# W81XWH-14-C-0101) (www.advancedmodularmanikin.com).

## Virtual reality simulators

VR simulators were considered the future of healthcare education in the early 1990s. After more than 20 years developers are still working to improve VR systems, to meet surgical education requirements. Realistic graphics and physics, as seen in videogames, although impressive are unfortunately not sufficient for surgery and very expensive to develop with current methods. Robot-assisted surgery simulators use VR today for basic tasks, like moving objects or suturing drills. Some intermediate training exercises for procedural task training are under development, as well as systems that allow for an interaction between the first operator from the console and a second operator maneuvering laparoscopic instruments. Robotic VR trainers (Figure 75.8) are on the market as stand-alone products or as upgrades for the actual robotic console.

## Hybrid simulators and future technologies

Hybrid simulators have been designed in the attempt to match the physical feedback of inanimate models to data collection and assessment capabilities of VR technologies. These systems, like the Electronic Data Generation for Evaluation (EDGE; Simulab, Seattle, WA, USA) or the LapX Hybrid (Epona, Rotterdam, The Netherlands), and the ForceSense (Medishield B.V., Delft, The Netherlands), are still just based on FLS tasks and take advantage of video tracking and several sensors to record performance and eventually assess in real time. This concept could be enhanced by applying augmented reality to synthetic models. The advent of three-dimensional printing is facilitating fast and cheap reproduction of physical models and instruments, which could accelerate adoption of technical skills training. This technology, coupled with biologic printing materials [54], could lead to the creation of *standardized* printed organs, designed to address training requirements and producible on site.

Given the variety of simulators available, many learning objectives can be met today. These range from simple inanimate trainers like E-BLUS, up to Human Patient Simulators that allow training of team skills [55–58]. In any case, citing Richard Satava, “the simulator is just

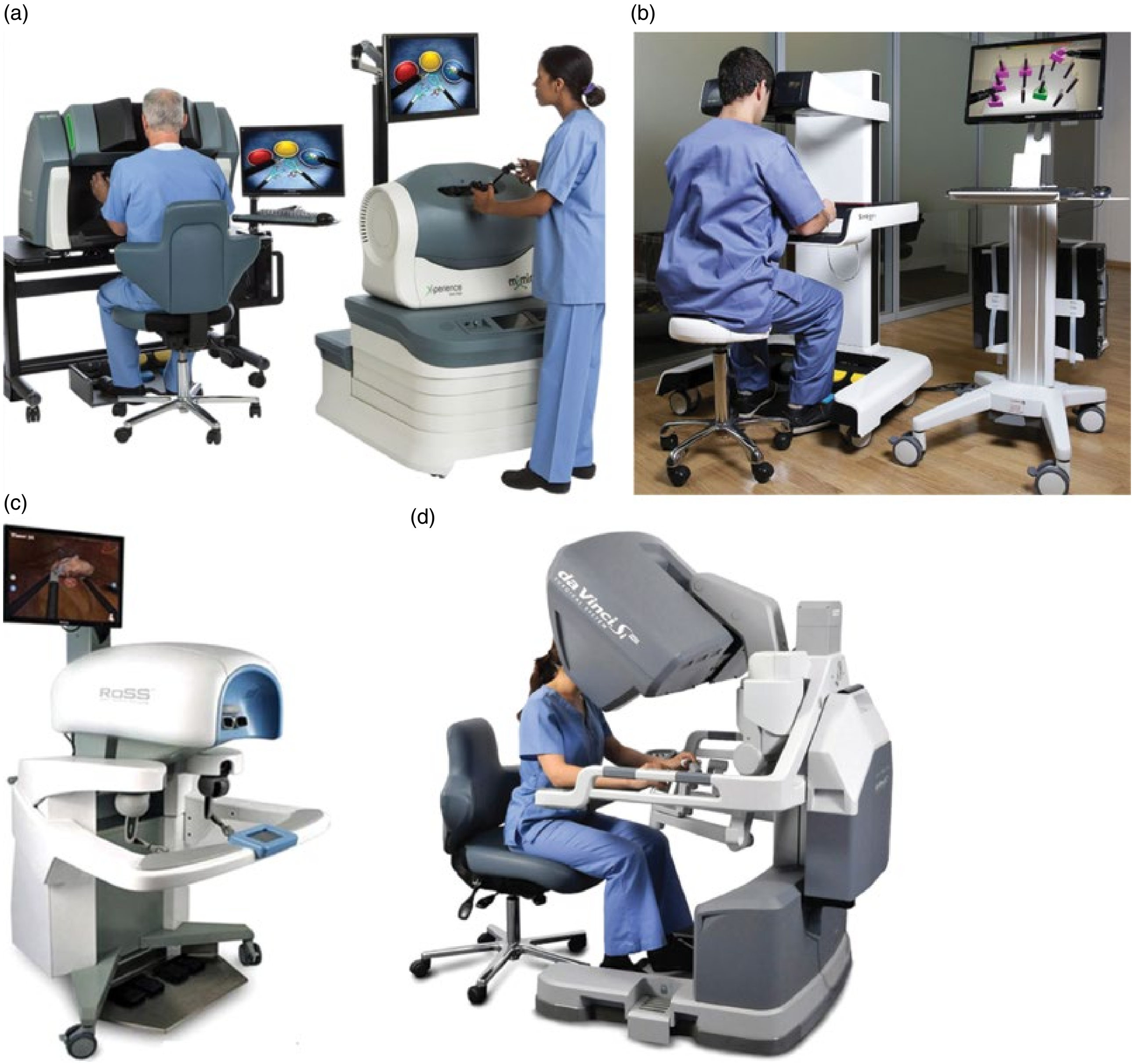


**Figure 75.8** Robotic VR trainers: (a) dV trainer by Mimic, (b) RobotiX Mentor by Simbionix, (c) RoSS by Simulated Surgical Systems, (d) backpack by Intuitive Surgical on a da Vinci console.

another tool, and it is the curriculum that will determine the training of the surgeon" [59].

For further information on available and future simulation technologies, please refer to Video 75.1.

## Validation: facts and controversies

The desire to validate simulators has been an important and necessary effort from the very beginning. After all, we need to know if time spent on a simulator provides value. Today we have a tendency to use the term *validation* in a generic sense of "does it do what it is supposed to do?" We need to consider this term from different points of view. While the surgical community considers simulators to prepare for patient care and increase safety, the education community talks about formative feedback and summative evaluation. Many important questions have been combined under this rubric, each with their own challenges:

- If I keep practicing on a simulator, do I get better?
- If I keep practicing on a simulator, do I get better in the operative room?
- How many times should I repeat an exercise or how long should I practice until I am done?

Let's consider these questions individually. If you keep practicing on a simulator you will always get better at doing that *specific* task on a simulator, which does not necessarily relate to the surgical task that we are preparing for. The second question moves us closer in that direction as it considers training transfer. Indeed, if the simulator was not designed properly you might actually get better on the simulator but worse in the operative room, which is known as negative training transfer. The third question, although not directly related to validation, is also a critical one. Unfortunately it is neither time nor repetition that can establish an end point. The correct answer has to be "until you reach proficiency," as each individual learns at a different rate. The only thing that really matters is that, whenever a trainee stops practicing on the simulator they must be deemed safe to take care of patients.

To further complicate the notion of *validating* a simulator, we need to consider some other items:

- Did the trainee properly study the didactic content preparing them for the exercise?
- Has a mentor observed and provided the trainee with formative feedback so that they get better at what they are doing?
- Was the trainee instructed properly on how to practice on the simulator?

If trainees do not understand the instructions, the simulator might not help them and, at the same time, even a mediocre simulator could allow them to learn if they were working with an excellent mentor.

None of these questions directly relate to validation as defined by the educational community, which will clearly state that one can only validate an assessment instrument, to basically state that it correctly measures what was intended to be measured. That process is rigorous and complex, reflected in the fact that there are very few simulators that are *formally* validated. The standards for validation are published in *Standards for Educational and Psychological Testing*, 2014 edition [60].

Validation is not a process that can be undertaken as an afterthought, as it relates to intent: what were the learning objectives we had in mind? How are we assessing that these learning objectives are reached? What is the prescribed training protocol? As the Holy Grail is to assess whether time spent on a simulator translates to better patient care, we also should create assessment instruments that can be used both with the simulators and in the clinical environment. Then we could compare data directly and determine whether or not training transfer took place.

## The role of assessment and certification

When discussing training, we also need to consider assessment. Without assessment we cannot tell if training is leading to improvement. Without assessment we cannot tell the trainees how to improve their performance, or decide if the trainee is ready to move on to the next level.

Creating a reliable assessment instrument is a difficult task. For example, time to completion has been widely used for assessment of technical skills, while studies have shown that time is *not* a valid measure for surgical performance; in fact, speed increases errors. In 1990 Miller created a template for the assessment of cognition and behavior in a clinical setting (Figure 75.9) [61]. He underlined the importance of separating the assessment of cognition from behavior: the examinee shows the they *know* the basic science and demonstrates that they *know how* to relate it to the procedure. After demonstrating cognitive skills, the trainee *demonstrates how* they apply their cognitive knowledge to the procedure and, finally, that they are able to actually *do* it. This whole process reminds us once again of the procedural training template depicted in Figure 75.2 and of the relevance of modular hands-on training as a pattern of step-by-step skills assessment, during the "show how" phase. Assessment may include evaluation of both technical and nontechnical skill markers, such as the Global Evaluation and Assessment of Robotic Skills (GEARS) [62] and the Non-Technical Skills for Surgeons (NOTSS) [63]. Crowdsourcing is now also being studied as an alternative to conventional tools, mostly based on expert evaluation. Indeed recent studies [64, 65] demonstrate how "crowd scores can provide similar or nearly identical concordance with faculty panel ratings and pass-fail decisions" in approximately 48 hours, which is 60 times faster than the expert counterpart. Moving ahead, electronic sensors or video analysis could improve the measurement of technical skills, just as VR-based simulators claim to do.

Indeed, relying on a solid assessment tool is critical when we talk about certification and licensing. In 2009, the American Board of Surgery (ABS) mandated that, in order to be eligible to sit for the board exam in General Surgery [66], a certificate documenting the successful completion of the FLS exam had to be

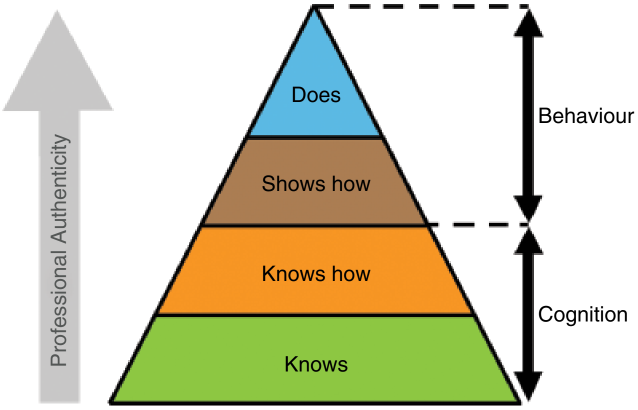


**Figure 75.9** The assessment of clinical skills/competence/performance.

submitted along with the application. Similarly, the E-BLUS exam includes an online cognitive part to be completed before moving on to the technical skills part, to be certified. Creating a high-stakes exam requires tremendous scrutiny and rigor. When a surgical society endorses an exam as "high stakes" it certifies that, by passing the exam, the applicant is considered by the society competent to perform the procedure with full autonomy. Urology board certifications in America, Europe, and Australia include today only cognitive assessment and rely on logbooks to certify practical skills. The addition of technical skills assessment as an integral part of board exams would definitely improve the validity of these high-stakes exams, leading to improved patient safety.

As documented in the literature, assessment and certification in surgery are evolving with much room for improvement. Considering the role of simulators in civil aviation training, licensing, and re-certification today, it would not be a surprise to see similar requirements in the laparoscopic and robotic surgery fields in the years to come.

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# Patient Preparation and Operating Room Setup for Laparoscopic and Robotic Surgery

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## Introduction

Laparoscopic and robot-assisted procedures have become the cornerstone of a urologist's surgical armamentarium over the past two decades. These minimally invasive procedures require additional equipment and operating room setup. Patient and operating room preparation are key features to successful and efficient surgery.

It is imperative that the operating room personnel and surgeon are familiar with all equipment systems and proper preparation of equipment. Urology surgical team members also need to be able to troubleshoot unexpected occurrences during a case. Without proper preparation and positioning, patient safety and surgical outcomes may be compromised. In this chapter we describe key features of patient preparation and operating room configuration for common laparoscopic and robotic surgeries.

## Patient preparation

Careful patient selection for minimally invasive urologic procedures is critical for successful outcomes. Patient selection begins with a thorough history and physical examination, including attention to cardiopulmonary status and previous abdominal surgeries. Medical and/or cardiovascular clearance may be warranted. Patients with chronic obstructive pulmonary disease require pulmonary clearance, including pulmonary function tests, because of the risk of hypercarbia. Appropriate laboratory data, such as complete blood count, basic metabolic panel, prothrombin time, partial thromboplastin times, and urinalysis with culture should be considered. Radiologic imaging is helpful for surgical planning. For example, computed tomography (CT) with intravenous contrast is valuable for delineating the renal vascular supply for laparoscopic nephrectomy or partial nephrectomy, or for identifying crossing vessels prior to pyeloplasty.

The indications for laparoscopic and robotic urologic procedures are almost identical to those of open surgery. Absolute contraindications to minimally invasive surgery include uncorrectable coagulopathy, abdominal wall infection, massive hemoperitoneum, and generalized peritonitis [1]. Intestinal obstruction was formerly considered an absolute contraindication; however, many general surgeons will perform diagnostic laparoscopy for small bowel obstruction if the bowel is not too dilated. Historically, relative contraindications to minimally invasive surgery included morbid obesity, extensive prior abdominal/pelvic surgery, pelvic fibrosis, organomegaly, ascites, pregnancy, hernias, and iliac or aortic aneurysms. However, in this current day and age laparoscopic and robotic surgery can be safely performed in patients with morbid obesity and previous abdominal surgery with minor technical adaptations. For example, Trocar placement for laparoscopic renal surgery can be shifted laterally for obese patients and the Veress needle can be introduced off site from abdominal scars in patients with previous abdominal incisions during initial insufflation. Pregnancy is no longer considered a contraindication for laparoscopy.

## Informed consent

All patients should understand the risks, benefits, and alternatives of the proposed procedure. Complications associated with minimally invasive procedures are

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similar to their open counterparts with the exception of a few unique complications, including $CO_2$ embolism, hypercarbia, postoperative crepitus, and shoulder pain from pneumoperitoneum. Every patient who undergoes a laparoscopic or robotic procedure should understand the potential for conversion to an open procedure and this should be documented in the written consent.

### Consent for blood products

For surgeons who have experience with laparoscopy, blood type and screen can be sufficient for most minimally invasive urologic procedures. Type and cross for 2 units of packed red blood cells is appropriate for more extensive procedures, such as partial nephrectomy and radical cystectomy. We do not recommend preoperative donation of autologous blood prior to robot-assisted radical prostatectomy because of lower estimated blood loss due to pneumoperitoneal compression of venous blood supply with the laparoscopic approach [2].

## Bowel preparation

Preference for bowel preparation varies from surgeon to surgeon. It is our recommendation that patients take a half bottle of magnesium citrate the day before surgery for transperitoneal laparoscopic or robotic renal procedures. Many minimally invasive urologic surgeons do not routinely administer a bowel preparation prior to laparoscopic or robotic renal or prostate surgery.

Our preference for bowel preparation prior to robot-assisted radical cystectomy is mechanical bowel preparation only with an oral electrolyte solution. We no longer routinely administer antibiotic bowel preparation (i.e. oral neomycin and metronidazole); however, broad-spectrum antibiotics are administered intravenously within 60 minutes of incision.

## Operating room setup

Operating room setup, experienced nursing staff, and a team approach are keys to a smooth procedure. All operating room personnel should be familiar with the operating room setup and basic equipment function. Minimally invasive procedures require more equipment than standard open procedures; thus, the operating room should be large enough to accommodate the laparoscopic tower and the robotic system.

All equipment should be tested prior to each procedure to make sure it is functional, including the aspiration–irrigation system, electrocautery, $CO_2$ insufflation, camera, and light source. If anticipated to be used, the argon beam electrocautery or saline-enhanced radiofrequency cautery should also be tested prior to partial nephrectomy. Lists of equipment necessary for laparoscopic and robotic renal surgery, as well as robotic pelvic surgery, are given in Boxes 76.1–76.3. An open tray should be either set up or immediately available in the room in the event rapid conversion to open surgery is needed.

The room configuration for renal surgery varies from left to right side and from laparoscopic to robotic cases. Aerial diagrams of room setup for laparoscopic transperitoneal renal surgery and robotic pelvic surgery are shown in Figures 76.1–76.3.

Most laparoscopic renal surgeries are performed with the surgeon and assistant on the same side of the table. Thus, two video monitors are ideal with the main laparoscopic tower (containing video monitor, light source, camera, and insufflators) placed on the side opposite the surgeons. The $CO_2$ insufflator is placed in the surgeon's view to allow for continuous monitoring of the intraperitoneal pressure. The second video tower is placed in view of the second assistant and the scrub nurse who are stationed on the side opposite the surgeons along with the instrument table. Incoming lines from the camera, light cord, $CO_2$ insufflation tubing, aspiration–irrigation tubing, and electrosurgical devices enter from the contralateral side of the table or from the head or foot of the table. Additional lines from equipment, such as a Harmonic scalpel, LigaSure (Covidien, Boulder, CO, USA), or argon beam coagulator, should be arranged in an orderly fashion to prevent them from getting tangled during surgery. Pre-existing or improvised pockets in the laparoscopic drape can be helpful for organizing equipment.

**Box 76.1 Basic equipment for laparoscopic surgical procedures.**

Mobile video cart with monitor
Secondary video cart
$CO_2$ insufflator with $CO_2$ tank or wall supply
$CO_2$ insufflation tubing
Camera, high resolution, and control box
0 and 30° 5- or 10 mm laparoscopes
Scope warmer
High-intensity light source
Fiberoptic light cable
Electrosurgical cords
Electrosurgical unit with foot pedal (monopolar, LigaSure, HARMONIC, ENSEAL, and/or Thunderbeat)
Aspiration–irrigation system with double canister suction apparatus
High-definition video recorder (optional)

### Box 76.2 Equipment for laparoscopic renal surgery.

One Veress needle
One 5 mm Trocar
Two 12 mm Trocars
One aspiration–irrigation tubing and probe
Two 5 mm laparoscopic atraumatic grasping forceps (blunt)
One 45 mm endovascular stapler
Two endovascular stapler reloads
One 5 mm laparoscopic monopolar scissors

*Additional equipment for laparoscopic partial nephrectomy*
Four bulldog clamps with remover
Two 5 mm laparoscopic needle drivers
One Satinsky clamp
Additional 12 or 15 mm Trocar for assistant
Laparoscopic ultrasound
0 polyglactin CT-1 suture
FloSeal Hemostatic Matrix (Baxter, Deerfield, IL, USA)
Mini-laparotomy pads
Hem-o-lok ligation system (Teleflex Medical, Research Triangle Park, NC, USA)
Lapra-Ty absorbable suture clips (Ethicon, Somerville, NJ, USA)
2-0 polyglactin SH suture
Closed suction drain

*Additional equipment for robot-assisted procedures*
0 and 30° robot camera lens
One robot fenestrated bipolar grasper
Two robot large needle drivers (Mega cut, Large needle driver)
8 mm robot Trocars
One robot Prograsp grasper
One robot monopolar scissors

During robotic procedures the surgeon console can be positioned in a corner of the operating room, depending on room configuration. In the newer-generation robotic surgical systems, the optical viewer, arm rest, and foot pedals can be easily adjusted for surgeon comfort. For robotic renal surgery, the assistant is positioned on the

### Box 76.3 Equipment for robot-assisted laparoscopic radical prostatectomy.

One Veress needle
Four 8 mm robotic Trocars (for da Vinci S, Si, Xi, X)
One 12 mm Trocar
One 5 mm Trocar
One aspiration–irrigation tubing and probe
Robotic monopolar scissors
Robotic fenestrated bipolar grasper
Robotic Prograsp grasper
One 5 mm laparoscopic needle driver
One 5 mm atraumatic grasping forceps
Hem-o-lok ligation system (Teleflex Medical, Research Triangle Park, NC, USA)
One 2-0 polyglactin CT-1 suture cut to 10 inches for dorsal vein stitch
One 3-0 barbed poliglecaprone RB-1 suture for posterior reconstruction stitch (optional)
Two 3-0 barbed poliglecaprone RB-1 suture as a "double-armed" stitch
One 10 mm Endocatch bag
One 18 Fr Foley catheter (intraoperative catheter)
One 20 Fr Foley catheter (final catheter)
Closed suction drain

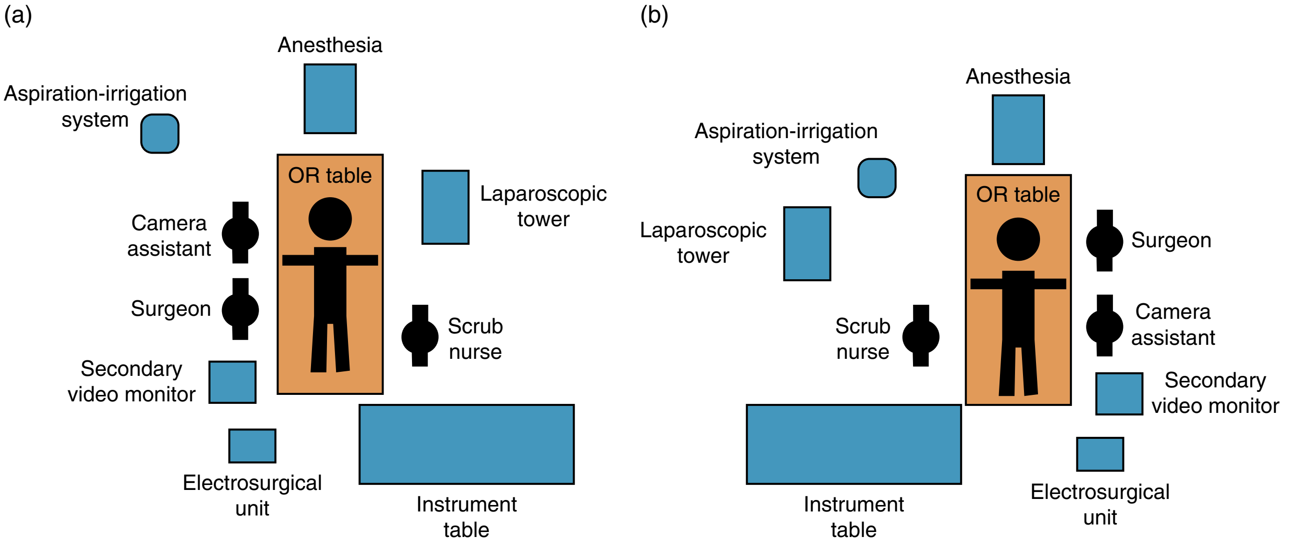
(a)
Anesthesia
Aspiration-irrigation system
OR table
Laparoscopic tower
Camera assistant
Surgeon
Scrub nurse
Secondary video monitor
Electrosurgical unit
Instrument table
(b)
Anesthesia
Aspiration-irrigation system
OR table
Laparoscopic tower
Surgeon
Camera assistant
Scrub nurse
Secondary video monitor
Instrument table
Electrosurgical unit

**Figure 76.1** Operating room (OR) setup. (a) Left-sided laparoscopic transperitoneal renal surgery. (b) Right-sided laparoscopic transperitoneal renal surgery.

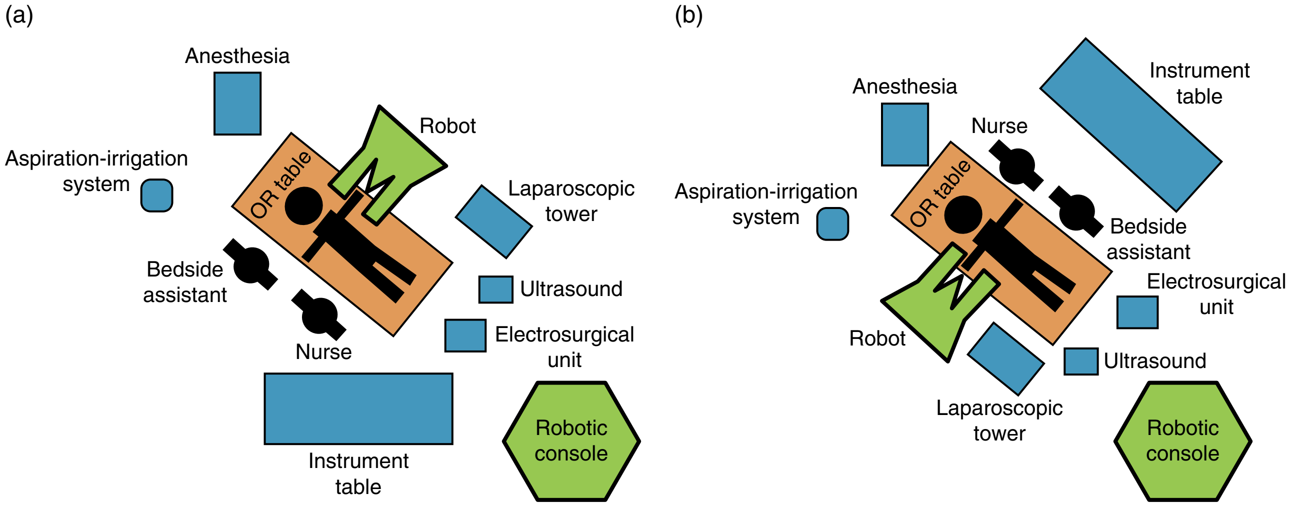
(a)
Anesthesia
Robot
Aspiration-irrigation system
OR table
Laparoscopic tower
Bedside assistant
Ultrasound
Nurse
Electrosurgical unit
Instrument table
Robotic console
(b)
Instrument table
Anesthesia
Nurse
Aspiration-irrigation system
OR table
Bedside assistant
Electrosurgical unit
Robot
Ultrasound
Laparoscopic tower
Robotic console

**Figure 76.2** Operating room (OR) setup. (a) Left-sided robotic transperitoneal renal surgery. (b) Right-sided robotic transperitoneal renal surgery.

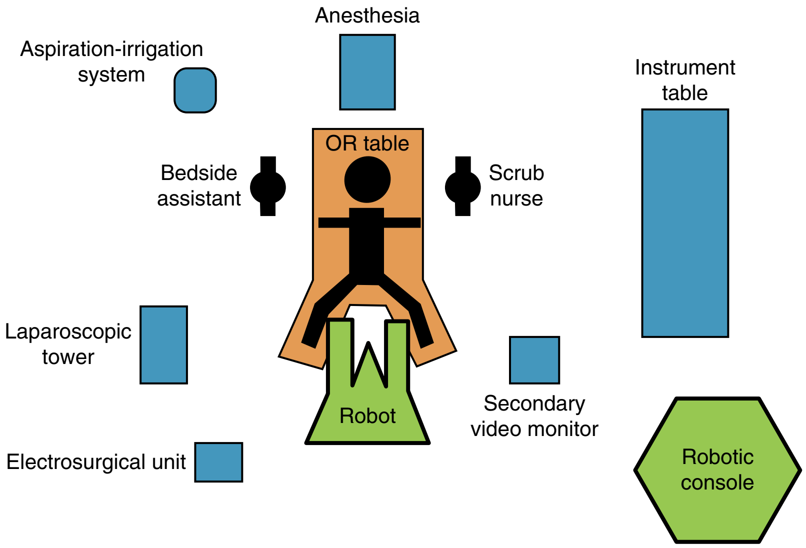
Anesthesia
Aspiration-irrigation system
Instrument table
OR table
Bedside assistant
Scrub nurse
Laparoscopic tower
Robot
Secondary video monitor
Electrosurgical unit
Robotic console

**Figure 76.3** Operating room (OR) setup for robotic pelvic surgery.

side opposite the surgical site. For robotic pelvic surgery, the authors' preference is for the bedside assistant to sit or stand on the patient's right side with the scrub nurse on the patient's left side. One advantage of having the scrub nurse and assistant on opposite sides of the table is that the scrub nurse can be positioned close enough to the table to actively participate in the surgery, such as during Foley catheter manipulation and for applying perineal pressure. A disposable plastic instrument holder can be secured to the laparoscopic-assisted vaginal hysterectomy (LAVH) drape next to the bedside assistant for convenient intraoperative storage of frequently used instruments. This helps minimize instrument passage across the patient's body. Alternatively, a sterile Mayo stand can be positioned next to the bedside assistant as a "mini table" to hold the frequently used instruments. It should be noted that some surgeons prefer the bedside assistant to be located on the patient's left side, allowing the fourth arm to be placed on the patient's right side and the two grasping instruments to be used simultaneously. A second video monitor is helpful for the remainder of the operating room staff. If laparoscopic ultrasound is used, the screen should be placed within the assistant's direct line of vision.

Once the robotic and assistant ports are placed, the robot is docked. It is important to align the base of the slave unit with the camera port. This allows for proper docking of the robotic instruments in order to have adequate range of motion and to avoid arm collisions. With the da Vinci Si Surgical System, it is important that the blue arrow on the camera arm be aligned within the "sweet spot" to ensure the slave unit is docked within the correct distance from the operating table to accommodate appropriate range of motion of all instruments. To reduce instrument and robotic arm collisions, the robotic ports are placed at least four fingerbreaths apart from each other, and the elbows of the robotic arms are rotated outwards.

With the da Vinci Xi Surgical System, the patient cart is brought over the patient by aligning the laser crosshairs on the boom over the camera port. With the robot arm docked to the camera port and the camera focused on the target anatomy, the autotargeting button on the camera is pressed to rotate the boom to optimize the position of the remaining robot arms. The robot ports are placed at least 6–8 cm apart from each other. To minimize external robot arm collision, we adjust the space between the elbows of each robot arm to accommodate the size of a hand's fist.

## Patient positioning

### Laparoscopic renal surgery

In traditional open renal surgery, the patient is positioned in flank position in the lateral decubitus position with the kidney rest elevated and the table flexed. In contrast, laparoscopic transperitoneal renal surgery can be effectively performed with the patient in the modified flank position [3] (Figure 76.4). The patient is placed in the supine position with a 4 kg sandbag or gel roll under the ipsilateral side, creating a 30–45° rotation. The bottom leg is slightly flexed at the hip and knee, and the top leg is left straight. Pillows are placed between the legs as a cushion and to slightly elevate the upper leg in line with the torso. The chest and hips are secured to the table with 8 cm silk tape. The ipsilateral arm is then padded and secured in a modified "sling" position, similar to the position used by orthopedics for clavicular fractures. The contralateral arm should be secured to an arm board. All pressure points are padded with egg-crate foam or gel pads. Neither the kidney rest nor an axillary roll is necessary in this modified flank position. The table is then maximally rotated laterally, thus creating a true 90° angle relative to the horizontal. The lateral rotation of the bed should be tested prior to draping the patient and the anesthesia team should ensure patency of arterial and venous access. This positioning is ergonomic for the patient and surgeon.

Positioning for retroperitoneal laparoscopic renal surgery is similar to that for open nephrectomy. The patient is placed in the full lateral position in the center of the table with the table flexed. An axillary roll is placed to prevent brachial plexus injury.

Bilateral lower extremity antiembolic stockings and pneumatic compression devices should be in place prior to induction of anesthesia. An upper body and/or lower intraoperative warming device should be placed before the patient is prepped and draped. There is debate about optimal surgical site preparation and preoperative antibiotics for prevention of incisional infections. A prospective randomized clinical trial comparing chlorhexidine–alcohol to povidone–iodine for surgical site preparation demonstrated a statistically significant reduction in both superficial and deep surgical incisional infections with the use of chlorhexidine–alcohol [4]. The entire abdominal wall should be prepped from the nipples to the pubis. The genitalia should be prepped in the

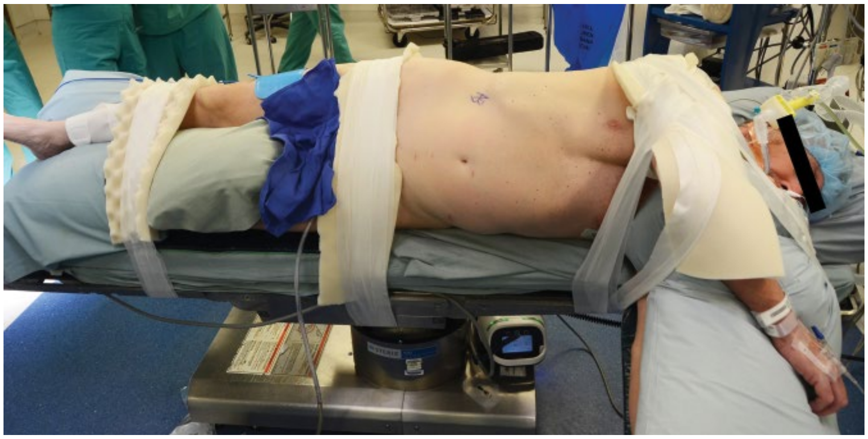

**Figure 76.4** Patient positioned in modified flank position for laparoscopic and robotic transperitoneal renal surgery.

field for minimally invasive nephroureterectomy and ureteral reimplant to allow for sterile Foley catheter placement on the field. Antibiotic prophylaxis should be administered within 60 minutes of the surgical incision. The American Urological Association's best practice policy statement on urologic surgery antibiotic prophylaxis is an excellent resource for selecting specific preoperative antibiotics [5]. Prior to insufflation, an orogastric tube and Foley catheter should be in place in order to decompress the stomach and bladder to avoid inadvertent injury to these hollow viscera.

## Robotic pelvic surgery

For robotic pelvic surgery the patient is ultimately placed in a steep Trendelenburg position with the legs in a low lithotomy position (Figure 76.5). For the da Vinci Xi, we use the split-leg position (without hyperextension of the hip) as the robot docks from the patient's side rather than between the legs (Figure 76.6). This position allows gravity to pull the abdominal viscera away from the operative field and the assistant to access the perineum and genitalia intraoperatively. The operating table is prepared with egg-crate foam taped to the table and a folded sheet placed under the egg-crate foam to facilitate securing the arms. The friction between the egg-crate foam and the patient's skin will help prevent cephalad slippage or movement when the table is in the full Trendelenburg position. Some centers advocate the use of a gel pad instead of egg-crate foam between the operating table and the patient's skin because of reports of chafing and skin breakdown. The patient is placed in the supine position with the buttocks at the end of the table break. Prior to induction of anesthesia, compression stockings and sequential compression devices are placed on the patient's lower extremities. The legs are placed in Allen Yellofin stirrups (Allen Medical Systems, Acton, MA, USA) with the knees flexed. The foot of the table is then lowered until it is perpendicular to the floor. Care should be taken to align the toe, knee, and opposing shoulder, to ensure the heels are touching the heel of the boot, and to check that the calves have adequate space to avoid popliteal artery occlusion, peroneal nerve injury [6], or the devastating complication of lower extremity compartment syndrome [7]. The anesthesiologist should evaluate

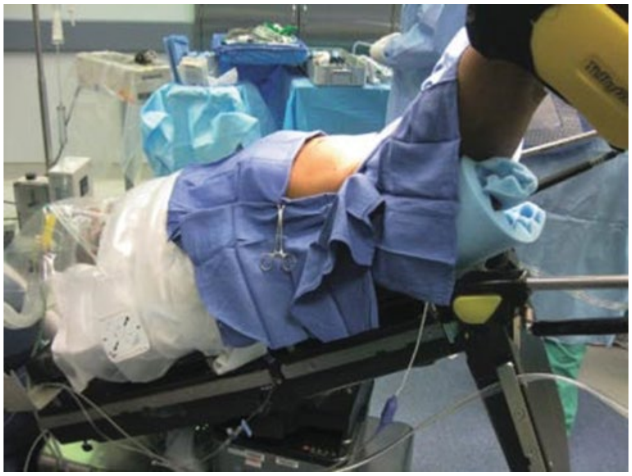

**Figure 76.5** Patient positioning in low lithotomy with the full Trendelenburg position for robotic pelvic surgery.

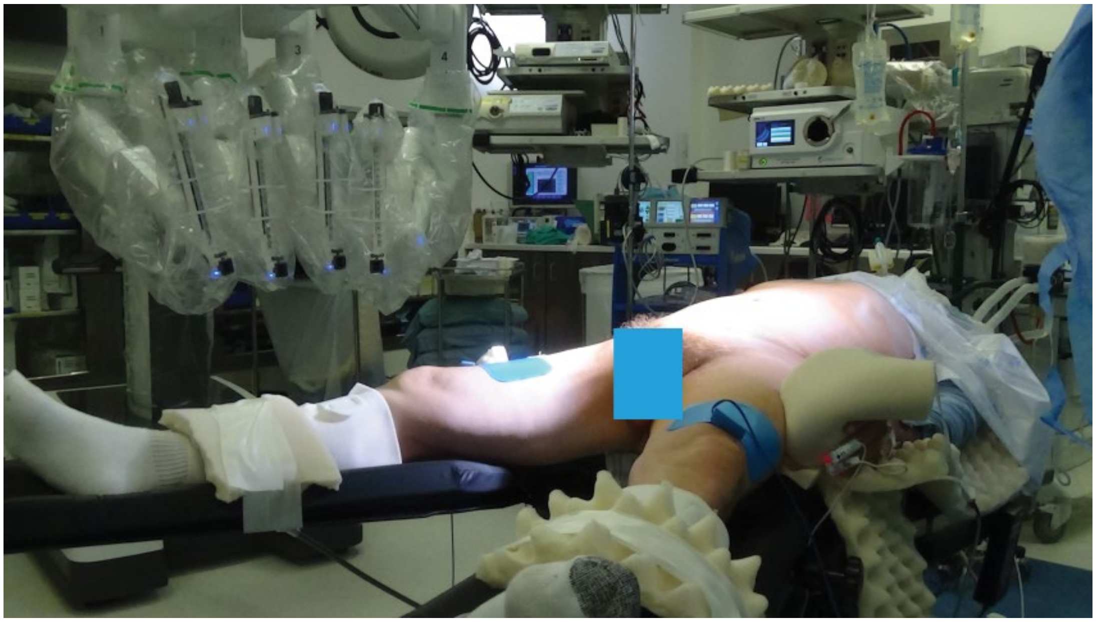

**Figure 76.6** Patient positioning in split-leg position for robotic pelvic surgery.

the position of the patient's head before and after applying the Trendelenburg position in order to monitor for slippage. The arms are tucked at the patient's side with the preplaced sheet under the gel pad. Alternatively, arm sleds can be utilized to secure the arms without tension; however, excess arm compression can result in temporary neuropraxia. The fingertips are positioned at the anterolateral thigh. The elbows and wrists are protected with gel padding, and small foam rolls are placed in the patient's hands. Care should be taken to ensure that vascular lines and the pulse oximeter are properly functioning. The arms should be secured low enough for the prepped field to include the area lateral to the anterior superior iliac crest. Obese patients may require an arm board on the side of the table to support the arms. We do not recommend routine use of shoulder straps or taping the shoulders in a harness fashion because of the risk of brachial plexus injury [8, 9]. We recommend using foam-wrapped 8 cm cloth tape across the chest to prevent cephalad slippage in obese patients only. Care should be taken to ensure the chest tape does not impede mechanical ventilation.

The patient is then prepped and draped from the costal margin to the mid thighs, including the genitalia and perineum. Surgical site preparation and preoperative antibiotic prophylaxis recommendations are the same as for laparoscopic renal surgery. An LAVH drape is useful for robotic pelvic surgery as it is a combination leg and laparoscopic drape. The field is established such that the bedside assistant can have access to the perineum and genitalia for intraoperative application of perineal pressure during initial anastomotic suture placement and for Foley manipulation. An 18 Fr Foley catheter is placed, sterile, on the field and the anesthesia team should place an orogastric tube.

After initial insufflation and port placement, the patient should be placed in a steep Trendelenburg position. For the da Vinci Si and earlier-generation robots, the robot is brought in for docking between the legs. The Allen Yellowfin stirrups should be low enough to accommodate the robot. For the da Vinci Xi robot, our preference is to use the split-leg position and dock the patient cart to the patient's side. Once the robot is docked, there should be no additional manipulation of the table position.

## Positioning pitfalls

Suboptimal positioning can not only lengthen operative times and lead to surgeon frustration, but can lead to devastating complications. Despite proper patient positioning and preparation, patient injuries have been reported as a consequence of positioning during laparoscopic and robotic surgeries [6, 10]. Wolf et al. reported on 1651 procedures that resulted in 46 neuromuscular injuries in 45 patients (2.7%), including abdominal wall neuralgia, extremity sensory deficit, extremity motor deficit, clinical rhabdomyolysis, shoulder contusion, and back spasm. Patients with rhabdomyolysis were more often male, were heavier, and underwent longer procedures. Patients with motor deficits were older. Preexisting nerve dysfunction predisposes patients to motor nerve injury.

It is important for the surgeon to remain comfortable throughout the procedure to avoid pain or fatigue. Interestingly, 28% of surgeons in the 18 academic institutions included in Wolf et al.'s study reported frequent neck pain and 17% reported frequent shoulder pain [6]. Measures taken by surgeons to alleviate neuromuscular strain included lowering the table maximally, using lifts on the floor, altering the manner in which they held instruments (without fingers through the handles), and altering the position of the monitors.

A devastating complication of robotic pelvic surgery is lower extremity compartment syndrome, which can occur when the patient is placed in Allen Yellofin stirrups in the extreme Trendelenburg position. This complication may require lower extremity fasciotomy [7, 11]. Proper positioning is key to prevention, specifically ensuring the patient's ankle, knee, and contralateral shoulder are aligned in the stirrup, and that gel pads are used directly in contact with the patient's skin to avoid cephalad slippage while in the Trendelenburg position. A high index of clinical suspicion will facilitate early recognition and prompt treatment.

There have been reports of patients developing ischemic optic neuropathy after laparoscopic radical prostatectomy, thought to be a result of a combination of long operative time and the Trendelenburg position [12]. Intraocular pressure measurements in surgical patients confirmed a higher intraocular pressure in patients in the Trendelenburg compared to the supine position [13]. However, the direct clinical consequences of sustained elevated intraoperative intraocular pressures are not known.

## Positioning for other robotic procedures

### Other robot-assisted laparoscopic pelvic surgery

Positioning for a robot-assisted laparoscopic radical cystectomy and for robot-assisted ureterovesical reimplant is similar to that for robot-assisted laparoscopic radical prostatectomy. The only difference is shifting port placement slightly cephalad to allow for proximal ureteral dissection and for extended bilateral pelvic lymphadenectomy. The camera port is placed 2 cm above the umbilicus and the two robotic ports are placed approximately at the level of the inferior border of the umbilicus.

### Transperitoneal robot-assisted laparoscopic renal surgery

Positioning for robot-assisted laparoscopic kidney surgery is similar to that for the pure laparoscopic approach. Depending on operating room configuration, the operating table may need to be rotated 90° to accommodate docking the robot. For the da Vinci Si and earlier-generation robots, the robot is docked at an angle from the ipsilateral side of the table in a direct line between the camera port and the renal hilum. For the da Vinci Xi, the robot is docked perpendicular to the patient's back, followed by adjustments with the boom to target its position over the camera port as previously described.

## Conclusions

Time spent properly setting up the operating room and positioning the patient is invaluable. The entire urologic team should be involved in the process with the goal of optimizing outcomes.

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## 77

# Patient Preparation and Operating Room Setup for Robotic Surgery

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## Introduction

Since the advent of robotic surgery less than two decades ago, urologists have been on the leading edge of research into this technology's role in the care of surgical patients. Robotic approaches have now supplanted laparoscopic and even open surgery for many common urological diseases. As the indications and complexity of robotic urological surgery has grown, so too has the body of research describing its relative risks and benefits. Though few randomized trials exist, the common thread among this work is encouraging. Robotic urological surgery is at least as efficacious as the conventional techniques that it complements, often with decreased postoperative pain, less blood loss, faster recovery, shorter hospital stays, and improved cosmesis. Critics of robotic surgery point to higher costs, while other analyses actually suggest potential for substantial cost savings [1]. Additionally, there exists the intangible benefit of improving patient access to minimally invasive surgery not always available with conventional laparoscopy. Much of this work is ongoing, but one thing has become clear: patients who are candidates for robotic surgery pose a unique set of clinical and technical challenges. Knowledge of these factors preoperatively is critical to ensuring the highest likelihood of successful surgical outcomes. The purpose of this chapter is to provide a comprehensive review of patient preparation and operating room setup for robotic urological surgery.

## Patient selection

### History and physical

Many considerations in patient selection for robotic surgery are the same as those for conventional laparoscopic surgery. As with all preoperative consultations, this begins with a thorough history and physical examination. Urologists should pay particular attention to cardiac and pulmonary comorbidities. In all patients, abdominal insufflation with carbon dioxide raises the risk of clinically significant hypercarbia. Patients with chronic obstructive pulmonary disease (COPD) are at particularly high risk. When pneumoperitoneum is combined with steep Trendelenburg positioning for certain pelvic organ access, anesthetic considerations including higher driving pressures for adequate ventilation may arise. Urologists should be similarly cautious in patients with structural cardiac disease. Hypercarbia may be arrhythmogenic in such patients when superimposed on preexisting dysfunction. In patients with these or other concerning comorbidities, preoperative medical consultation for further testing, risk stratification, and medical optimization is reasonable before proceeding with elective surgery. Physical examination in anticipation of robotic surgery is the same as that before any urological surgery. However, one should pay special attention to the presence of surgical scars which may suggest a surgical history that patients have forgotten to disclose. Although some retrospective studies have demonstrated equivalent outcomes in such patients with

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a history of intra-abdominal surgery who go on to have open or laparoscopic urological surgery, this may be the result of appropriate patient selection rather than true equipoise [2]. Patients with a history of multiple abdominal surgeries may be better served with an open or retroperitoneal approach as indicated.

### Indications and contraindications

The indications for robotic urological surgery are essentially the same as those for the corresponding open or laparoscopic techniques. As the body of comparative research grows, we may soon be able to delineate which patients stand to benefit the most from robotic surgery. In the meantime, the decision is largely a matter of surgeon preference, comfort, technical expertise, and robot availability.

There are relatively few absolute contraindications to robotic surgery. These include uncorrectable coagulopathy, significant abdominal wall infections, massive hemoperitoneum, generalized peritonitis, intestinal obstruction unless accompanied by an intention to treat, and suspected malignant ascites. Given that the majority of urological robotic surgeries are performed on an elective basis, these absolute contraindications to robotic surgery would likely be impediments to the corresponding open or laparoscopic alternatives as well.

In contrast, robotic surgeons disagree more readily regarding the relative contraindications to robotic surgery. The most well studied of these is obesity. Urologists have traditionally hesitated to offer robotic surgery to morbidly obese patients out of a concern for the physical constraints imposed by a thick body wall. This includes the possibility of inadequate robotic instrument length, a decreased ability to pivot Trocars, and higher pressures required for equivalent pneumoperitoneum. Recent work has validated some of these concerns, with a study of over 1600 robot-assisted radical prostatectomies demonstrating increased operative time and estimated blood loss in patients with a body mass index (BMI) over 40 kg/m$^2$ [3]. Garcia-Roca et al. reviewed their experience with renal transplantation in patients with an even higher BMI cutoff of 45 kg/m$^2$; their group found no difference in patient and graft survival rates [4]. Surprisingly, it remains less clear whether the risk of complications with robotic surgery in obese patients is related to the degree of obesity. Two recent studies of patients undergoing robot-assisted radical prostatectomy (RARP) demonstrated conflicting results. Khaira et al. found that BMI >30 kg/m$^2$ was associated with longer anastomotic times, but that there was no significant difference in the total duration of surgery or the frequency of postoperative complications [5]. In contrast, Ahlering et al. found that obese men with BMI >30 kg/m$^2$ had more surgical complications and a slower recovery of urinary function, and required more time to return to baseline activities after RARP [6]. Although obese patients in this study had high levels of preoperative urinary and sexual dysfunction that may have confounded these findings, this serves as an important reminder for urologists to counsel obese patients about their increased surgical risk, even when the surgery is performed robotically.

Other relative contraindications to a robotic approach include pelvic fibrosis, organomegaly, large-volume ascites, hernias, vascular aneurysms, and pregnancy. The last of these is controversial, with some arguing that robotic surgery may still be performed safely in pregnant women. O'Connor et al. reported performing laparoscopic nephrectomy in a pregnant woman, which has now been replicated robotically by Ramirez et al. [7, 8]. When urologists have access to a multidisciplinary team including specialists in obstetrics, anesthesia, and high-risk maternal fetal medicine, gravid women may be reasonably counseled about the risks and benefits of undergoing robotic urological surgery. Further research is necessary to precisely delineate the risks and benefits of robotic urological surgery in this high-risk group.

Irrespective of the presence of relative contraindications to a robotic approach, all patients should be counseled preoperatively about the risk of conversion to an open procedure. Contemporary analyses suggest that this risk is somewhere between 1 and 3% in case series of robotic nephrectomy and prostatectomy, as an example [9, 10]. The conversion rate may be elevated for high-risk patients and those surgeries done at low-volume centers, although retrospective studies are likely affected by patient selection, with high-risk patients encouraged to undergo forego robotic surgery, thus lowering the resulting conversion rate [9].

## Patient preparation

Urological and general surgery have both seen recent paradigm shifts in the management of anticipated postoperative ileus. Whereas extensive bowel preparations preoperatively and prolonged bowel rest postoperatively have long been the norm, both conventions are now being questioned. In one large study of over 700 men undergoing radical prostatectomy with or without preoperative mechanical bowel preparation, Sugihara et al. found no difference between the two groups with respect to overall complications, operative time, length of stay, and total costs [11, 12]. Perhaps even more convincingly, Ramirez et al. performed a systematic review to describe the incidence of postoperative ileus in patients after radical cystectomy with all types of urinary diversion [13]. Not only did mechanical bowel preparation fail to prevent postoperative ileus, but in many studies was in fact associated with a prolonged time to first bowel movement [13]. Although practice patterns continue to vary, such data have been used to guide the continued refinement of early recovery care pathways for patients undergoing urological surgery [14].

Other components of preoperative preparation are either less standardized or have not yet been studied rigorously. Most urologists elect to type and screen patients preoperatively, rather than to crossmatch for blood. Studies of robot-assisted partial nephrectomy versus open nephrectomy have demonstrated lower transfusion rates for the robotic cohort [15]. Similar data exist for large studies of patients undergoing robot-assisted radical prostatectomy, who require fewer transfusions than do those who undergo open surgery [16]. Additional preoperative preparation is largely driven by individual patient needs. The American Urological Association (AUA) has issued a comprehensive best practice policy statement on perioperative antimicrobial prophylaxis, and should be used to guide decision making for robotic surgery as well [17].

## Operating room

### Robotic surgical system components and physical setup

The physical layout of operating rooms used for robotic urological surgery varies. However, adherence to certain key principles is necessary to ensure optimal patient outcomes and to minimize costly operative time. First, the room size itself may become rate-limiting; operating rooms used for robotic surgery must not only accommodate a large amount of additional equipment, but be large enough to facilitate variable patient positioning and the movement of robotic components. The robotic surgery platform that is currently in widespread use is the da Vinci Robotic System (Intuitive Surgical, Sunnyvale, CA, USA). This system is composed of three main components: the patient-side cart (robotic tower), the surgeon console, and the vision system (Figure 77.1). The patient-side cart is the operative component or “slave” unit of the system which contains robotic arms that hold the Endowrist instruments that are used to perform surgery. The surgeon console consists of the stereo viewer that integrates the imaging of the surgical field acquired by the endoscopy, the master controller by which the surgeon can manipulate the surgical instruments, and foot pedals which control camera movement, robotic arm selection, and energy delivery. Additionally, a central touchscreen control panel allows for management of various functions. The vision system houses the image processing equipment, light source, insufflator, and electrosurgical unit, along with a monitor and various minor components. The specific positioning of these components depends on the constraints of individual operating rooms, as well as patient positioning for the procedure in question. The introduction of the da Vinci Xi system allows for flexibility in operating room setup as the new device enables improved anatomic access regardless of

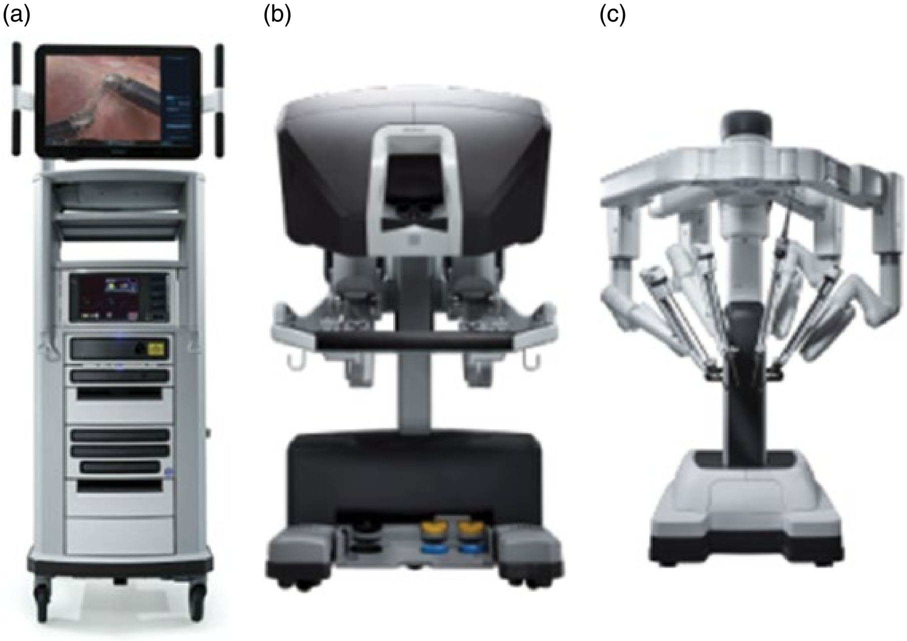

**Figure 77.1** (a) da Vinci Xi vision cart, (b) surgeon console, and (c) patient-side cart. *Source:* Intuitive Surgical, Inc., Calfiornia, USA. Reproduced with permission of Intuitive Surgical, Inc.

patient-side cart position and allows the endoscope to be placed via any surgical port. Longitudinal studies suggest that the presence of ancillary staff who are familiar with and can efficiently troubleshoot the robotic surgery equipment is critical to success [18]. Lastly, but importantly, all operating rooms equipped for robotic surgery should have a complement of open instruments either open or immediately available, should the need for them arise. A complete list of suggested basic equipment for robotic surgery is provided in Box 77.1.

**Box 77.1 Basic equipment for robotic surgical procedures.**

Surgeon console
Patient-side cart
Mobile video cart with monitor[a]
Camera, high-resolution, and control box[a]
High-intensity light source[a]
Electrosurgical unit[a]
$CO_2$ insufflator[a] with $CO_2$ tank or wall supply
Secondary video cart/monitor
$CO_2$ insufflation tubing
0 and 30° camera lens
Scope warmer
Fiber-optic light cable
Electrosurgical cords
Aspiration–irrigation system with double canister suction apparatus
High-capacity media recorder (optional)
Veress needle
12 mm Trocar[b]
Three 8 mm robotic Trocars[c] (for da Vinci S, Si, Xi, or fourth arm)
5 mm Trocar (optional assistant)
Aspiration–irrigation tubing and probe
Robotic monopolar scissors
Robotic bipolar Maryland grasper
Robotic prograsp
Robotic fenestrated bipolar electrocautery (optional)
Robotic Harmonic scalpel (optional)
5 mm atraumatic grasping forceps
Laparoscopic needle driver
Laparoscopic scissors
Hem-o-lok ligation system (Teleflex Medical, Research Triangle Park, NC, USA)
10 mm titanium clip applier (optional)

[a] Components housed in the vision system.
[b] For Xi system, 12 mm Trocar is used as assistant port. For earlier systems, an additional Trocar is used as camera port.
[c] For Xi system an additional robotic Trocar is used as a camera port.

## Patient positioning: general concepts

As with all types of surgery, patient positioning for robotic urological surgery is largely predicated on the anatomical site in question; preparation and positioning for flank surgery is inherently different from pelvic surgery. However, certain principles are universal. Patients should be positioned in ways that maximize access for robotic instruments, are ergonomic for the assistant, and minimize the likelihood of positioning-related complications. Primary considerations in positioning include individual surgeon preference, surgical approach (transperitoneal vs. retroperitoneoscopic), laterality, and organ of interest.

## Patient positioning: retroperitoneal kidney

For retroperitoneal surgery in the upper abdomen, the patient is placed in the lateral decubitus position, with the site of interest easily accessible. The patient’s bottom leg is flexed, the upper leg straight, and all pressure points are padded with pillows, foam, and typically an axillary roll. The table is flexed to increase the distance between the 12th rib and the iliac crest, maximizing access to the flank. Following port placement, the assistant remains facing the front of the patient. The robot patient-side cart is then docked on the contralateral side (i.e. the patient’s back), or from the side of the patient’s head (Figure 77.2).

## Patient positioning: transperitoneal kidney

For transperitoneal surgery in the upper abdomen, a modified lateral decubitus position is used (Figure 77.3). The robot is docked from the table’s contralateral side (Figure 77.4). This maximizes the assistant’s mobility while minimizing interference from the robotic arms.

## Patient positioning: pelvic

Lastly, for pelvic surgery, the patient is placed in the Trendelenburg position, either supine (da Vinci Xi) or with the legs either on split-leg positioners or in stirrups (da Vinci Si) (Figure 77.5). The additional mobility and rotational capability of the Xi patient-side cart allows for positioning at the patient’s side. However with the Si, the patient-side cart is docked between the patient’s legs, allowing the assistant to stand on either side (Figure 77.6). The addition of auxiliary video monitors provides flexibility in the location of the bedside assistant, can limit the necessity of moving the vision tower for different procedures, and provide a view of the procedure for the scrub assistant throughout the case.

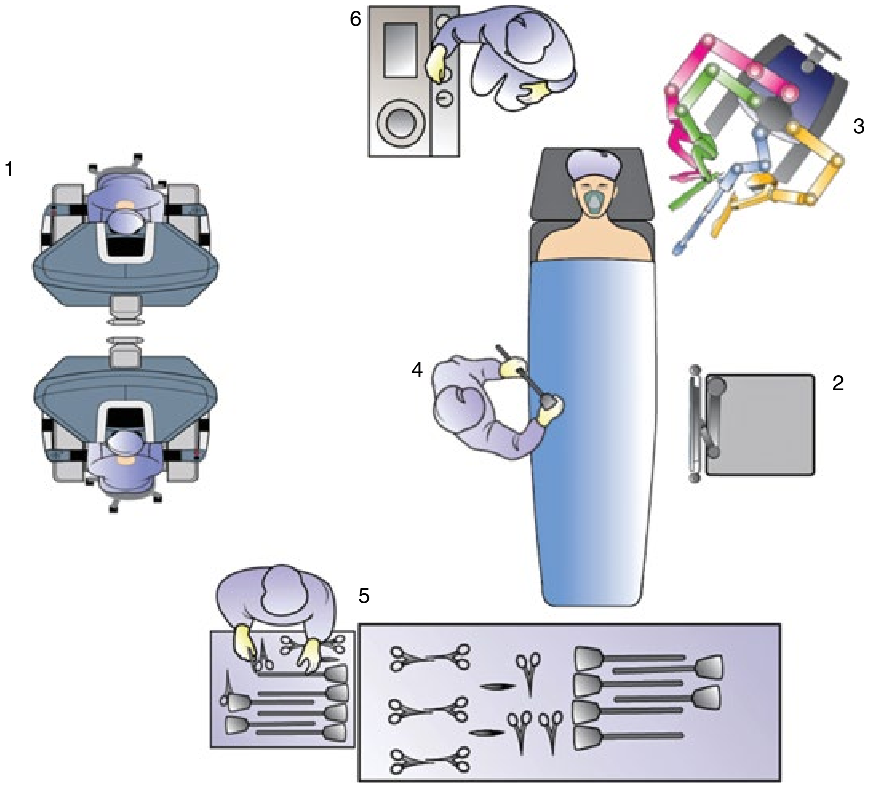

**Figure 77.2** Patient positioning for left retroperitoneoscopic upper tract surgery. Surgeon console (1), robotic tower (2), patient-side cart (3), bedside assistant (4), scrub assistant (5), anesthesia (6). *Source:* Intuitive Surgical, Inc., Calfiornia, USA. Reproduced with permission of Intuitive Surgical, Inc.

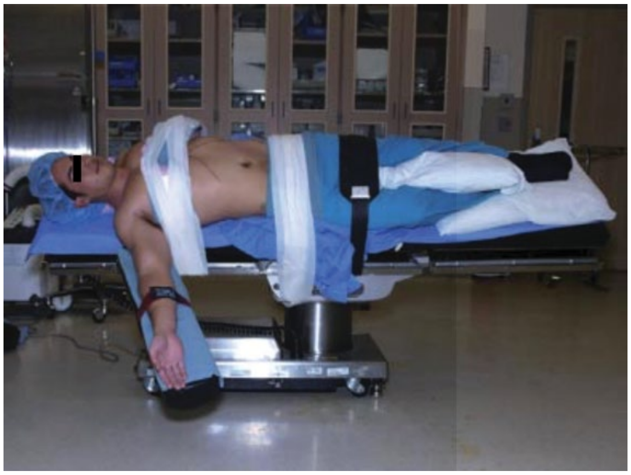

**Figure 77.3** Modified lateral decubitus position used for robotic transperitoneal renal surgery.

## Complications

Failure of the da Vinci system itself is quite rare, and likely becoming even more so as surgeon and engineering experience grows. In a single institution study of 1797 procedures performed with the early da Vinci S system from 2005 to 2008, there were 43 cases of mechanical failure (2.4%). However, these required that only three cases (0.17%) be converted to open or laparoscopic approaches [19]. In a larger study of 11 high-volume institutions performing over 8000 robotic cases, the rate of critical failure causing either conversion or case cancellation was 0.4% [20]. While such events are clearly problematic and reinforce the need for appropriate preoperative patient counseling, they are exceedingly rare and often outside of the surgeon's purview.

In contrast, urologists must remain constantly vigilant of the pitfalls of positioning when preparing patients for robotic surgery. These dangers are similar to those seen with other types of surgery. However, because robotic surgery often prolongs operative time, patients are exposed to these dangers to a greater degree. For example, the use of stirrups is associated with popliteal artery occlusion, peroneal nerve injury, and even lower-extremity compartment syndrome. In one study of 17 high-volume centers performing RARPs in the United Kingdom between 2004 and 2011, lower-extremity compartment syndrome was diagnosed following nine of 3110 procedures, for an incidence of 0.29% [21]. Although this rate is low, seven of nine patients went on to require lower extremity fasciotomy. The authors identified console time over 4 hours, early surgeon learning curve with fewer than 20 robotic cases, BMI >30 kg/m$^2$, and peripheral vascular disease as risk factors [21]. Although some of these risk factors are not easily modifiable, this study serves as an important reminder for the surgeon to check all aspects of positioning before beginning a case.

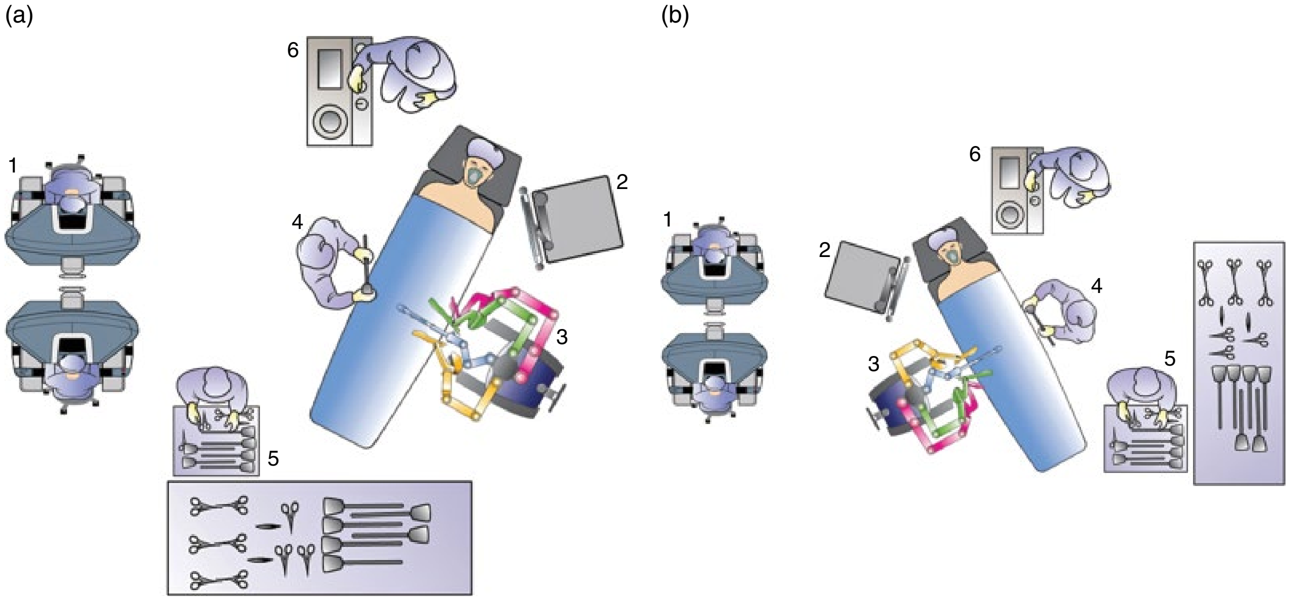

**Figure 77.4** Patient positioning for left (a) and right (b) transperitoneal renal surgery. Surgeon console (1), robotic tower (2), patient-side cart (3), bedside assistant (4), scrub assistant (5), anesthesia (6). *Source:* Intuitive Surgical, Inc., Calfiornia, USA. Reproduced with permission of Intuitive Surgical, Inc.

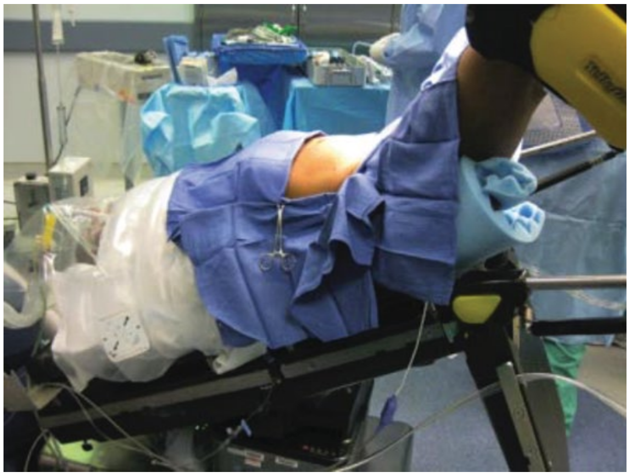

**Figure 77.5** Patient positioning in low lithotomy with legs in stirrups for pelvic surgery.

Similar risks exist to a patient's upper extremities. Older laparoscopic literature suggests that patients may be at risk of abdominal wall neuralgias, injuries to peripheral nerves, and musculoskeletal injury [22]. These same risks would be expected for robotic approaches to urological surgery, given the similarities in positioning. Case reports have now emerged of neurological injury following robotic surgery. In one study, Devarajan et al. identified three patients with upper and middle brachial plexus trunk injury following RARP [23]. The authors theorized that positioning in steep Trendelenburg caused abnormal distraction forces on the abducted arm, which over several hours led to brachial plexus neuropathy [23]. Echoing similar research described above, the authors argued for particular caution in patients who undergo cases with a prolonged operative time.

An additional complication that is thought to be related to positioning in steep Trendelenburg is the development of ischemic optic neuropathy (ION). This phenomenon was described by Weber et al. after two patients developed postoperative ION following laparoscopic radical prostatectomy. The authors theorized that this complication was due to venous stasis and facial edema caused by a prolonged surgical time with the head of the bed down [24]. Alarmingly, similar findings and even complete postoperative visual loss have now been reported after robotic pelvic surgery [25]. To clarify this relationship, Wen et al. used a national database to identify positioning-related complications in patients following robotic or conventional laparoscopic radical prostatectomy [26]. Although ocular complications contributed the most to the overall cohort's complication rate of 0.4%, the authors found that robotic surgery was associated with a decreased risk as compared to conventional laparoscopy [26]. Further research is clearly necessary to delineate risk factors such that urologists may take pre-emptive steps to minimize the likelihood of positioning-related complications.

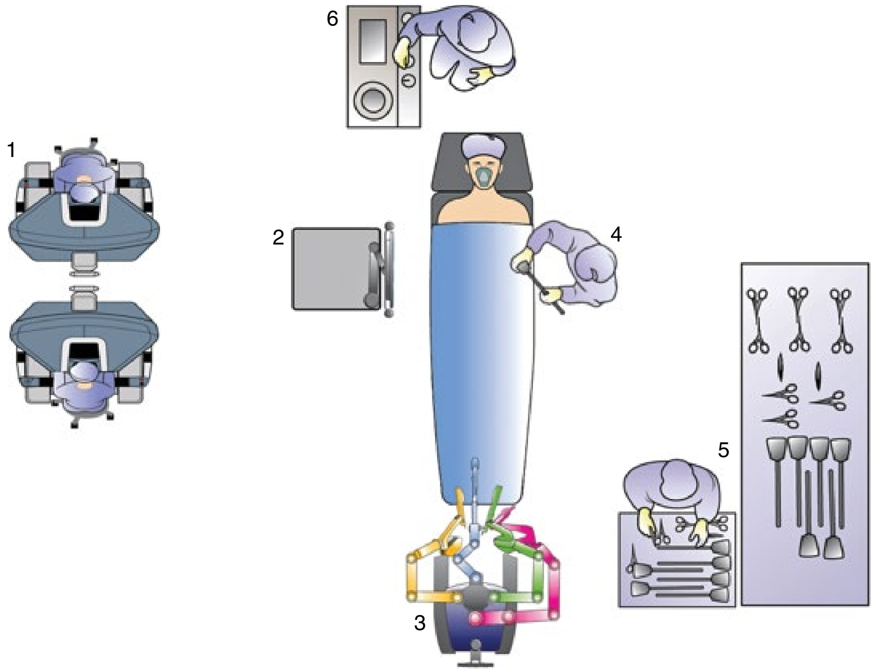

**Figure 77.6** Patient positioning for pelvic surgery. Surgeon console (1), robotic tower (2), patient-side cart (3), bedside assistant (4), scrub assistant (5), anesthesia (6). *Source:* Intuitive Surgical, Inc., Calfiornia, USA. Reproduced with permission of Intuitive Surgical, Inc.

## Conclusion

Robotic surgery is becoming an increasingly important part of the urologist's armamentarium, with robotic techniques emerging as the standard of care throughout the scope of urological practice. However, this development requires caution. Success in robotic surgery requires extensive preparation on the part of the patient, urologist, and operating room team. Although existing work has begun to clarify some of these issues, further research is necessary to continually improve perioperative care. Such work will ensure that robotic surgery performed by urologists in the future will be done even more safely and effectively than today.

Review accompanying Video 77.1.

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# 78

# Physiologic Considerations in Laparoscopic and Robotic Surgery

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## Introduction

Laparoscopic and robotic surgery challenge the patient with unique physiologic stresses. These stresses are primarily due to abdominal insufflation, but may be due to positioning requirements. Pneumoperitoneum, the result of abdominal insufflation, is considered necessary for visualization of the target organs, and may be maintained for prolonged periods of time. This can result in physiologic disturbances both during and after surgery as a result of increased abdominal pressure and absorption of the insufflated gas.

The introduction of laparoscopic cholecystectomy in 1990 and laparoscopic nephrectomy in 1991 proved pivotal for the future of laparoscopy, as for the first time solid organs could be removed with laparoscopic instrumentation [1, 2]. Following these advances, two major changes occurred in the field of laparoscopic surgery: first, the complexity and – consequently – the duration of minimally invasive surgical cases increased dramatically. Second, the patients selected for laparoscopic and robotic surgery covered an increasingly broader spectrum of disease states, with many patients having underlying cardiac and pulmonary comorbidities. As a result, the minimally invasive surgeon today must give significant consideration to the physiologic impact of prolonged pneumoperitoneum. While most patients tolerate the physiologic changes associated with laparoscopy well, there are occasional life-threatening complications as a result of the physiologic reaction to the laparoscopic environment.

Pneumoperitoneum and patient positioning required for laparoscopy have several well-understood physiologic effects which will be reviewed extensively in this chapter, along with the complications of pneumoperitoneum and consideration of methods of altering pneumoperitoneum that mitigate certain unwanted side effects.

## Impact of patient positioning

A number of patient positions are used during laparoscopy to more easily target the organ of interest. In urology, the lateral position is commonly used for upper urinary tract and retroperitoneal procedures; this position has little effect on hemodynamics unless there is extreme flexion or improper use of the kidney rest such that the vena cava is compressed, wherein venous return to the heart can be reduced [3]. The lateral position can lead to ventilation–perfusion mismatch and changes to pulmonary compliance for the dependent lung, as well as over-inflation and potential barotrauma to the nondependent lung.

During upper abdominal surgery, which is uncommon for urologic procedures, the patient can be placed head up (reverse Trendelenburg) to drop the bowel away. In most cases, this position demonstrates improved pulmonary mechanics [4–6]. However, this position also decreases cardiac output [7, 8] and can lead to profound hypotension and cerebral hypoperfusion, particularly in patients with pre-existing dysfunction of cerebral autoregulatory mechanisms, such as those with chronic hypertension, history of cerebrovascular accident, or carotid occlusive disease.

A position more commonly used by the urologist is Trendelenburg (head down), which can facilitate pelvic, lower urinary tract surgery such as radical

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

prostatectomy. This position increases cardiac output modestly [9–12]. Additionally, it restricts diaphragmatic movement and increases ventilation–perfusion mismatch [5, 13, 14]. As one might expect, the effects on cardiovascular and respiratory physiology are stronger with steeper head-down angles [15]. Table 78.1 compares the cardiovascular effects of the head-up and head-down positions.

## The gaseous medium: carbon dioxide and other insufflation agents

Today, the vast majority of laparoscopic and robotic cases are performed with carbon dioxide ($CO_2$) pneumoperitoneum. During the development of laparoscopy, the early cases were performed using oxygen and room air for insufflation [16]. These proved to be dangerous and quickly abandoned due to the significant potential for venous air embolism, intra-abdominal explosion, and combustion. Carbon dioxide was selected as it met a number of important criteria for the ideal gas for insufflation: it is readily available, inexpensive, noncombustible, rapidly soluble in plasma, and removed via respiration [17].

Due to the favorable properties of $CO_2$, it was adopted quickly. The rapid absorption of $CO_2$ decreased the chance of postoperative abdominal distention, and lowered the probability of developing a gas embolism. These same properties have dangers as well: they can lead to hypercapnia, hypercarbia, and cardiac dysrhythmia. While these sequelae are typically self-limiting, they can be problematic for patients with poor cardiopulmonary function and those with chronic obstructive pulmonary disease, as the minute ventilation may not be able to be increased sufficiently to compensate for the increased $CO_2$ absorption.

Other insufflation agents such as nitrogen dioxide ($N_2O$) and helium are possible alternatives in the select patient. While $N_2O$ came into favor in the 1970s and 1980s due to low cost, decreased peritoneal irritation, and fewer cardiovascular adverse effects compared to $CO_2$, case reports of intraoperative explosions due to its combustibility severely limited its use in the therapeutic setting [18–21]. In fact, it should be limited to cases where electrosurgical equipment is not needed. Helium, in contrast, is both inert and noncombustible. Rademaker et al. demonstrated favorable effects of helium on atrial partial pressure without hypercarbia or acidosis in a porcine model [22]. Helium insufflation may be useful in select patients with pulmonary disease who would not tolerate the hypercarbia associated with $CO_2$ insufflation [23]. The main drawback of helium is its low blood solubility, which may portend to a higher risk of gas embolism [24].

Considering the widespread, nearly exclusive use of $CO_2$ insufflation for laparoscopic procedures, the remainder of the chapter will focus on pneumoperitoneum with $CO_2$.

**Table 78.1** Effects of patient position on hemodynamic parameters compared to the supine position.

| Hemodynamic parameter | Head up | Head down |
|---|---|---|
| Heart rate | ↑ | ↓ |
| Mean arterial pressure | ↓ | ↑ |
| Systemic vascular resistance | ↑ | ↓ |
| Cardiac output | ↓ | ↑ |
| Intracranial pressure | ↓ | ↑ |

## Physiologic organ changes caused by insufflation with carbon dioxide

### Effect on the lungs

Pulmonary physiology is affected by a number of aspects during laparoscopic surgery. Patient size and the existence of underlying pulmonary pathophysiology certainly affect how the patient will respond to insufflation. The mechanical effects of pneumoperitoneum and the absorption of $CO_2$, however, are the main drivers of the physiologic changes seen during laparoscopy (Table 78.2).

As pneumoperitoneum increases the intra-abdominal pressure (IAP), it exerts a mechanical limitation to excursion of the diaphragm. This limitation results in decreased lung capacity and compliance, with eventual ventilation–perfusion mismatch and shunting [25, 26]. Consequently, there is an overall decrease in vital capacity, functional residual capacity, total lung volume, and

**Table 78.2** Respiratory effects of laparoscopy with intra-abdominal pressure of 10–20 mmHg.

| Respiratory parameter | Change |
|---|---|
| Chest wall mechanical resistance | ↑ |
| Peak inspiratory pressure | ↑ |
| Pulmonary compliance | ↓ |
| Alveolar dead space | ↔ or ↑ |
| Functional reserve capacity | ↓ |
| Forced vital capacity | ↓ |
| $FEV_1$ | ↓ |
| Peak expiratory flow | ↓ |

pulmonary compliance, alongside increases in peak inspiratory pressure [4, 5, 27]. These changes are exacerbated by obesity or other causes of pre-existing atelectasis and decreased lung volumes [4, 28].

Carbon dioxide has many properties, including its rapid solubility and quick absorption into the circulation, making it the ideal gas for insufflation. As such, it must be eliminated efficiently by the lungs. While normal $CO_2$ production in the average adult ranges from 150 to 200 ml/min [29, 30], the rate of $CO_2$ absorption during laparoscopy is 14–48 ml/min [31–33]. Adjustments must be made in minute ventilation by either increasing tidal volume or respiratory rate to mitigate the effects of increased blood levels of $CO_2$. If not corrected for, hypercarbia can lead to respiratory acidosis, which can depress cardiac function and cause arrhythmia. Subcutaneous emphysema, increased IAP, extraperitoneal insufflation, and prolonged surgery can also increase the rate of $CO_2$ absorption [34].

The minimally invasive surgeon must be aware of the compounding effects of $CO_2$ absorption over time, and how they can linger in the postoperative period. In a prospective study of changes in end-tidal $CO_2$ for healthy patients undergoing laparoscopic cholecystectomy, Meftahuzzaman et al. showed that significant alteration occurs 40 minutes after insufflation during cholecystectomy [35]. Many urologic cases can extend well past this period of time, and close monitoring of end-tidal $CO_2$ is imperative. Additionally, some degree of $CO_2$ is also sequestered in the skeletal system, which is the largest reservoir in the body, and it is eliminated slowly in the postoperative period. This can be particularly problematic for patients with pre-existing cardiopulmonary dysfunction, and these patients must be monitored closely [36].

## Effect on the heart and hemodynamics

Several hemodynamic effects are seen as a result of increased IAP, including decreased cardiac output, increased mean arterial pressures (MAP), increased systemic vascular resistance (SVR), and increased pulmonary vascular resistance (Table 78.3). At low insufflation pressures (<10 mmHg) there is an initial increase in venous return; this “auto-transfusion” causes the cardiac output and cardiac index to increase. Conversely, above 20 mmHg, venous return is hindered and there is a considerable decrease in cardiac output [37].

**Table 78.3** Hemodynamic effects of laparoscopy with intra-abdominal pressure of 10–20 mmHg.

| Hemodynamic parameter | Change |
|---|---|
| Central venous pressure | ↑ |
| Systemic vascular resistance | ↑ |
| Heart rate | ↑ |
| Mean arterial pressure | ↑ |
| Cardiac output | ↓ |

Patient factors can attenuate the cardiac response to pneumoperitoneum. Volume status is important as hypovolemic patients tend to have a more exaggerated drop in cardiac output in response to increased IAP. This was demonstrated by Ho et al. using a porcine model of acute hemorrhage [38]. Therefore generous volume loading can be recommended for patients undergoing laparoscopic procedures. Additionally, there is evidence that vagal stimulation from peritoneal distention can also decrease cardiac output. In fact, pneumoperitoneum causes excessive stretching of the vagal nerve endings, which are richly distributed throughout the abdominal cavity, which can lead to bradycardia [39]. Patient positioning, particularly for deep pelvic surgery, also has a significant impact. The Trendelenburg position decreases venous return. This exacerbates the effect of increased IAP, which further decreases venous return due to caval compression [40] and increased venous resistance [41, 42]. Of note, the opposite effect occurs with reverse Trendelenburg.

Increased SVR and MAP are also attributable to the sympathoadrenal effects of increased IAP and $CO_2$ insufflation [43]. There is increased catecholamine production, presumably from both surgical stress and directly from the increased IAP. Early hypercarbia may also exacerbate this sympathomimetic effect; however, as hypercarbia progresses and acidosis becomes more profound, a cardiodepresent effect predominates. The renin-angiotensin system and vasopression are also postulated to be contributors to the increases in SVR [44–48]. There is a rapid increase in plasma renin activity during induction of pneumoperitoneum, and increased plasma renin activity positively correlates with MAP [49–51]. Additionally there is a significant increase in anti-diuretic hormone (ADH), which controls arterial blood pressure via receptors in vascular smooth muscle; this can provoke intense vasoconstriction and likely plays a key role in regulating hemodynamics during laparoscopy [46, 48].

A recent study by Rosendal et al. [52] sought to determine changes in preload, afterload, and cardiac function in the different phases of robotic prostatectomy, including induction of anesthesia, initiation of pneumoperitoneum, immediately after a 45° head-down tilt, 15 minutes later into the head-down tilt, after release of pneumoperitoneum, and 5 minutes after returning to a horizontal position. Central venous pressure increased threefold from baseline after induction of anesthesia, but no other preload parameters showed overload or demand. There was no change in cardiac contractility over time. Afterload increased significantly during $CO_2$ pneumoperitoneum and decreased compared with baseline after the release of pneumoperitoneum at the end of the case. Heart rate and cardiac index increased significantly during robot-assisted laparoscopic prostatectomy [52].

### Effect on the kidneys

Oliguria is a well-characterized side effect of sustained pneumoperitoneum. This is important to know, as relying on urine output alone as an indicator of fluid status can lead to fluid overload in overzealous hands. There are several possible causes of oliguria in this setting, which appear to occur at an IAP around 15 mmHg [53]. It is well documented that elevated IAP causes significant renal hypoxia and decreased renal blood flow [54]. One theory as to why this occurs is that there is a Page kidney effect, whereby applying renal parenchymal compression causes a decrease in urine output, glomerular filtration rate (GFR), and effective renal blood flow. Razvi et al. proved this experimentally by placing a pressure cuff at 15 mmHg on the left kidney of canines, thereby causing overall urine output to decrease [55]. Using a porcine model, Chiu et al. demonstrated that pneumoperitoneum-induced oliguria may also be due to increased serum aldosterone levels [56].

Elevated IAPs are thought to stimulate endogenous catecholamine release, another potential contributor to oliguria. Circulating levels of endothelin, a catecholamine, is increased in response to pneumoperitoneum [57]. Studies of unilateral renal vein compression in a rat model and a canine model showed decrease in GFR and urine osmotic pressure in both kidneys. In each case, circulating endothelin increased [53, 58].

Vasopressin has also been implicated as a contributor to oliguria. Krisch et al. demonstrated in a rat model that using vasopressin antagonists during periods of increased IAP improved renal function compared to control [59].

Other possible causes of oliguria have been studied and disproven. The decreased cardiac output seen with increased IAP is unlikely to affect renal output; studies have shown that normalization of the cardiac output with fluid resuscitation does not lead to increased urine output [60, 61]. Ureteral obstruction, similarly, is unlikely to contribute significantly. Patients with ureteral stents, which presumably remain unobstructed, do not have increased urine output [62]. Additionally, animal imaging studies with intra-operative urography show no evidence of ureteral obstruction during pneumoperitoneum [56].

Importantly, the renal effects from increased IAPs tend to subside in the immediate postoperative period in healthy patients with normal renal function [63]; however, those with pre-existing renal dysfunction may experience longer delays to return to baseline GFR [64]. A rabbit model of severe hydronephrosis showed that obstructed kidneys were more likely to suffer acute kidney injury when exposed to pneumoperitoneum [65]. While pneumoperitoneum was certainly feasible in rats with impaired baseline renal function, it appeared worse for those with acute kidney injury than chronic renal insufficiency [66]. Patients with significant cardiovascular dysfunction such as decompensated congestive heart failure also appear to be more susceptible to the adverse renal effects of pneumoperitoneum [67].

### Effect on the brain

Changes in cerebral blood flow during laparoscopy can occur even at a mildly increased IAP, and are due to several factors: cardiovascular changes, alterations in $P_aCO_2$, patient positioning, and the increased intra-abdominal and intra-thoracic pressures. Rosenthal et al. demonstrated increases in intracranial pressures (ICPs) and IAPs above 8 mmHg in a large-animal model [68]. This is thought to be due to compression of the vena cava, which increases central venous pressures and decreases drainage from the central nervous system.

Studies have also shown that cerebral blood flow velocity increases due to the increase in $P_aCO_2$ that results from $CO_2$ pneumoperitoneum [69]. Additionally, hypercapnia causes cerebral vascular vasodilation which increases ICP. This effect can be mitigated by hyperventilation.

A retrospective review of measured ICPs in patients undergoing laparoscopic ventriculoperitoneal shunt placement confirmed a correlation between IAP and ICP. The maximum recorded ICP was 25 mmHg, which can be dangerous for certain patients, particularly those with increased ICP at baseline or head trauma [70]. A study of patients undergoing robotic prostatectomy in steep Trendelenburg quantified the increase in ICP in these patients with ultrasonic evaluation of optic nerve sheath diameter, a surrogate measurement for ICP. This found a 12.5% increase during $CO_2$ pneumoperitoneum. Of note, three of the 20 patients studied showed ICPs above 20 mmHg without a deterioration of cerebral oxygen saturation or any neurologic complications [71].

### The stress response to insufflation

Several studies have compared open versus laparoscopic procedures in regards to the associated stress response elicited in the patient. Laparoscopy is generally shown to produce a decreased stress response compared to open procedures, but these results are often mixed.

Laparoscopy certainly does increase the MAP and SVR compared to open surgery. This increase in arterial pressure, in turn, increases ADH, plasma renin, and aldosterone levels [49]. Additionally, cortisol, human growth hormone, vasopressin, and other endogenous cathecholamines such as epinephrine and norepinephrine have been associated with an increase in IAP [45].

However, in a series of studies, acute-phase reactants typically seen during surgery, such as C-reactive protein and interleukin-6, are significantly lower as compared to open procedures [49, 72, 73]. There is also less hyperglycemia and leukocytosis seen [72, 73]. Notably, a recent study of patients undergoing laparoscopic adrenalectomy at varying IAPs showed that significantly higher levels of acute phase reactants were seen in patients given standard insufflation (12–14 mmHg) versus low pressure pneumoperitoneum (6–8 mmg) [74]. Such a difference was not seen in a prospective study by Landman et al., which concluded that stress factors, inflammatory markers, and other markers of immune activity were not statistically different between patients undergoing open versus laparoscopic nephrectomy. They postulate that the extent and length of surgery required for laparoscopic nephrectomy is often greater than laparoscopic cholecystectomy and that above a certain threshold (for laparoscopic or open surgery) the immune response reaches an upper limit [75].

Other markers of inflammatory response also point to the superiority of laparoscopy to standard open surgery. To demonstrate this, Dalgic et al. experimentally performed cecal-peritoneal abrasions in rats using either a standard open technique or laparoscopy with $CO_2$ pneumoperitoneum. There was a decreased inflammatory response seen, as well as decreased adhesion formation in the laparoscopy group [76].

Lastly, laparoscopic surgery, by virtue of causing tissue injury, activates the coagulation and fibrinolytic pathways, another part of the inflammatory cascade. In a prospective randomized trial of patients undergoing laparoscopic versus open cholecystectomy, Tsiminikakis et al. showed significantly less activation of the clotting system in laparoscopic surgery compared to open surgery [77].

## Complications of obtaining and maintaining pneumoperitoneum

While a number of physiologic changes occur due to pneumoperitoneum itself, some complications can occur during the establishment of pneumoperitoneum. A misplaced Veress needle or Trocar with subsequent insufflation can cause a number of potential problems.

Subcutaneous emphysema is the most common result of an improperly placed Veress needle or Trocar, but can also be due to excessive IAPs, malfunctioning equipment, or leaks around a laparoscopic port placed with an open technique. While it is usually harmless, it can in some circumstances lead to hypercarbia [78–80]. In rare cases, it can enter the pleural or extrapleural space, the mediastinum, or the pericardium. Subcutaneous, retroperitoneal, or extraperitoneal gas, unlike intraperitoneal gas, is not limited by the peritoneum and can therefore traverse a variety of tissue planes: for example, $CO_2$ can dissect along the great vessels or from the anterior neck into the mediastinum and, from there, rupture into the pericardium or travel along the pulmonary vessels into the pleural space [81]. Several early case reports describe this to result in pneumopericardium [82–84] or pneumothorax [81, 84, 85]. Most small pneumothoraces can be managed conservatively in the absence of hemodynamic or respiratory compromise, but large or symptomatic pneumothoraces may require treatment with needle aspiration or, rarely, chest tube placement.

Gas embolism is a potentially fatal complication in which the Veress needle is inadvertently placed into a vein, thereby injecting gas directly into the venous system. The incidence is estimated between 0.002 and 0.08% [37]. This complication can also arise from venous injury during the laparoscopic procedure [86, 87]. The gas bubble travels to the right heart and lodges in the atrium or pulmonary arterial system. The result can be catastrophic as the gas lock can obstruct venous return to the atrium resulting in a sharp drop in cardiac output. Alternatively, it could obstruct the pulmonary blood flow causing pulmonary hypertension and right heart failure. The diagnosis of gas embolism is suggested by dramatic, sudden cyanosis, hypoxia, hypercarbia, arrhythmia, or hypotension during insufflation or after venotomy. The pathognomonic "mill wheel" murmur may also be present and widening of the QRS complex with a right heart strain pattern on ECG can also be seen. Capnography may be useful in early diagnosis of gas embolism [88]. The most sensitive detector of gas embolism is transesophageal echocardiography, which can detect a $CO_2$ embolus as small as 0.02 ml [86, 87, 89]. In experimental animal cases of gas embolization caused by direct venotomy, the degree of embolization correlated with the decrease in central venous pressure due to blood loss or distal venous compression, the duration and amount of manipulation of the venotomy and the intraperitoneal pressure [86]. As such, in the event of significant venous injury during laparoscopy it is important to maintain intravascular volume and occlude the site of bleeding directly.

Treatment of gas embolism includes immediate desufflation, initiation of 100% inspired oxygen, and resuscitative measures. The patient should be turned laterally with the right side up and head down; this position prevents further air from entering the pulmonary circulation and the air bubble can be aspirated with a central venous catheter in the right atrium.

Cardiac dysrhythmias can occur as a result of the establishment and maintenance of pneumoperitoneum. Two studies early in the development of laparoscopy reported several anomalies [90, 91]. Bradycardia occurred shortly after initiation of $CO_2$ insufflation in several patients, thought to be due to reflex vagal stimulation from stretching of the peritoneum. Ventricular arrhythmias were also reported thought to be due to ventilator insufficiency. Extraventricular beats were also seen in 17% of patients with $CO_2$ pneumoperitoneum compared to 4% with $N_2O$ pneumoperitoneum, which may point to hypercarbia as a cause [91].

## Considerations with obesity

Obesity, defined as having a body mass index >30 $kg/m^2$, continues to increase in prevalence in the United States, now affecting over 30% of patients. Laparoscopy and robotic surgery may be more suitable than open surgery for many of these patients, but they carry unique risks and physiologic challenges from pneumoperitoneum. These patients tend to have a host of other comorbidities including diabetes mellitus, hypertension, hypercholesterolemia, arthritis, and asthma [92].

Obesity impacts respiratory mechanics, such that morbidly obese patients have reduced functional residual capacity, lower chest wall compliance, and increased carbon dioxide production at baseline [27, 28]. Pneumoperitoneum will reduce compliance to a greater degree in obese patients compared with normal-weight control subjects. Obese patients required 15% higher minute ventilation to maintain normocarbia in the supine position. Interestingly, changing to a Trendelenburg position had little impact on overall outcome, suggesting that obese patients who tolerate the induction of anesthesia and pneumoperitoneum in the supine position will likely tolerate the Trendelenburg position [27, 28]. This paradoxical finding was thought to be due the mechanical effects of pneumoperitoneum, which opposed the gravitational shift of abdominal contents.

A "tilt test" has been found to be helpful in many cases. Once the patient is intubated and positioned, the patient can be placed in a steep Trendelenburg for 2–5 minutes and the cardiac and respiratory status can be monitored. If tolerated, meaning the patient remains normotensive with inspiratory pressures at 30–40 mmHg, the abdomen can then be insufflated and monitored. If the patient continues to tolerate insufflation, they are likely to tolerate the remainder of the laparoscopic procedure [93].

## Modifying pneumoperitoneum

A number of modifications to standard $CO_2$ pneumoperitoneum have been investigated, in the hope of mitigating the adverse effects of increased IAP and the absorption of insufflant. Low-pressure or gasless laparoscopy has been extensively investigated, and there are now commercially available abdominal wall elevators that are secured to the operating table (Laparolift, Origin Medsystems, Menlo Park, CA, USA). A number of different devices were created and employed to do a similar task: elevate the anterior abdominal wall away from the intra-abdominal organs, thereby creating a working space and eliminating the need for insufflation. This has allowed for completion of numerous laparoscopic procedures at pneumoperitoneum pressures down to 4 mmHg, which may be preferable for patients who would otherwise be unable to tolerate increased IAPs or hypercapnia [94–96]. These wall-lifting methods have been shown to reduce stress response compared to standard pneumoperitoneum [97]. They have proven to be safe, to preserve pulmonary function, and in some cases decrease hospital stay [98]. While the low-pressure environment certainly limits surgeon comfort, it has been shown to decrease postoperative pain [99].

Others have looked at altering the temperature of the gaseous medium but reports on the physiologic benefits are mixed. A study compared insufflation with warm $CO_2$ to insufflation with $CO_2$ at room temperature, finding that warm $CO_2$ lead to higher core temperatures, increased urine output, and increased cardiac index [100]. This is thought to be due to regional vasodilatation of the renal vasculature which restores both renal blood flow and urine output. These improvements can be of particular benefit to those patients with renal dysfunction. Fluid management becomes more predictable with more reliable urine output

Other perceived benefits of warmed and humidified insufflant have not panned out. While one multicenter double-blind study randomized controlled trial showed no attenuation of the early inflammatory cytokine response [101], another study of patients undergoing laparoscopic cholecystectomy with warmed versus room temperature insufflation showed improvement in core temperature by 0.32 °C, but no major clinically relevant differences were seen [102]. In fact, a Cochrane review of the subject concluded that heated gas insufflation, with or without humidification, has minimal benefit on patient outcomes [103].

AirSeal® (Surgiquest, CT, USA) is a novel valve-free and membrane-free insufflation and Trocar system that enables a stable pneumoperitoneum with continuous smoke evacuation and $CO_2$ recirculation during laparoscopic surgery. It responds immediately to slight changes in IAP, and may be associated with reduced $CO_2$ use and absorption. Horstmann et al. prospectively compared the AirSeal Trocar system to a standard Versaport Plus V2 Trocar for assisting robotic radical prostatectomy. While there was no significant decrease in operative time, blood loss, camera cleaning, or overall $CO_2$ consumption, the AirSeal Trocar provided a more stable pneumoperitoneum with only one episode of pressure loss during 19 cases, as compared to 38 pressure-loss episodes in 17 cases performed with the standard port [104]. Further clinical studies are underway to characterize the potential benefits of the system [105].

## Conclusion

The physiologic effects of laparoscopy and robotic surgery are the result of patient positioning and the effects of insufflation of the abdomen. Pneumoperitoneum is most frequently created with carbon dioxide gas, as it is inexpensive, colorless, odorless, non-flammable, and rapidly eliminated from systemic circulation. It creates a number of physiologic challenges due to increased IAP and the absorption of $CO_2$, for the cardiovascular, pulmonary, renal, brain, and endocrine systems. Complications such as subcutaneous emphysema, cardiac arrhythmia, and gas embolism may arise. In addition, special considerations for the obese patient and those with cardiopulmonary compromise must be made. While studies to improve laparoscopy and the effects of pneumoperitoneum continue, the effects of pneumoperitoneum are generally well tolerated.

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# 79

# Anesthetic Management During Laparoscopic/Robotic Surgery

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## Introduction

Minimally invasive surgical techniques are rapidly becoming the accepted standard of care worldwide for many procedures performed by urologists. Laparoscopy is being increasingly utilized in nephrectomies (radical, partial, and living donor), nephroureterectomy, pyeloplasty, radical prostatectomy, pelvic lymph node dissection, varicocelectomy, and total cystectomy with ileal conduit formation. Significant advantages include decreased hospital length of stay, reduced blood loss, and fewer complications including in-hospital deaths when compared to open surgery for many procedures [1, 2]. Additional benefits include less postoperative pain, lower narcotic requirements, improved cosmetic results, and earlier return to normal activity. Robotic technology offers a three-dimensional view of anatomic structures, superior precision, and dexterity, and may be associated with a significantly faster learning curve than conventional laparoscopy [3, 4]. The anesthesiologist should be aware of the surgeon's expertise in this area as it has a profound influence on the postoperative management of the patient.

## Anesthetic considerations

The anesthesiologist is presented with a number of perioperative challenges during minimally invasive urologic surgery, and anesthetic management is guided by surgical complexity, patient positioning, duration of procedure, potential for blood loss, and the patient's baseline status. Patient access may be severely limited during robotic surgeries, and the physiologic consequences of extreme positioning and pneumoperitoneum may not be well tolerated. Rapid port removal and robot disengagement may become necessary during the case and requires clear communication with operating room personnel familiar with the equipment and operating room environment. Teamwork and effective communication are essential to assure optimal patient outcomes.

## Preoperative assessment

Patients scheduled for elective procedures should be evaluated in a preoperative clinic to ascertain patient specific and procedural risk factors, facilitate a perioperative management plan, and manage comorbid conditions. Previous studies show that visiting an anesthesiologist-led preadmission testing clinic before surgery can reduce preoperative consultations, decrease surgical cancellations, reduce costs associated with unnecessary testing, and reduce in-hospital mortality [5–7]. A complete history and physical exam should be performed with a focus on cardiopulmonary function and potential airway problems. Any pre-existing neuropathies should be investigated and documented to avoid being misdiagnosed as a complication of surgical positioning. More extensive preoperative testing should be guided by the patient's functional capacity, comorbidities, type of procedure, and surgical expertise. Current American College of Cardiology/American Heart Association guidelines should be followed for patients with known or suspected cardiac disease [8].

There are few, if any, agreed-upon absolute contraindications to laparoscopic surgery, and its safety in high-risk patients has been documented extensively [9–12]. Contraindications include patient conditions that preclude major surgery by any approach, such as severe decompensated cardiopulmonary disease or uncontrolled bleeding diatheses [13]. Patient-specific factors

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that may lead to procedural difficulties and prolonged surgery include morbid obesity, adhesions, and prior radiation therapy [14]. Patients considered high risk should be counseled in the rare event that a planned laparoscopic procedure must be converted to an open procedure.

## Anesthetic management

The goal of anesthetic management is to provide optimal and safe surgical conditions while managing the physiologic and hemodynamic responses associated with laparoscopic surgery. General anesthesia with a secured airway and controlled ventilation is the most common technique used during laparoscopy. Although supraglottic airway devices have been used in laparoscopic cholecystectomies and short laparoscopic gynecologic procedures, their use in longer procedures requiring steep Trendelenburg position has not been sufficiently studied to recommend [15, 16]. Induction of general anesthesia and endotracheal intubation are usually accomplished with intravenous administration of propofol and an intermediate-acting muscle relaxant. Etomidate and ketamine may be used in patients who cannot tolerate the hemodynamic effects of propofol. The endotracheal tube should be secured immediately after the cuff passes the vocal cords to prevent possible right endobronchial migration after abdominal insufflation [15, 17, 18]. Carbon dioxide pneumoperitoneum with Trendelenburg position increases endotracheal tube cuff pressure, leading to significant postoperative patient discomfort [19]. This can be avoided by periodically measuring the cuff pressure during the case. Anesthesia can be maintained with a volatile anesthetic combined with an opioid or total intravenous anesthesia (TIVA) with propofol. TIVA with propofol has been shown to decrease the incidence of early postoperative nausea and vomiting (PONV) in patients undergoing robot-assisted radical prostatectomy (RALP) [20]. Complete muscle relaxation with controlled ventilation is recommended to provide optimal surgical conditions and prevent hypercapnia. Patient movement must be avoided at all costs when incorporating robot assistance. Minute ventilation may need to be increased as much as 30% to maintain normal $P_aCO_2$ levels [21]. Oxygenation and respiratory mechanics are similar whether ventilation is volume- or pressure-controlled during laparoscopy, even in morbidly obese patients [22, 23]. Constant application of 5 $cmH_2O$ of positive end-expiratory pressure (PEEP) effectively maintains $P_aO_2$ levels during prolonged pneumoperitoneum [24] and, combined with low tidal volumes (6 ml/kg), may decrease postoperative pulmonary complications [25]. In addition, application of PEEP is associated with decreased blood loss during RALP [26]. The use of nitrous oxide, although not contraindicated, is frequently avoided due to its ability to cause bowel distention and contribute to PONV. Additionally, it can worsen the effects of air embolism and pneumothorax [27, 28].

Standard patient monitoring should include electrocardiogram, noninvasive arterial blood pressure, pulse oximetry, capnography, peripheral nerve stimulator, airway pressure, and temperature probe. Invasive blood pressure monitoring may be indicated in patients with significant cardiopulmonary disease, particularly when access to the upper extremities is restricted. Frequent blood gas analysis may be necessary in patients with increased dead space ventilation (i.e. chronic obstructive pulmonary disease, asthma, acute respiratory distress syndrome), as end-tidal $CO_2$ is an unreliable estimate of $P_aCO_2$ in these conditions. Two large-bore intravenous lines should be placed when significant intraoperative blood loss is anticipated or patient position precludes later placement should additional access become necessary. All lines and monitors should be rechecked after the patient is positioned to confirm they are functioning properly. A central line is rarely indicated. A fluid warmer and warming blanket is used to mitigate the effect of cold insufflated gasses on core body temperature. Even mild hypothermia is associated with adverse cardiac events, bleeding, and impaired wound healing [29].

Neuraxial techniques have been utilized successfully in a number of laparoscopic procedures, including transperitoneal nephrectomy, ureterolithotomy, and nephrolithotomy [30–32]. Drawbacks associated with the use of spinal and epidural anesthetics include inadequate abdominal relaxation, shoulder tip pain, urinary retention, and respiratory insufficiency secondary to carbon dioxide pneumoperitoneum. Benefits include less PONV and decreased need for postoperative analgesics. Laparoscopic cholecystectomy under epidural anesthesia has been successfully performed in high-risk chronic obstructive pulmonary disease patients classified as “too sick” for general anesthesia and endotracheal intubation [33].

Meticulous attention to patient positioning is imperative to prevent nerve injury and other complications. Positioning is even more critical when the robot is employed because the camera system and working arms must be accommodated. All pressure points and dependent areas must be padded and avoidance of extreme flexion, extension, and abduction should be followed to help minimize neuromuscular injuries. The back of the head should be padded and the face protected with foam pads or a mayo stand to prevent contact with the robot camera. If foam pads are used over the face, they should be easily removable in case of an airway emergency. When steep Trendelenburg position is required, egg-crate foam or surgical gel pads placed directly under the patient are commonly used to prevent cephalad migration on the operating room table. Shoulder straps, shoulder braces, and head rests are associated with neuromuscular injuries, particularly brachial plexus injury [34]. Chest straps are often utilized, but may decrease chest wall compliance. Some authors recommend placement of a throat pack to prevent gastric reflux through the lacrimal ducts with resulting chemical burns to the cornea [35]. For patients in the lateral decubitus position, a chest roll placed under the dependent hemithorax relieves tension on the brachial plexus by preventing compression of the axilla and shoulder. If an upper or double arm board is used, it must be properly set to prevent compression of the radial nerve at the posterior aspect of the humerus [36]. Excessive pressure on the dependent ear and eye should be avoided. Adhesive eye shields or Tegaderms can be used for eye protection.

## Fluid management

Although evaporative losses and fluid shifts are significantly reduced during laparoscopic surgery compared to open procedures, the ideal strategy for fluid replacement remains elusive. Patient condition, type of procedure, and patient position during the case help inform intraoperative fluid replacement therapy. Heart rate, blood pressure, urine output, and central venous pressure are not reliable measures of volume status. Pneumoperitoneum and Trendelenburg position make goal-directed fluid therapy indices difficult to interpret, and no single hemodynamic goal or monitoring method has been accepted across the literature [37, 38]. Restrictive fluid regimes have been associated with longer hospital length of stay and delayed postoperative wound healing in patients undergoing laparoscopic surgery, while fluid loading has successfully decreased rates of PONV [39, 40]. Conservative intravenous fluid administration during RALP decreases the amount of urine obscuring the operative field and may also reduce postoperative laryngeal edema resulting from prolonged Trendelenburg position [34].

## Physiologic changes

The physiologic changes that accompany laparoscopic surgery are well tolerated in healthy (American Society of Anesthesiologists [ASA] grade I or II) patients. They are produced by the interaction of several factors, including pneumoperitoneum, carbon dioxide absorption, patient position,surgical procedure, and the patient's baseline cardiopulmonary status.

### Pneumoperitoneum

Pneumoperitoneum has profound effects on the cardiovascular, cerebrovascular, and respiratory systems. Displacement of the diaphragm cephalad decreases tidal volume, pulmonary compliance, and functional residual capacity. Peak inspiratory pressure and plateau pressures increase secondary to atelectasis and narrowing of the large airways. Moderate Trendelenburg position does not seem to affect these changes, even in the morbidly obese [41, 42]. Steeper levels of Trendelenburg may worsen lung compliance [43]. Atelectasis may be more prominent in older people due to increased closing capacity with age. Strategies to mitigate the effects of these changes are discussed under Anesthetic management. Cardiovascular changes associated with pneumoperitoneum are related to the degree of increased intra-abdominal pressure and position of the patient. Intra-abdominal pressures up to 12 mmHg can cause an initial rise in cardiac output by increasing preload as blood volume is forced from the splanchnic vessels into the inferior vena cava. When intra-abdominal pressure rises above 15 mmHg, reductions in preload and cardiac output can be seen secondary to caval compression. A rise in systemic vascular resistance (SVR) is due to many factors, including compression of the arterial vasculature, the release of catecholamines and vasopressin, and activation of the renin-angiotension system. Odeberg et al. reported a 58% increase in central venous pressure and a 32% increase in pulmonary capillary wedge pressure in healthy patients after abdominal insufflation in the horizontal position when intra-abdominal pressure was maintained between 11 and 13 mmHg. Cardiac filling pressures were further increased by 40% when patients were placed in the Trendelenburg position [44].

Lestar and colleagues found a threefold increase in central venous pressure in ASA grade I–II patients undergoing RALP in 45° Trendelenburg position with an intra-abdominal pressure of 11–12 mmHg. Mean pulmonary artery pressure and pulmonary capillary wedge pressure increased twofold, but cardiac performance was unaffected [45]. It should be noted that the effects of intra-abdominal hypertension may be exaggerated in hypovolemic patients or those with cardiovascular disease, particularly if the reverse Trendelenburg position is used. Severe reflex bradycardia resulting from stretching of the peritoneum during insufflation has also been reported [46].

Pneumoperitoneum decreases renal blood flow, although the clinical significance of this is unknown [47]. This decrease in blood flow is pressure dependent and intensified by the reverse Trendelenburg position. Mechanical compression of the renal vein and increased secretion of antidiuetic hormone decrease glomerular filtration and urine output. The renin-angiotensin-aldosterone system is activated, leading to further reductions in renal blood flow. Pneumoperitoneum-associated hemodynamic changes in kidney donors can negatively affect transplanted kidney function [48]. Suggested measures to protect renal function, particularly during laparoscopic live donor nephrectomy, include maintaining a positive intravascular fluid balance and limiting intra-abdominal pressure to a maximum of 12 mmHg [49]. Ureteral obstruction due to mechanical pressure has not been shown to play a significant role in renal dysfunction associated with pneumoperitoneum [50].

### Carbon dioxide absorption

Carbon dioxide ($CO_2$) is the gas most commonly used for abdominal insufflation during laparoscopy because it is highly soluble, inexpensive, nontoxic, nonflammable, and easily eliminated through the lungs. Its high solubility makes it less likely than air to cause clinically significant gas embolus. $CO_2$ is systemically absorbed during laparoscopy, potentially causing respiratory acidosis. During carbon dioxide pneumoperitoneum, end-tidal $CO_2$ progressively increases, reaching a plateau after 40 minutes if minute ventilation is kept constant [51]. Thereafter, $CO_2$ accumulates in the body and $CO_2$ output may be increased for up to 30 minutes after abdominal decompression [52]. Factors contributing to a higher degree of $CO_2$ absorption include higher insufflation pressure, longer insufflation time, and subcutaneous emphysema [53–56]. Hypercarbia can cause arrhythmias and contribute to increased SVR during laparoscopy. Excess $CO_2$ is easily eliminated in healthy patients by increasing minute ventilation. However, hypercarbia can induce pulmonary vasoconstriction that may be poorly tolerated in patients with pulmonary hypertension. Alternatively, permissive hypercarbia causes vasodilatation and shifts the oxyhemoglobin dissociation curve to the right, improving tissue perfusion and oxygen delivery [57]. Elevated $P_aCO_2$ has also been shown to reduce shunting by increasing blood flow to noncollapsed lung regions [58].

### Patient position

The most common positions for laparoscopic and robotic urological procedures are the low dorsal lithotomy with steep (35°) Trendelenburg position, followed by the lateral jackknife decubitus position. Neurological complications after prolonged periods of steep Trendelenburg have been reported [59]. Schramm and colleagues used transcranial Doppler to investigate the time course of cerebral autoregulation during RALP. Their findings suggest a slow deterioration of cerebral autoregulation during extreme Trendelenburg position combined with pneumoperitoneum [60]. Kim et al. used optic nerve sheath diameter to assess intracranial pressure in 20 patients undergoing RALP. In 15% of patients optic nerve sheath diameter increased to levels equivalent to an intracranial pressure >20 mmHg. No postoperative neurological complications were noted in their study [61]. Although not strictly contraindicated, laparoscopic surgery in Trendelenburg position has been safely performed in patients with ventriculoperitoneal shunt [62].

Intraocular pressure (IOP) has been shown to increase significantly over time in patients undergoing RALP with steep Trendelenburg. However, no perioperative visual loss has been attributed to steep Trendelenburg positioning alone in patients without pre-existing ocular disease [63, 64]. There is at least one case report of a patient with primary open-angle glaucoma undergoing RALP. The IOP was measured after induction of general anesthesia and every 15 minutes thereafter. Increased IOP was treated with intravenous acetazolamide and mannitol. The patient's visual acuity postoperatively remained unchanged [65]. Preoperative consultation with the treating ophthalmologist is recommended for patients with glaucoma as intraoperative treatment for increased IOP may be warranted.

Some degree of lateral positioning is commonly used for kidney surgery depending on the surgical approach, i.e. transperitoneal or retroperitoneal. Advantages to the retroperitoneal approach include less need for visceral retraction and lack of peritoneal irritation from insufflated carbon dioxide. Transperitoneal is associated with a larger increase in peak inspiratory pressure and plateau pressure when compared to retroperitoneal [66]. This may be attributed to greater interference to diaphragmatic excursion when the transperitoneal is used. Which approach results in less $CO_2$ accumulation is the subject of debate. Bannenberg et al. found arterial $CO_2$ levels increased significantly more during intraperitoneal insufflation compared to extraperitoneal insufflation in piglets [67]. This is presumably due to the increased diaphragmatic surface area exposed to $CO_2$. Streich et al. and Mullet et al. found retroperitoneal carbon dioxide insufflation causes more carbon dioxide absorption than intraperitoneal insufflation [68, 69], and Ng et al. found no difference in carbon dioxide absorption when comparing the retroperitoneal to the transperitoneal approach [70].

## Enhanced recovery after surgery

Enhanced recovery programs (ERPs) have been utilized in urology for both open and minimally invasive procedures, but adoption has been slow. ERPs are increasingly being implemented to improve patient outcomes and reduce healthcare costs through standardized, evidence-based perioperative care. Minimally invasive surgery alone represents a major opportunity to enhance recovery and reduce morbidity, especially when combined with other aspects of an ERP. Although most of the literature on this topic is derived from colorectal surgery, many elements have been effectively applied to ERPs in other specialties. It should be noted that the number and type of ERP elements varies widely across the literature and the impact of any individual element on outcomes is not clear. Successful ERPs require a multidisciplinary, team-based approach and coordination of evidence-based care throughout the perioperative continuum. Anesthesiologists are responsible for delivering many elements in an ERP, highlighting the importance of their commitment to this process. Collaboration between the surgeon and anesthesiologist is essential for an ERP to be effective and sustainable. An ERP begins when surgery is scheduled and ends when the patient returns to their preoperative functional status. ERP interventions can be classified as preoperative, intraoperative, and postoperative. The anesthesiologist plays an important role in the shared decision-making for many of these interventions, including:

1) identification and optimization of patient's comorbid conditions before surgery,
2) utilizing opioid-sparing anesthetic techniques, including regional blocks, that minimize postoperative pain and allow for rapid recovery,
3) aggressive prophylaxis and treatment of PONV,
4) utilizing effective pre-emptive analgesics and an opioid-sparing multimodal strategy for postoperative pain management,
5) providing goal-directed or zero-balance fluid therapy perioperatively (when evidence-based).

Common elements found in many enhanced-recovery or "fast-track" protocols for gastrointestinal and urologic surgery are listed in Table 79.1. Inclusion, modification, and/or elimination of elements in a protocol should be evidence-based and procedure-specific.

Magheli et al. studied 50 patients undergoing laparoscopic radical prostatectomy randomized to conventional or enhanced recovery fast-track care. Patients in the fast-track group mobilized earlier, had lower pain scores and a decreased overall complication rate, and were discharged home earlier than patients in the conventional group. Postoperative pain in the fast-track group was managed with a COX-2 inhibitor [71]. Dudderidge and colleagues reduced intraoperative and postoperative opioid use by incorporating a pre-emptive transversus abdominis plane (TAP) block as part of a standardized anesthetic technique into their care pathway for laparoscopic radical prostatectomy. Some 78% of patients who received a TAP block were discharged home on postoperative day 1, and 7% went home on the evening of surgery [72]. Enhanced recovery protocols have been utilized in robot-assisted laparoscopic cystectomy and laparoscopic nephrectomy with promising results [73, 74]. More studies are needed in minimally invasive surgery as part of the enhanced recovery paradigm to assess and clarify its influence on patient outcomes and cost effectiveness.

## Postoperative pain management

Minimally invasive laparoscopic procedures are known to cause less pain than open procedures. However, characteristics of the laparoscopic approach such as insufflation of the abdomen with $CO_2$ can create unique postoperative pain management challenges. Postoperative pain associated with robotic/laparoscopic surgery is caused by tissue trauma at port incision, peritoneal distention, and diaphragmatic irritation that leads to referred shoulder pain. Although there are no procedure-specific guidelines for pain management in urologic surgery the goal is to provide adequate analgesia while curtailing the administration of systemic opioids. Opioids are associated with a

**Table 79.1** Common elements of enhanced recovery protocols.

| Preoperative | Intraoperative | Postoperative |
|---|---|---|
| Patient education and counseling<br>Preoperative risk assessment and optimization (hypertension, diabetes, anemia)<br>Carbohydrate drink (clear) night before and 2 hours before surgery<br>Preoperative administration of non-narcotic analgesics<br>Avoidance of mechanical bowel preparation<br>Alcohol and tobacco abstinence<br>Thromboembolic prophylaxis | Fluid optimization to maintain euvolemia<br>Fluid warmer and warming blanket to maintain normothermia<br>Minimally invasive surgery<br>Pre-incision regional block/local anesthetic infiltration<br>Opioid-sparing techniques<br>Prophylactic antiemetics, antimicrobial prophylaxis | Multimodal, opioid-sparing analgesia<br>Antiemetics<br>Early routine mobilization<br>Early enteral nutrition<br>Avoidance of nasogastric tubes<br>Avoidance of peritoneal drains<br>Early removal of catheters<br>Rehabilitation plan |

number of undesirable side effects, including nausea, vomiting, pruritus, urinary retention, respiratory depression, and delayed return of bowel function. For this reason, opioid-sparing multimodal analgesic techniques are increasingly being utilized to control postoperative pain and promote early recovery [75]. Multimodal protocols use combinations of analgesic medications with different mechanisms of action and sites of administration to provide optimal pain relief. Strategies for the management of postoperative pain frequently include the perioperative administration of nonsteroidal anti-inflammatory agents, NMDA inhibitors, steroids, and acetaminophen combined with regional block or wound infiltration with a local anesthetic. Supplemental opioid may be added for breakthrough pain. There is evidence that the preoperative administration of COX-2 inhibitors and gabapentin may be more effective than opioids and other nonsteroidal anti-inflammatory drugs in reducing postoperative pain [76]. Preoperative systemic dexamethasone and perioperative ketorolac and ketamine have also been found to be effective adjuncts to reduce postoperative pain and opioid consumption in a variety of clinical settings [77–79].

Local anesthetics used for peripheral nerve blocks and local infiltration have been shown to reduce postoperative opioid requirements in laparoscopic surgery. Infiltration of a local anesthetic into laparoscopic port sites and other incisions is a common practice shown in the short term to decrease pain scores and the need for supplementary analgesia [80]. A meta-analysis of laparoscopic surgery clinical trials demonstrated that preemptive administration of local anesthetic at the port incision site reduced postoperative pain compared with placebo but was found to have an analgesic effect similar to that of postincisional anesthetic infiltration [81]. Pre-emptive timing of administration was only significant for intraperitoneal infiltration. The analgesic duration of most local anesthetics when administered as a single injection is less than 4–6 hours and may not provide significant long-term postoperative analgesia. Liposomal bupivacaine is a delayed-release local anesthetic approved for injection into the surgical site to produce postsurgical analgesia. Knight et al. found there was no significant difference with respect to opioid consumption and pain control between liposomal bupivacaine and free bupivacaine following injection of incision sites in laparoscopic and robot-assisted urologic surgery cases [82].

The TAP block is a peripheral nerve block that anesthetizes the abdominal wall and is used as part of a multimodal strategy to optimize postoperative pain outcomes. While advocates of the TAP block propose that the analgesia provided reduces postoperative pain, opioid consumption, and related side effects, evidence for TAP block use has been inconsistent. De Oliveira et al. detected a beneficial effect of TAP block on analgesia outcomes after laparoscopic surgery with the preoperative period as the optimal time for administration of the block [83].

A variety of methods have been tested to reduce the incidence and severity of shoulder tip pain. Guido et al. found no difference in shoulder pain after laparoscopic tubal ligation by gasless laparoscopy versus $CO_2$ pneumoperitoneum while Goldberg and Maurer found the compromised surgical exposure and lack of benefits in terms of postoperative discomfort rendered this method unsuitable [84, 85]. Sarli et al. performed laparoscopic cholecystectomy comparing 9 mmHg carbon dioxide pneumoperitoneum with 13 mmHg pneumoperitoneum and noted a decreased incidence and frequency of shoulder tip pain [86]. Sajid et al. concluded that the use of heated humidified $CO_2$ for pneumoperitoneum in laparoscopic procedures is associated with lower postoperative pain and analgesic requirements when compared to dry $CO_2$ [87]. Intraperitoneal local anesthetic nebulization has been found to reduce postoperative pain and referred shoulder pain after laparoscopic cholecystectomy and laparoscopic gynecologic surgery [88–90].

## Postoperative nausea and vomiting

PONV is a common but distressing complication of surgery with a reported incidence of 25–36% [91]. The incidence of PONV has been found to be as high as 79% in certain high-risk populations [92]. It can result in delayed postanesthesia care unit discharge, unplanned hospital admission, and increased healthcare costs. Patient anesthetic- and procedure-related characteristics that confer increased risk for PONV include female gender, history of PONV, nonsmoking status, history of motion sickness, younger age (<50), use of volatile anesthetics and nitrous oxide, duration of anesthesia, postoperative opioids, abdominal procedures, and the laparoscopic approach [91, 93, 94]. While there is no specific guidance for laparoscopic urologic surgery, $CO_2$ insufflation, which causes peritoneal stretching and irritation, is thought to play important role in postoperative PONV [94]. The most recent American Society of Anesthesiologists evidence-based guidelines advocate a comprehensive approach to PONV management. The guidelines include the use of risk scores to ascertain high-risk patients and the implementation of strategies to reduce these risks, such as the use of regional anesthesia and TIVA and minimizing perioperative use of opioids. TIVA with propofol has been shown to reduce the incidence and severity of PONV in patients undergoing RALP [20]. Recommended pharmacologic antiemetic agents for PONV prophylaxis include 5-hydroxytryptamine receptor antagonists, neurokinin-1 receptor antagonists, antihistamines, corticosteroids, butyrophenones, and anticholinergics. Prophylactic antiemetics are recommended only following consideration of patient and procedure risk factors, adverse effects and cost. While 5-hydroxytryptamine receptor antagonists, corticosteroids, and butyrophenones have a documented effect on reducing PONV with similar levels of efficacy, the use of combination therapy utilizing drugs from different classes is preferable. If PONV prophylaxis fails, it is recommended that an antiemetic from a different class than the prophylactic regimen is used [95].

## Complications

### Carbon dioxide embolism

Clinically significant carbon dioxide embolism is a rare but dangerous complication of laparoscopic surgery with a reported incidence of 0.0014–0.6% and an associated mortality rate of 29% [96, 97]. Although a variety of monitoring devices can be utilized to detect gas embolism, transesophageal echocardiography (TEE) is the most sensitive. Kim et al. reported the presence of $CO_2$ embolism in 100% of patients undergoing total laparoscopic hysterectomy with TEE monitoring [98]. Subclinical $CO_2$ embolism was discovered in 17% of patients undergoing laparoscopic radical prostatectomy when TEE was used for detection [99]. Cases of clinically relevant gas embolism have been reported for bariatric, cholecystectomy, radical prostatectomy, hysterectomy, and pediatric laparoscopic procedures [99–103]. The mechanism of embolism is thought to be unintended injection of carbon dioxide into a large vein, artery, or solid organ during initial peritoneal insufflation [104]. Clinical signs of gas embolism depend on the volume of gas and its rate of entry into the circulation and include a sudden drop in end-tidal $CO_2$, hypotension, tachycardia, cardiac arrhythmias, increased central venous pressure, the presence of a "mill-wheel" murmur, cyanosis, and electrocardiogram changes [100]. Immediate treatment requires release of pneumoperitonium, placing the patient in the left lateral decubitus (Durant maneuver), and Trendelenburg position. The patient should be hyperventilated with 100% oxygen to correct hypoxemia and reduce the size of the gas embolus. Volume loading and the Valsalva maneuver elevate central venous pressure and may reduce further gas entry. Vasopressors and inotropic agents are administered as indicated. If these measures are not effective, a multiport central venous catheter may be introduced to aspirate gas from the right atrium or ventricle. If necessary, cardiopulmonary resuscitation should be initiated for persistent hypotension or arrhythmia [105]. Cardiopulmonary bypass and hyperbaric oxygen have both been used successfully to treat symptomatic gas embolism [106, 107]. A prompt collaborative response by the anesthesiologist and surgeon is necessary to limit morbidity when this potentially fatal complication occurs.

### Well-leg compartment syndrome

Well-leg compartment syndrome (WLCS) following surgery in the lithotomy position is a rare complication that requires rapid diagnosis and treatment to prevent serious morbidity and mortality [108]. Reports on the frequency of compartment syndrome in patients who underwent procedures in the lithotomy position range from 1 in 500 to 1 in 3500 [109, 110]. Gluteal and upper extremity compartment syndrome have also been reported following robot-assisted urologic surgery [111]. The pathophysiology involves increased intracompartmental pressure with subsequent decreased tissue perfusion, ischemia of the muscles and nerves, and tissue necrosis [112]. Risk factors include prolonged operative time (>4 hours), patient position (lithotomy and lithotomy-Trendelenburg), obesity, systemic hypotension, muscular lower limbs, type of leg holder, epidural anesthesia, and peripheral vascular disease [109]. Clinical signs and symptoms of WLCS include paresthesia, disproportionate pain in the affected compartment, pain on passive stretch, and tight calves. Supplementary compartmental pressure measurement is recommended when the clinical signs are unclear [113]. Once a diagnosis is made, fasciotomy should be performed urgently to minimize the likelihood of adverse sequelae. Untreated compartment syndrome or delayed fasciotomy can result in limb loss, renal failure, and death [114]. Clinicians must maintain a high level of vigilance in patients with risk factors and explore ways to reduce this risk. Proposed risk-reduction strategies include use of the modified lithotomy position, periodic mobilization of the lower extremities, avoidance of the Trendelenburg position, and ankle dorsiflexion and heel support [115]. Of interest, intermittent compression stockings have been reported to be a risk factor as well as a preventive measure to reduce the risk of WLCS [109, 116].

### Mesenteric ischemia and bowel infarction

There have been several reports of mesenteric ischemia and bowel infarction after routine laparoscopic procedures. Many of these complications occurred in patients with evidence of preoperative cardiovascular, hepatic, or renal compromise. Bandyopadhyay et al. describe a case of large bowel ischemia involving a 78-year-old man who died within 30 hours after an elective laparoscopic transperitoneal inguinal hernioplasty. An autopsy revealed thrombosis of the inferior mesenteric artery and an infrarenal aortic aneurysm with thrombotic plaque on its wall [117]. At least nine cases of small bowel ischemia following laparoscopic cholecystectomy have been reported, many of them fatal [118]. $CO_2$ pneumoperitineum may play a role in this devastating event by reducing mesenteric perfusion in at-risk patients [119]. Techniques that utilize the lowest possible insufflation pressure and intermittent decompression of gas during pneumoperitoneum have been suggested as preventive measures [120]. Intestinal ischemia should be considered whenever nonspecific abdominal symptoms are present after transperitoneal laparoscopic surgery.

## Ocular injuries

Ocular complications of robot-assisted urologic surgery can range from more frequent corneal abrasions to the rare but devastating postoperative visual loss. Corneal abrasions can cause considerable patient pain and discomfort. Possible etiologies include lagophthalmos during general anesthesia resulting in corneal drying, direct mechanical trauma, and chemical injury. Advanced age, general anesthesia, length of surgery, and Trendelenburg positon have been confirmed as perioperative risk factors for corneal abrasions [121]. A retrospective review of 1500 consecutive patients undergoing robotic prostatectomy found corneal abrasions to be the most common anesthesia-related complication, occurring in 3% of cases with the use of eye tape [122]. This incidence was reduced to 1% following the introduction eye patches. In a United States nationwide sample of patients undergoing radical prostatectomy the overall incidence of corneal abrasion was reported as 0.18% [123]. Proposed measures to protect against corneal abrasions include the use of eye patches, and transparent occlusive dressings [122, 124].

Postoperative visual loss (POVL) is a rare complication following robot-assisted laparoscopic surgery. Prolonged operative times in steep Trendelenburg have raised concerns about increased venous congestion in the head, facial edema, and elevated IOP interfering with optic nerve perfusion. Lee et al. reported three cases of POVL from the ASA POVL registry from 2006 to 2011 secondary to posterior ischemic optic neuropathy following RALP [125].

A small randomized trial by Raz et al. found that modifying the Trendelenburg position by placing the head and shoulders horizontally during RALP lowered IOP and accelerated its recovery to the normal range without affecting the procedure [126]. An ophthalmology consult should be considered in patients with history of severe ocular disease and older adults who may have elevated baseline intraocular pressure.

## Peripheral nerve injuries

Nerve injuries related to patient positioning are injuries that occur when a peripheral nerve is subjected to stretching or compression during surgery. Mills et al. reviewed 334 adult urological robot-assisted cases at their institution over a 2 year period and found 22 documented positioning injuries (6.6%). Twenty eight percent of these injuries persisted beyond 6 months. Retroperitoneal lymph node dissection was associated with the highest percentage of patients with injuries (40%), followed by adrenalectomy (17%). Patients at greatest risk for injury were those with a higher ASA classification [127]. Factors associated with positioning nerve injuries can be classified as patient- or procedure-related. Patient-related factors include ASA physical status, body mass index (BMI), variant anatomy, and comorbidities such as diabetes mellitus and vascular disease. Procedural risk factors include patient position and operative duration [127–129]. Lower extremity neuropathies involving the common peroneal, obturator, lateral femoral cutaneous nerve and sciatic nerve from prolonged standard and low lithotomy positioning have been documented with a frequency of 1 in 3608 [130]. Manny et al. reported a lower extremity neuropathy rate of 1.7% in RALP and prostatectomy cases with patients in the low lithotomy position [131]. Koc et al. reported that patients who developed lower extremity neuropathies had a significantly longer operative time than average and that use of a split-leg table was found to put the femoral nerve at risk for injury [132]. Elements of correct lithotomy positioning include the use of boot stirrups, hip flexion of 60–120°, knee flexion of 90–120°, hip adduction of 90° or less, minimal external hip rotation, and the use of specific padding to prevent pressure against the peroneal nerve at the fibular head [133]. Larger BMI is a risk factor for upper extremity injury [128]. Mills et al. reported that 59% of all nerve injuries involved an upper extremity, with the highest proportion of injuries occurring when one upper extremity was adducted while the other was tucked beside the patient. The majority of these injuries occurred in the tucked extremity [127]. Brachial plexus injuries are the most commonly reported peripheral nerve injuries and have been linked to the use of shoulder braces and prolonged steep Trendelenburg positioning [134]. Most guidelines discourage the use of shoulder braces in favor of nonsliding mattresses [133]. Devarajan et al. described three patients who developed brachial plexus injuries with the use of beanbag body supports in steep Trendelenburg position. The authors recommended adduction or tucking of the upper extremities and the use of nonslipping operating table mattresses to prevent cephalad migration of the patient in steep Trendelenburg position [135]. The use of padded arm boards, chest rolls, and elbow padding are also recommended [133]. Documentation of perioperative positioning actions with intermittent assessment of patient positioning is essential.

## Pneumothorax, pneumomediastinum, and pneumopericardium

Pneumothorax (PTX), pneumomediastinum, and pneumopericardium are well-known complications of laparoscopic surgery and can cause significant morbidity. Laparoscopic procedures performed near the diaphragm, inadvertent pleural or diaphragmatic injury, and congenital diaphragmatic defects have been identified as routes for $CO_2$ entry into the mediastinal and pleural spaces [136–138]. PTX has a reported incidence of less than 1% during renal surgery and 3% during adrenalectomy [139, 140]. Risk factors associated with PTX during laparoscopic surgery include prolonged operative times, older age, intraoperative end-tidal $CO_2$ above 50 mmHg, and operator inexperience [140]. Signs of PTX during surgery include hypercapnia, increased airway pressure, hypoxemia, billowing of the diaphragm, and absent breath sounds. Concomitant hemodynamic instability indicates the PTX is likely under tension. While most cases are diagnosed intraoperatively, a valveless Trocar may obscure typical signs of PTX, impeding diagnosis [139]. The authors recommend a chest X-ray in the immediate postoperative period when using a valveless Trocar for procedures close to the diaphragm. Treatment of PTX consists of immediate release of pneumoperitoneum, hyperventilation with 100% oxygen, PEEP, and hemodynamic support.

Severe PTX or cases secondary to underlying lung disease may require immediate simple aspiration or chest tube drainage. Given the favorable absorptive properties of $CO_2$, asymptomatic or hemodynamically stable patients with PTX can be treated conservatively and allowed to resolve spontaneously [141].

## Cardiac patients

Patients with cardiac dysfunction undergoing laparoscopic surgery present a variety of challenges to the anesthesiologist. The physiological effects of $CO_2$ pneumoperitoneum and extreme positioning may be poorly tolerated in these patients. Pneumoperitoneum activates the release of catecholoamines leading to tachycardia, increased afterload, and hypertension. Furthermore, mechanical compression of the aorta by insufflated $CO_2$ may further increase SVR [142]. The tachycardia and increased afterload increase myocardial oxygen demand and the likelihood of ischemia. Further increases in intra-abdominal pressure as insufflation continues decreases venous return, preload, and end-diastolic volume, with the magnitude of decrease in cardiac index directly related to the insufflation pressure [143]. By occupying a less-advantageous position on the Frank–Starling curve, cardiac output can subsequently decrease. Preload augmentation prior to pneumoperitoneum may be necessary. Limiting insufflation pressures should also be considered, as patients with limited cardiac reserve or compensated failure may not tolerate associated hemodynamic changes. Decreased cardiac output leads to decreased oxygen delivery to the periphery with a concomitant decrease in mixed venous oxygen saturation. Patients with severe congestive heart failure and valvular lesions are more likely to develop complications than those suffering from ischemic cardiac disease [144]. The possibility of rising arterial carbon dioxide tension may lead to, or exacerbate, pulmonary hypertension, resulting in right heart strain and ischemia. Standard monitoring may need to be supplemented with invasive monitoring in this patient population. TEE can be used to assess regional wall motion abnormalities, hydration status, and the degree of preload and end-diastolic volume. Invasive arterial monitoring may be useful and pulmonary arterial catheterization may help maximize cardiac output and measure mixed-venous oxygen saturation. Alternatively, noninvasive measures of hemodynamic parameters are commercially available. Noninvasive hemodynamic monitoring provides ease of use while eliminating the risks associated with the placement of invasive monitors. Algorithmic analysis of the Pleth Variability Index (PVI) has been advocated as a method for measuring intraoperative fluid balance, hemodynamic parameters, and hemoglobin. This method utilizes algorithmic analysis of the waveform generated from a standard or modified pulse-oximeter probe. Hemodynamic parameters are derived from respiratory variations in the pulse oximeter waveform amplitudes [145]. While PVI has been shown to reliably predict fluid responsiveness in the mechanically ventilated there are few data to support the use of these monitors in those undergoing laparoscopic procedures [146]. In addition, the impact of abdominal insufflation on the validity of these noninvasive monitors is still unclear. Some data suggest that PVI is falsely elevated with abdominal insufflation. This could assign a false state of hypovolemia and result in the unnecessary, and potentially deleterious, administration of volume expanders [145]. The hemodynamic effects of steep Trendelenburg position commonly used in many robot-assisted urologic procedures appears to be mitigated by the increased intra-abdominal pressures associated with insufflation [142].

## Older patients

Older patients are more susceptible to adverse surgical outcomes because of decreased functional reserve and an increased number of coexisting diseases [147]. Most significantly, changes due to the physiologic stresses of pneumoperitoneum need to be anticipated in this surgical population as the customary insufflation pressures of 10–15 mmHg may cause significant physiologic disturbances. Increased intra-abdominal pressure in octogenarians may decrease the cardiac output by 30% [148]. Heart rate typically increases in an effort to maintain oxygen delivery to the tissues. This compensatory increase may be diminished by medications typically taken by older people, particularly beta-blockers. Elevations in heart rate, SVR, and mean arterial pressure that typically accompany pneumoperitoneum can increase myocardial workload and the risk of ischemia. The presence of atrial fibrillation further decreases cardiac reserve due to loss of the atrial contribution to ventricular filling.

The pharmacokinetics and pharmacodynamics of drugs are significantly altered in older people. Elderly patients tend to have increased adipose tissue, decreased muscle mass, and decreased total body water accounting for many of the pharmacokinetic changes [149]. The subsequent decreased volume of distribution can lead to exaggerated hemodynamic responses to induction agents and other drugs. Older people, particularly the malnourished, have a lower serum albumin concentration resulting in considerably higher plasma concentrations of unbound drug. Drug doses should be lowered and titrated to effect in these patients to avoid relative overdose. While is important to recognize age-related physiologic changes, age alone has not been associated with an increased risk of intraoperative or postoperative complications [150]. Laparoscopic renal and adrenal surgery, radical prostatectomy, and robot-assisted radical cystectomy in older adults have all been shown to be well tolerated with low perioperative morbidity.

## Pregnancy

Pregnancy-induced anatomical and physiological changes must be understood to provide optimal care to these surgical patients. Approximately 1–2% of pregnant patients require a non-obstetric surgical intervention during their pregnancy, representing approximately 80 000 cases per year [151]. Laparoscopic partial nephrectomy for renal cell carcinoma in the pregnant patient has been described in the literature [152]. While there are numerous case reports that support the use of laparoscopy during pregnancy, by the end of the second trimester the size of the uterus often interferes with the laparoscopic approach and open surgery may be indicated [153]. Additionally, many laparoscopic-specific maternal and fetal complications bear consideration, including uterine and/or fetal trauma, fetal acidosis from carbon dioxide absorption, decreased maternal cardiac output, and decreased uteroplacental blood flow secondary to increased intraperitoneal pressure [151]. Pneumoperitoneum can initiate premature labor. Preservation of maternal hemodynamics, uteroplacental blood flow and avoidance of maternal and fetal hypoxia is paramount. While the retroperitoneal approach to the kidney for laparoscopic nephrectomy has been described, the best approach remains controversial. The transperitoneal approach affords the surgeon a larger working space while the retroperitoneal approach provides for early control of the renal vasculature and minimizes bowel and uterine manipulation, thereby potentially decreasing the risk of premature labor [154]. The Society of American Gastrointestinal Endoscopic Surgeons (SAGES) has issued guidelines for laparoscopic surgery during pregnancy that include deferring surgery until the second trimester and maintaining low pneumoperitoneum pressures (<15 mmHg) [155]. Close interdisciplinary communication and cooperation is essential in the provision of perioperative care of these high-risk patients. The mother should be fully informed of the low risks of teratogenicity of most anesthetic agents, and of the significant risk of preterm labor.

## Obesity

Many of the complexities of caring for the obese surgical patient have been well described. Careful attention to the comorbidities unique to the obese aids in their safe management. These comorbidities include pulmonary, airway, and cardiac changes, among other concerns. Morbidly obese patients have a higher potential for difficult mask ventilation, laryngoscopy, and intubation. The obese patient's large tongue, redundant oropharyngeal tissue, atlantoaxial joint limitation, and presternal fat deposits inhibit movement of the laryngoscope and increase the difficulty of direct laryngoscopy. Factors such as Mallampati classification and neck circumference are predictive of a difficult airway [156].

Chest wall compliance is decreased in the obese due to increased adipose load on the chest and abdomen. Lung compliance is decreased secondary to increased pulmonary blood volume and is proportionate to the degree of obesity. Expiratory reserve volume is decreased and may be exceeded by the closing volume, leading to air entrapment. Pneumoperitoneum may exacerbate these changes. Surprisingly, the decrease in lung compliance upon insufflation in normal weight patients has been shown to be equal to or even greater than the decrease seen in morbidly obese patients [157]. Morbid obesity is associated with sleep apnea, elevated pulmonary pressures, and right ventricular hypertrophy and failure. Pre-existing pulmonary hypertension may be aggravated by insufflation induced hypercarbia. Thorough preoperative assessment and optimization and continued postoperative monitoring of respiratory parameters is essential in patients with these comorbid conditions. Positioning of the obese patient for laparoscopic surgery can be challenging, as these patients are at greater risk for nerve injury. The most frequently reported complication is ulnar neuropathy and careful attention to and padding of stress points is imperative [158].

BMI is associated with major complications following laparoscopic surgery for renal cancer with risk increasing by 14% for every unit increase [159]. Once again, the use of noninvasive monitoring techniques may aid in the management of these patients. The limitations of PVI, however, may be pronounced in obese patients.

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# 80

# Laparoscopy Surgery: Basic Instrumentation

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## Introduction

Even in the face of significant advances in robotic and endoscopic surgery, laparoscopy remains the method of choice for multiple urologic procedures and advances continue to be made in instrumentation. Significant technological improvements have been made over the last decade to ameliorate problems, including limitations of previous generations of optics, maintenance of pneumoperitoneum, intracorporeal retractors, and hemostasis. Well-established instruments such as graspers, clip appliers, intracorporeal bags, and fascial closure devices have remained largely constant with few adjustments.

Advanced laparoscopy, much like robotics and endoscopic surgery, is only limited by instrumentation, both in availability and applicability. Therefore, it is the author's firm belief that extensive knowledge of laparoscopic instrumentation is necessary to continue to offer the best surgical care for our patients.

## Access

### Transperitoneal

Laparoscopic instrumentation has not changed much since the introduction of the Veress needle in 1947 [1]. The Veress remains widely used as a safe and efficient access to the peritoneal cavity while causing minimal trauma [2]. It is a 2 mm needle with a spring-loaded blunt obturator that is hidden during penetration of firm structures, such as fascia or skin (Figure 80.1). The blunt obturator deploys beyond the beveled edge of the needle when encountering softer, mobile structures such as bowel or intraperitoneal organs. Although a blind access technique, several tests such as aspiration, monitoring of insufflation pressure, and the "saline drop" tests can be used in combination to confirm entry into the peritoneal cavity [3] (Video 80.1).

For those uncomfortable with blind access or for patients with extensive previous abdominal surgery, the Hasson technique, open entry through a small incision with direct visual entry, provides a nearly failsafe alternative. Special blunt-tipped camera Trocars are manually deployed upon confirmation of entry for camera placement and insufflation. These Trocars will be described in subsequent sections [1].

### Retroperitoneal

The retroperitoneal space is only a potential space, making it ineffective for access and initial insufflation with a Veress technique. Access can be achieved by the Hasson technique with the use of a balloon dilator under laparoscopic vision. Although older reports describe filling a surgical glove or condom with air or saline once the proper space is entered, modern dilating balloons allow for manually controlled dilation with air while still maintaining visualization with a laparoscope [4]. Balloons are typically either spherical or oval in shape (Figure 80.2). Once the potential space is created correctly, the balloon port is switched to a traditional Hasson port to prevent loss of insufflation and dislodging.

## Insufflation

Carbon dioxide insufflator technology has remained unchanged for several years. The regulator box limits the inflow of the gas to the surgeon's preference, with auto-adjustment based on desired cavity pressures, while constantly displaying actual cavity pressure (Figure 80.3).

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

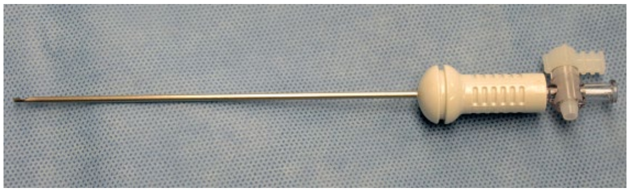

**Figure 80.1** The Veress needle is used for blind percutaneous access to the peritoneal cavity.

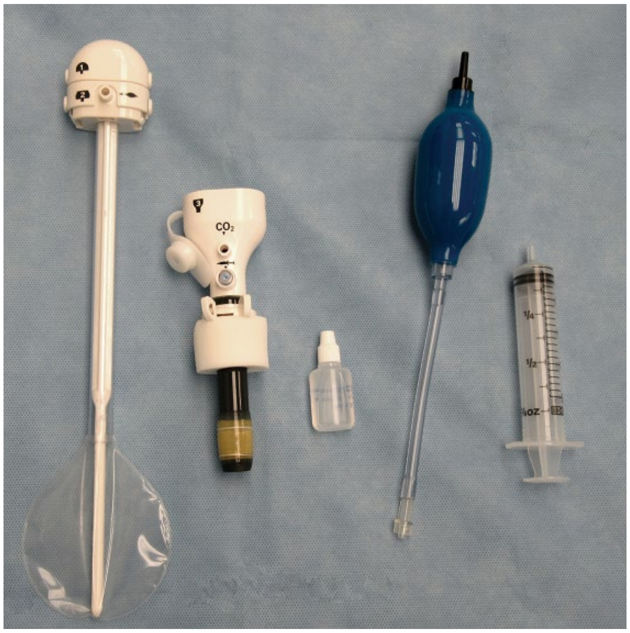

**Figure 80.2** Retroperitoneal access balloon set is used to expand the potential space of the retroperitoneal cavity.

Although initially described for patients with chronic obstructive pulmonary disease (COPD), helium gas is seldom used due to poor availability and very little practical need [5,6]. It is the author's experience that even patients with severe COPD can undergo laparoscopic surgery with $CO_2$ insufflation, with necessary adjustments to lower pressure or the volume and/or frequency of the ventilator.

One advance in insufflation is the advent of the AirSeal® system (SurgiQuest, Milford, CT, USA), which uses recirculated $CO_2$ to allow for a valveless Trocar while simultaneously providing insufflation and preventing loss of pneumoperitoneum. Without valves, this Trocar does not cause "smudging" with camera insertion and has no impedance to transfer of needles, hemostatics, bags, and specimens to and from the peritoneal or retroperitoneal cavity. This system also provides excellent smoke evacuation and can be switched to "conventional" insufflation if desired.

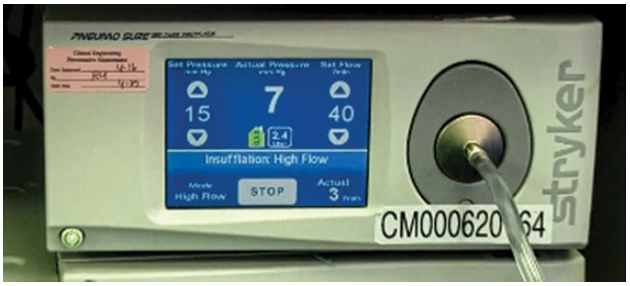

**Figure 80.3** An insufflator is used to deliver inert gas and regulate intraperitoneal pressure throughout the operation.

## Trocars

### Hasson

Usually used for the camera Trocar, Hasson Trocars are deployed into the access site created by the Hasson technique. They come in either a wedge/plug configuration or with a small-volume intracorporeal anchoring balloon. These additions to the simple cylindrical Trocar are essential for open or Hasson port placement to prevent constant loss of pneumoperitoneum and dislodgement of the port, as the size of the fascial incision is larger than with a puncture technique. To prevent loss of pneumoperitoneum during instrument exchange, these Trocars have an internal rubber diaphragm.

### Visual entry

Visual entry Trocars are cylindrical in shape and generally have a clear sheath and obturator with a dilating cone tip. The obturator is unique in that it will allow a 10 or 5 mm laparoscope lens to fit inside and visualize entry through the layers of the abdomen (Figure 80.4). The Trocars' anti-slip mechanism is such that since no fascial incision is made upon placement shear forces are stronger and there are small ridges on the surface of the outer sheath to hold it in place. To prevent loss of pneumoperitoneum during instrument exchange, these Trocars have an internal rubber diaphragm.

### Reusable

Aesculap (Center Valley, CA, USA) offers a set of reusable, metal Trocars ranging from 3.5 to 12 mm in size (Figure 80.5). A series of reusable nipples and a mechanical internal one-way valve prevent loss of pneumoperitoneum during instrument exchange. These Trocars are deployed using a screw-technique, employing a threaded screw around the outside of the Trocar that both dilates and anchors the Trocar during surgery.

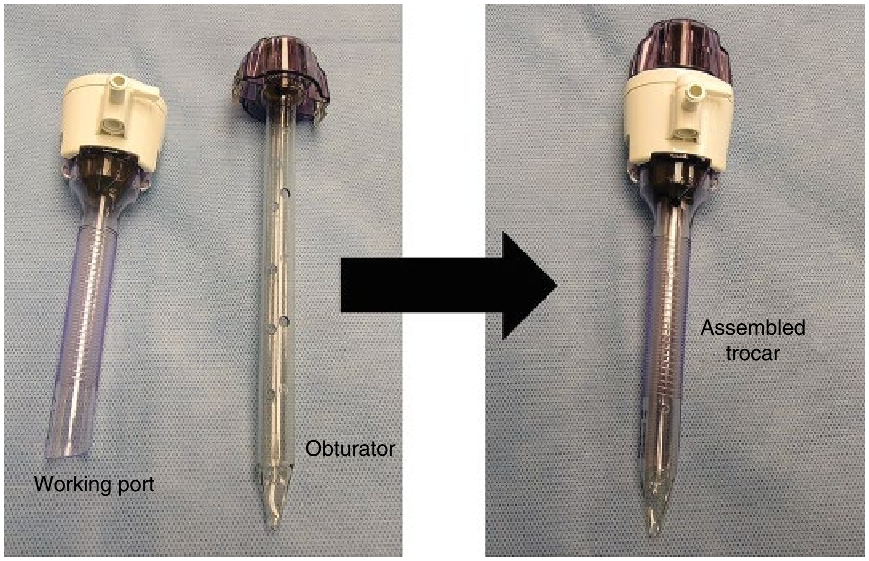

**Figure 80.4** Visual entry Trocar is used with a zero-degree lens laparoscope placed within the clear obturator to visualize penetration of the layers of the abdominal wall. Right: the assembled obturator-Trocar device.

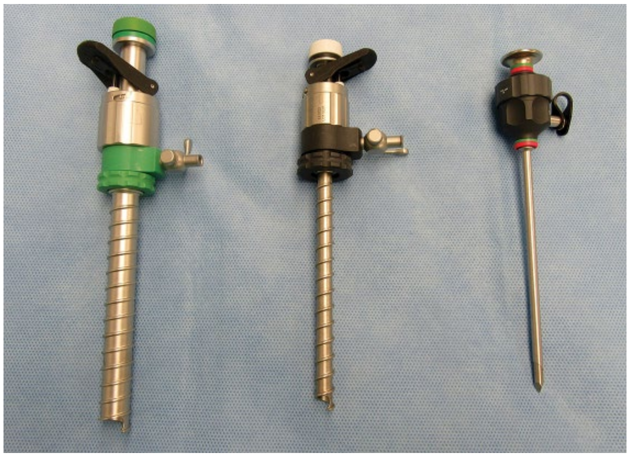

**Figure 80.5** Reusable Trocars can be deployed using blind or visual entry, utilizing a screwing motion with gentle downward pressure for precise Trocar placement.

### Internal dilating

The Step™ system (Medtronic, Minneapolis, MN, USA) is a radially dilating system of bladeless Trocars that are initially deployed by Veress needle. The Trocars dilate to full working size by placement of an internal dilator which opens the expandable Trocar sheath. This offers the advantage of minimal trauma to the abdominal wall and the small Trocars can be expanded to a larger diameter intraoperatively without the need to remove and replace [7]. Radially dilating Trocars have the smallest defect size when compared to single and triangular cutting bladed Trocars, but required the greatest insertion force [8].

Of note, there are a variety of other Trocars that have been developed and used for single-port and robotic surgery that will not be discussed in this chapter.

## Vision

Perhaps the greatest advances in laparoscopic surgery have been in intracorporeal visualization. Advances in resolution, magnification, three-dimensional (3D) optics, digital image processing, and advanced image enhancement has hastened the widespread adoption of laparoendoscopic surgery for even more complex procedures.

Currently, all laparoscopic optics require a reusable camera and lens system that can be sterilized and connected by cables to an image-processing set-top box. The laparoscopic tower holds one or multiple set-top boxes that are not sterilized and can digitally enhance and transmit the image to a monitor in the operating room (OR). The tower also houses the light source, a high-intensity bulb transmitting light to the laparoscope via a sterile cable (Figure 80.6).

### Rigid endoscopes

Rigid endoscopes are the traditional lenses used to transmit light from the intracorporeal cavity to an image-processing camera. They incorporate a separate fiber-optic channel to transmit light into the body along the outer edges of the lens. Currently, these lenses offer different degrees of angulation (0–45°) and increasing size, from 2.7 mm “needlescopes” to standard 10 mm lenses for laparoscopic procedures. Generally, increasing the angle and decreasing the overall diameter diminishes image quality. On average, rigid endoscopes provide a 70° visual field. These lenses require a separate “camera” and light-source cable attached to the extracorporeal laparoscopic tower to provide image transfer and light.

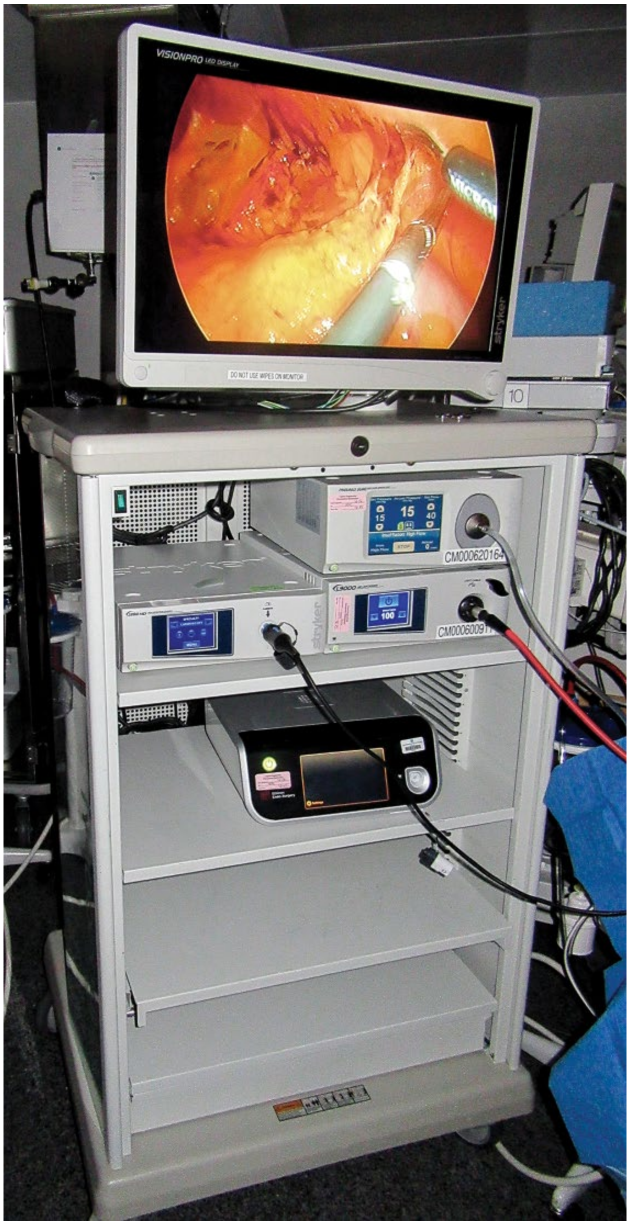

Figure 80.6 Laparoscopic set-top box tower with LCD display monitor, insufflation device, image-processing hardware, and light source.

### Flexible endoscopes

The Endoeye Flex 3D® (Olympus, Center Valley, PA, USA) is a 5 mm rigid-shaft digital endoscope with an articulating tip containing the camera and lens. This provides a high-definition (HD) image and angulation from 0 to 100°. Visual field is 85°. As with the other lenses, flexible endoscopes are sterilized using a standard autoclave. A single cord extends from the extracorporeal handle to the image-processing and light-supply tower.

## Light source

Halogen, xenon, and light-emitting diode (LED) are the most commonly used light sources. Aside from the LED, halogen and xenon can generate significant thermal energy when in contact with intraperitoneal contents. Currently, light sources are housed in an image-processing tower and transmit light using sterile fiber-optic cables [9].

## Image processing

Most image-processing occurs on the set-top box in the tower mentioned above. Processing can and usually does involve adjustments of brightness (automatic or manual), hue, contrast, and display size. Many vendors offer predetermined or memorized settings optimized to operation type or surgeon preference.

### Near-infrared technology

This technology requires injection of a fluorophore (commonly indocyanine green or ICG) that preferentially deposits in vascular tissues. A variety of different light sources can be used to excite the fluorophore and cause it to emit light. This light is then preferentially detected using one of several optical filters, highlighting the desired target tissues. In urology, the most common use for near-infrared technology is in identifying renal tumors and ureters.

### Narrow-band imaging

Narrow-band imaging uses wavelengths specific for limited green and blue visible light to highlight vasculature of mucosal surfaces. Although primarily used in endoscopic procedures, many image-processing platforms used in laparoscopy incorporate this technology.

### Three-dimensional imaging

3D imaging was popularized in surgery primarily by the da Vinci® surgical system. The da Vinci® system utilizes a binocular lens and camera that projects through two separate eyepieces into a surgeon console. This concept has been applied to laparoscopic surgery through binocular surgeon headsets. While studies have shown that the 3D systems improve surgeon performance, they have not been widely accepted or utilized due to reports of dizziness, operator discomfort, technological complexity, and high cost [10–12]. For laparoscopic surgery, single screen-suspended or set-top monitors have been used to display 3D images (see Display). Early versions of 3D imaging were limited to standard definition (SD), but newer products offer HD quality of 3D images.

### 4 K

Ultra-HD or 4 K imaging provides approximately four times the number of pixels over the same area as an HD image (4 K is 3840 × 2160; HD is 1920 × 1080). This increased resolution is best appreciated at close viewing distances and is highly applicable to laparoscopic surgery. Current limitations only include cost and availability, as displays and image-processing technology are already mature in nonmedical applications [13]. Although few ORs currently employ this technology, 4 K will certainly offer improved visualization in laparoscopic surgery.

### Ultrasound

A variety of vendors offer handheld ultrasound probes designed to fit through a 10–12 mm port. These are articulating and can offer Doppler overlay. BK Ultrasound and Hitachi Aloka Medical are widely available and can double for use in robotic surgery. This technology is essential for partial nephrectomy and can also be used to identify vessels hidden by scar tissue.

## Display

Monitors, either suspended from the ceiling with a boom or on a set-top box tower, are the standard choice for image display in the OR. An OR usually requires at least two monitors so that everyone in the OR can observe the operation and share the display, depending on the placement in the OR. In the United States, it is now commonplace to find HD monitors in the OR. In addition to being able to display high-resolution images, these monitors provide improved contrast and resolution to SD images.

Newer monitors can be integrated with 3D technology to provide 3D display to surgeons and others in the OR without the need for 3D glasses. There are several vendors through which these medical systems can be purchased.

## Extracorporeal assist devices

### Table-mounted instrument holders

Available from several vendors, table-mounted instrument holders are designed to take the place of a human bedside assistant by keeping secondary retracting instruments from moving during laparoscopic surgery. These often have either articulating or flexible locking arms that attach to the rails on the operating table. They are generally low in profile and can be mounted to allow the surgeon to operate unencumbered. The author has considerable experience with such devices from Thompson Surgical Instruments (Traverse City, MI, USA) that have performed reliably, but many different vendors offer table-mounted instrument holders.

## Graspers

Such a wide variety of laparoscopic graspers exists that here are recommended general categories that are felt to be essential to common laparoscopic procedures. In general, most are available in locking or nonlocking forms and rigid or rotatable forms. The author favors locking and rotatable instruments due to their versatility, but these instruments tend to be more fragile and sometimes more cumbersome and optional for straightforward procedures. Nearly every type of end-effector available in open surgery can be found in laparoscopic instrumentation.

### Bowel grasper

Bowel graspers have a long, single-hinged effector with small or large-gapped ridges to prevent slippage of tissue. Grip strength is purposefully weak to prevent crush injury. These are not meant for grasping needles or tissues with high turgor.

### Dissecting graspers

Dissecting graspers generally have a shorter end-effector, are single-hinged, and can be straight-tipped or carry varying degrees of curvature. They can range from a sharply tapered “dolphin-nose” effector to a broad tip. These tend to be the workhorse or most versatile instruments during surgery and have moderate grip strength. The author recommends having several different sizes and shapes of tips available for each case (i.e. curved versus right-angle versus straight tips).

### Needle-holders

Needle-holder graspers have short, single-hinged end-effectors with tremendous grip strength ideal for holding needles. They can be locking or nonlocking and sometimes “self-righting,” with a single matched pair of grooves in the end-effector to force the needle into a 90° position. These should not be used to grasp tissue due to the potential for crush injury.

## Clamps

Many standard graspers can serve as a “weak” clamp but do not resist tissue slippage very well. For this reason, various locking clamps are available. Small intracorporeal, spring-loaded “bulldog” clamps can be placed without losing the use of a port to keep them in place. Special handheld instruments passed through ports are used to deploy and remove these clamps. In addition, large “Satinsky”-style locking clamps with long handles can be used to clamp the renal hilum or major vascular injuries to the inferior vena cava. Of note these larger Satinsky-style clamps may require a flexible Trocar for deployment.

## Retractors

Although traditional locking graspers can be employed as retractors when clamped onto the body wall intracorporeally, several devices also exist for this purpose.

### Transabdominal stationary

These retractors are primarily designed to retract the liver or spleen and can be fixed-hook (e.g. Nathanson Hook®, Aesculap) or triangular self-forming (e.g. Lapro-Flex®, Mediflex Surgical Products, Islandia, NY, USA) in shape. The handle remains extracorporeal and can be held by a surgical assistant or, more often, by a table-mounted instrument holder.

### Transabdominal mobile

Held by a surgical bedside assistant, a “fan” retractor employs a collapsible set of long blades with blunt tips expanded to a triangle shape to retract large surface areas. This is available in disposable or reusable forms and comes in 5 and 10–12 mm sizes.

In disposable form, the Endo-Paddle™ (Medtronic) employs a collapsible, rectangular frame covered by a fabric mesh without fenestration. This is in only available in 12 mm size and is very useful for intestinal retraction due to the lack of fenestrations.

## Cutting

### Scissors

There have been no significant advances in laparoscopic scissors over the last 10 years, aside from the development of disposable blades. Blades can be either curved, which is more common and versatile, or straight with a fine tip, such as Potts scissors. Curved-tip scissors are available both with and without the ability to apply monopolar cautery. If used with cautery, the gentle curve can also be used for fine dissection much in the same way as a hook cautery device (also available in laparoscopic form). Curved scissors can be found most commonly in a 5 mm variety or in a heavy-duty 10 mm variety for heminephrectomy. The advent of disposable scissors allows consistently sharp blades best for fine dissection and delicate tissues. The entire instrument or just the tip can be single use. Microline Surgical (Beverly, MA, USA) and other vendors have such a line of “reposable” instruments, with single-use tips and a reusable handle and shaft.

## Hemostasis

Along with improvements in optics, advances in hemostatic technology for laparoscopic surgery have provided the significant benefit to surgeons over the last decade. Both energy-based instruments and biologic agents have seen a proliferation of options available during laparoscopic surgery and more are in development. There are so many options available at the current stage, with no single-proven single superior product, that surgeon preference after trying various competing products should drive choice.

### Energy-based devices

**Monopolar**

The oldest form of energy-based hemostasis employs the use of monopolar current. Common instruments that use monopolar current include shears and small dissecting hooks. In monopolar current, energy is dispersed from the active electrode to a larger return electrode, transferring heat from a single probe to vascular tissue and causing desiccation and coagulation. Injuries to surrounding tissues are common in monopolar cautery due the risk of capacitive coupling or breaks in the insulating coating; however, the advent of active electrode monitoring (AEM) has decreased the risk for injury [14,15]. This form of hemostasis remains useful in laparoscopy for its ease, precision, and speed.

**Argon beam**

The argon beam coagulator (ABC; Conmed, Utica, NY, USA) uses the inert gas argon to deliver monopolar electricity safely for hemostasis. In the ABC, a directed beam of argon gas ionizes to aid in the conduction of radiofrequency electric current. This is most useful for control of solid-organ surface bleeding on the liver, spleen, or kidney. It is important to vent the peritoneum during use to prevent buildup of pressure and gas embolism, the most serious danger of using an ABC [15]. In addition to the risks mentioned above, this method has become been utilized less due to the cumbersome equipment, the need for venting, and the improvement of deployable hemostatics.

#### Bipolar

Most newer energy devices use bipolar current, or the transfer of energy between two prongs of an instrument to contain heat transfer to the area between the prongs. This energy type is especially useful for ligation of small vessels (<8 mm) due to the utilization of simultaneous compression with coagulation and desiccation. The simplest bipolar device is a small grasping forceps that transfers a small amount of current between its two jaws. Newer devices with several vendors are more complex, offering impedance detection to verify when a vessel is truly “sealed,” an integrated cutting blade to combine sealing with division, and technologies to limit the spread of energy to surrounding tissues. Bipolar electrosurgery requires lower voltages than monopolar electrosurgery, resulting in a decrease in potential injury. These devices are very useful in laparoscopic surgery and have been shown to reduce blood loss, operative time, and the use of clips and ties intracorporeally [16,17]. Bipolar instruments range in diameter from 3 to 10 mm and come in a variety of tip shapes. Thermal spread of energy of devices ranges from 2 to 4 mm [18]. Some of the more advanced and widely used models are the Ligasure™ (Medtronic), Enseal® (Ethicon Endo-Surgery, Cincinnati, OH, USA), Caiman® (Aesculap), and PKS™ OMNI (Olympus) (Table 80.1).

#### Ultrasonic

Ultrasound technology can also be used for precise cutting and coagulation by converting electrical energy into vibration. The vibrations induce protein denaturation by causing internal cellular friction and breaking down hydrogen bonds [16]. The Harmonic Synergy® scalpel (Ethicon Endo-Surgery) utilizes pure ultrasonic energy through a vibrating cutting blade (55 kHz) to efficiently heat, compress, seal, and divide tissue and vessels that are less than 7 mm. The cutting blade does generate heat and should not be adjacent to delicate tissues not intended to receive high temperatures. Thermal spread is reported to be between 1.7 and 2.2 mm.

### Hemostatic agents

The development of deployable agents adds a useful tool to laparoscopic surgery. These agents have been in some form of development or use since the early twentieth century, but were initially fraught with problems and concerns of carrying viral or bacterial organisms. In modern times, improved sterilization techniques have negated this concern. In addition, allergic reactions are increasingly rare due to improved technology and decreased use of bone wax [19]. Many different vendors offer such agents, but over the last decade the categories of general types of agents have not changed. In general, there five categories: fibrin sealants, gelatin-based products, oxidized cellulose, collagen products, and microporous polysaccharide hemospheres [20,21] (Table 80.2). Different formulations of these products can be deployed by direct placement

**Table 80.1** The four most commonly used bipolar sealing devices are available within 5 and 10 mm shaft size, with opposing jaws for compression and delivery of energy. They all have the ability to sense tissue properties to confirm the seal and must be connected via cord to a nonsterile set-top box [16–18].

| | **Ligasure™** | **Enseal®** | **Caiman®** | **PKS™ OMNI** |
|---|---|---|---|---|
| Manufacturer | Medtronic | Ethicon | Aesculap | Olympus |
| Max vessel size | 7 mm | 7 mm | 7 mm | 7 mm |
| Mechanism | Delivers high current, low voltage along with pressure from the jaws to tissue and uses the body’s own collagen and elastin to create a permanent fusion zone | Delivers high uniform compression throughout the device tip and offset bipolar electrode design helps contain energy flow and concentrate energy on tissue and within the jaws | Pulse waveform modulation (PWM) monitors and delivers current in relation to power, voltage, and resistance | Plasma kinetic technology delivers a high current and very low voltage to the tissue while a series of rapid pulses allows a cooling phase during coagulation to decrease lateral thermal spread |
| Lateral spread [23,24] | 2–3 mm | <1 mm | <1 mm | 2–6 mm |
| Features | Fast sealing time (10 seconds)<br>Highest burst pressure (385 mmHg) | Offset electrode design reduces lateral thermal spread | Less operative time due to larger jaw<br>Tips close first to prevent slippage and provide uniform compression | Fast sealing time (11.1 seconds) |

**Table 80.2** Commonly used and widely available hemostatic agents can all be deployed laparoscopically on to bleeding tissues. Each agent has potentially different advantages depending on tissue type and situation, but selection is primarily surgeon-dependent [19–21].

| Category | Product | Manufacturer | Source |
|---|---|---|---|
| Fibrin sealants | Tisseel®/Artiss® | Baxter | Human |
| | Evicel® | Ethicon | Human |
| | Vivostat® | Pacific Medical Systems | Human |
| Gelatin-based products | FloSeal® | Baxter | Bovine |
| | Surgifoam® | Ethicon | Bovine |
| | Surgiflo® | Ethicon | Porcine |
| | GelFoam® | Pfizer | Porcine |
| Oxidized cellulose | Surgicel® (Snow) | Ethicon | Plant |
| Collagen products | Avitene™ | Bard | Bovine |
| | Instat MCH® | Ethicon | Bovine |
| Microporous polysaccharide hemospheres | Arista™ AH | Bard | Plant |

Baxter, Deerfield, IL, USA; Pacific, San Diego, CA, USA; Pfizer, New York, NY, USA. Other manufacturers are given in the text.

with forceps, spray, or even drip application. Prices of these agents may vary considerably with sometimes unclear differences in advantages for different purposes.

## Stapling

Multiple vendors offer reliable stapling devices to ligate and divide larger structures, ranging from large blood vessels >5 mm to intestines and even hepatic or adrenal tissues. Although powered options are available, most devices are manual, meaning the compression force is initiated manually and applied to the tissue being ligated immediately prior to deployment of the staples. It is important to note that there are different varieties of "load," or staple size and arrangement, that are optimized to certain tissues. Most commonly, vascular staples are small and closely situated in multiple rows while intestinal staples are larger with longer teeth to span the width of the intestinal wall. Staplers generally require a 12 mm port for use. The most useful stapling devices are able to rotate 180° or more along the shaft axis and articulate to >60°.

## Clips

Laparoscopic clip appliers come in two varieties, auto-reloading and manually reloading. Appliers range in size from 5 to 12 mm. The auto-reloading variety generally will carry 12–15 metal clips that are deployed by a variable squeezing mechanism in the handle. Once the clips are finished, another device must be opened to deploy more clips. In some cases, the clips can be removed by sliding them off gently, but this is not always possible.

Manually loaded clips are often plastic with a locking "clasp" that can also be removed using a different removal tool. An example is the Weck® Hem-o-lock® clips (Teleflex Medical, Research Triangle Park, NC, USA) that can ligate up to 16 mm structures. These clips are loaded individually at the bedside bench, generally by a scrub technologist, and handed to the surgeon for deployment intracorporeally.

## Suction-irrigation

These devices are essential for laparoscopy, except in cases of hand assistance. The primary purpose is to clear the area of dissection from blood or other spilled fluids to allow proper visualization. There are a limited number of widely used combination suction-irrigation devices. The two most widely used disposable devices are made by Bard Medical (Covington, GA, USA) and Stryker Corporation (Kalamazoo, MI, USA), but many acceptable alternatives exist. In addition, reusable metal instruments are also available. They are connected via sterile suction tubing to a battery-powered pump mechanism, saline bag, and reservoir near the operating table outside of the sterile field.

## Suturing instruments

Suturing during laparoscopy can be challenging due to decreased degrees of freedom, restricted space between instruments, and limited instrument access points due to port placement [22]. A variety of laparoscopic needle drivers are available. All available drivers have an end-effector needle-holding (short-nosed) forceps with high grip strength. Locking and nonlocking varieties exist. Some end-effectors have a slight curved tip that may be useful in small suturing spaces. Self-righting needle drivers with a shallow groove in the end-effector may be helpful because adjusting the needle angle on the driver laparoscopically can be cumbersome or challenging. The authors encourage laparoscopic surgeons to try both locking and non-locking varieties and multiple different handle types (such as a pistol, ringed, or straight grip) before committing to a certain driver.

An auto-suturing device (e.g. Endo Stitch™ by Medtronic) is also available that is very fast and easy to use for simple intracorporeal suturing. This device passes a small two-sided needle attached to a suture back and forth between two prongs on the end-effector. There are 5 and 10 mm devices available with a variety of suture sizes and types. Disadvantages of these devices include the inability to "back" a needle out to make a slight adjustment and difficulty navigating a complex curve or thick tissue due to the small, straight double-pronged end-effector.

## Entrapment bags

Entrapment bags are critical to oncology cases and useful in many other cases to avoid spillage and assist with extraction. These can be reusable, disposable, or even completely deployed off the laparoscopic device (e.g. LapSac® by Cook Urological, Spencer, IN, USA). Sizes of the bag vary considerably and all are made of impermeable materials atraumatic to the abdominal wall during extraction. Necessary port sizes to deploy the bags commonly range from 5 to 15 mm (Figure 80.7).

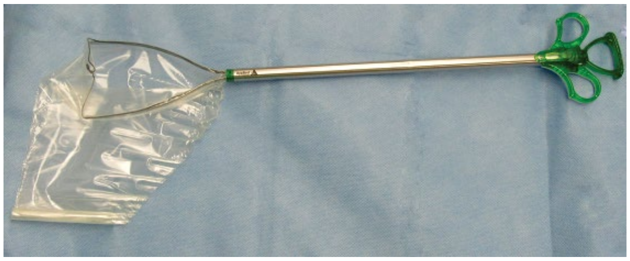

**Figure 80.7** Single-use entrapment bag, inserted into the abdomen through a 10–12 mm port while collapsed within the shaft and opened intracorporeally under laparoscopic vision. Once the specimen is within the bag, a drawstring is pulled to tighten the outlet to prevent spillage.

## Hand-assist ports

In intraperitoneal laparoscopic surgery, utilizing one hand intracorporeally can be a useful transition from a traditional open surgeon to laparoscopy. In addition, advanced laparoscopic surgeons may choose to utilize "hand-assistance" for complex operations. Although not necessary, multiple ports exist that can accommodate a hand while maintaining pneumoperitoneum and allowing quick and repetitive passage of the hand in and out of the abdomen. These ports span the entire abdominal wall with an anchoring ring inside the peritoneal lining and an outer anchoring ring on the skin surface. A popular choice is the GelPort® system (Applied Medical, Rancho Santa Margarita, CA, USA), which has a self-sealing gelatin-like matrix that can be cut to allow traditional laparoscopic ports in addition to a hand. Other ports may allow for adjustment of the circumferential pressure around the wrist and forearm based on surgeon preference.

## Closure devices

Because such small incisions are utilized to place laparoscopic ports (3–12 mm), closing the fascia may be cumbersome, especially in obese patients. Laparoscopic suture-passing devices have been developed to assist with fascial closure. These are 2 mm puncturing needles with a tip that can securely grasp and release the suture. The suture is passed through the abdominal wall, usually subcutaneously, and then regrasped intracorporeally under laparoscopic vision through a separate puncture on the opposite side of the incision to be brought out and tied extracorporeally. Devices range from a simple straight 2 mm grasping needle to a combination of needle and cone-shaped guides to produce more consistent throws and a predictably reliable closure (e.g. Carter-Thomason CloseSure System®; Cooper Surgical, Trumbull, CT, USA). This technique is nearly essential in the morbidly obese and can significantly decrease fascial closure time while also ensuring adequate closure.

## Other instruments

As more emphasis is placed on a quicker recovery and less time to return to normal activities after surgery, the footprint of laparoscopic surgery in urology is expanding to cases never before utilized, such as for urinary diversion and inferior vena cava thrombectomy. For this reason, and with the advancement of derivatives of laparoscopic surgery, namely single-site, natural orifice, and robotic surgery, new instruments are perpetually in development and are not all mentioned here.

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# 81

# Robotic Surgery: Basic Instrumentation and Troubleshooting

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## The da Vinci® System

The da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) consists of three core components: a surgeon console, a vision tower, and a patient cart with four robotic arms (Figure 81.1). One arm controls the camera and the remaining arms manipulate surgical instruments. On the da Vinci Xi Surgical System the camera can be placed on any of the four robotic arms, allowing for port hopping during a procedure. The instruments have seven degrees of freedom, including external pitch, external yaw, insertion, grip, roll, internal pitch, and internal yaw, allowing for wristed, articulated movement. The surgeon sits at the console and is presented with a high-resolution three-dimensional view of the surgical field.

### Surgeon console

The console includes a stereo viewer with sensors as a safety mechanism. If the surgeon's head is not positioned in the console, the system will be deactivated and the robotic arms will be locked in place. By using the two master controllers, the surgeon's hand movements are processed by a computer and sent to the patient cart, which controls the robotic instruments inside the patient's body in real time. Motion scaling can be performed to filter out physiologic tremor, allowing for finer movements [1]. Computer processing also facilitates intuitive motion, whereby movement of the surgeon's hands is translated to the movement of instruments. This differs from laparoscopic surgery, in which, to move the instrument tips left, right, up, or down, the surgeon must actually move his or her hand in the opposite direction.

Adjustments to the system, such as camera control, scope setup, audio volume, and console ergonomics, can be made while the surgeon is seated at the console. The console surgeon can also toggle between robotic arms. These tasks can be accomplished using the console's hand and foot pedal controls. The console is connected to the vision cart and patient cart components via cables.

### Optical system

The da Vinci system offers three-dimensional magnified vision. On the da Vinci Si Surgical System, a binocular telescopic camera lens system (0 or 30°) is attached to a high-resolution 3DHD camera, and together they are held on the main robotic manipulator arm. The da Vinci Xi Surgical System endoscope has "chip-on-tip" technology, where the digital image sensors are placed at the tip of the scope. The digital image information is then transmitted directly to the image processor. The binocular images are translated by the computer into a magnified 3D image when viewed at the surgeon console [2]. The robotic scope is either 12 mm (Si) or 8 mm (Xi) in diameter. On the Xi system, the 8 mm robotic endoscope fits through the standard robotic trocar, allowing for port hopping between trocars, giving surgeons the ability to have multiple vantage points in a single procedure.

### Patient cart (robotic arms and instruments)

The patient cart, consisting of the robotic arms and instruments, is draped and positioned alongside the patient table [3]. The patient cart has four arms. Robotic instruments have articulating joints (EndoWrist) near the tip that allow for wristed movement, providing seven degrees of freedom of movement for surgical tasks such

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

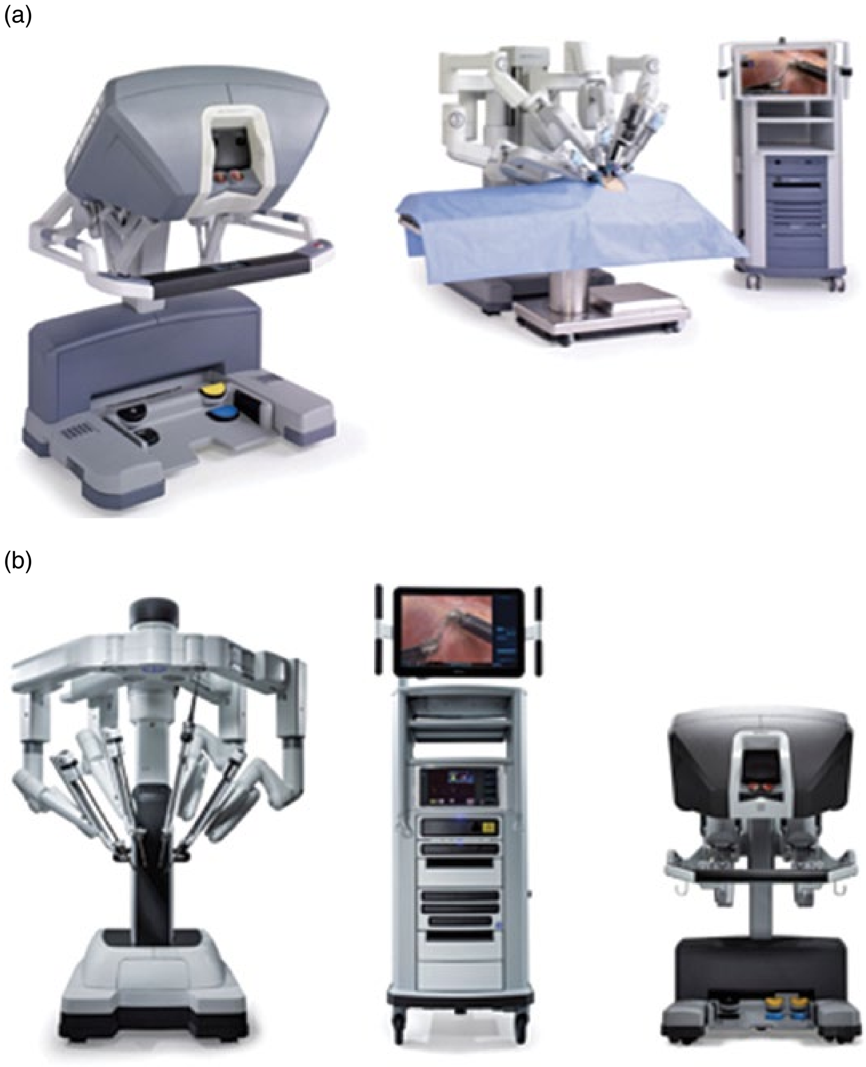

**Figure 81.1** The Surgeon Console, Patient-side Cart, and Vision System of the da Vinci Surgical System. (a) da Vinci Si Surgical System; (b) da Vinci Xi Surgical System.

as suturing and dissection. Robotic instruments are available with a variety of instrument tips in 5 or 8 mm diameter sizes.

The new da Vinci Xi™ Surgical System has four robotic arms attached to the mount of the patient cart, called the "boom." The Xi Surgical System has narrower arms and improved reach to minimize collisions between robotic arms. The endoscope can attach to any robotic arm through a robotic trocar, allowing flexibility in optimizing visualization of the surgical site. The "chip-on-tip" endoscope has a longer focal length and wider field of view. The rotating overhead boom allows for laser targeting and improved anatomical access from almost any position, which can help avoid the need for redocking and repositioning during surgeries such as nephroureterectomy.

## EndoWrist robotic instruments

The EndoWrist instruments are controlled by the surgeon at the console. The surgeon's finger movements are translated into movements of the instrument tips. The foot pedals can be used to toggle between instrument and camera movements, reset instrument movements (clutching) or initiate electrocautery [2]. Toggling between instruments allows a surgeon to control his or her own passive retraction using the third instrument arm. Clutching can also be performed using the finger clutch mechanism. If the robotic nondominant instrument is attached to cautery, care must be taken to avoid hitting the wrong foot pedal and causing thermal injury to the bowel or other structures [4].

Different EndoWrist robotic instruments offer different relative advantages for different procedures (Figures 81.2–81.5). Note: Some instruments may only be available on the Si or Xi system.

Commonly used EndoWrist monopolar cautery instruments include the Hot Shears™ monopolar curved scissors and monopolar cautery hook. Bipolar cautery instruments include the fenestrated bipolar forceps, Maryland bipolar forceps, PK™ dissecting forceps (Si only), and PreCise bipolar forceps (Si only), long bipolar grasper (Xi only), curved bipolar dissector, and microbipolar forceps. The robotic vessel sealer provides cauterization and coagulation of soft tissues and small vessels (less than 7 mm in diameter) using bipolar energy, with minimal thermal energy spreading, followed by cutting using the blade inside the instrument (see Figure 81.2).

Robotic grasper instruments include the, ProGrasp™ forceps, Cadiere forceps, double fenestrated grasper, and Cobra grasper (see Figure 81.3), as well as the tenaculum forceps and DeBakey forceps. In the nondominant hand, the fenestrated bipolar can be used for atraumatic dissection of vessels. However, the fine sharp tips of the Maryland bipolar forceps or PK dissecting forceps can be used for precise cauterization of small vessels and dissection of structures. The ProGrasp has no thermal energy but has the strongest closing force, making it a robust grasping instrument. In the dominant hand, the Hot Shears can be used for tasks such as cauterization, blunt and sharp dissection, as well as for tumor excision in cases such as robot-assisted partial nephrectomy [4]. The monopolar hook may be used for blunt dissection of vessels and dissection of tissue planes during extirpative procedures. Robotic ultrasonic shears are available, but they lack EndoWrist capability [5].

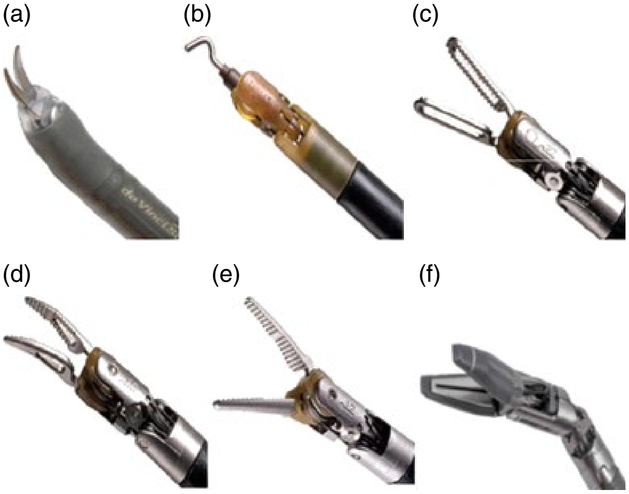

**Figure 81.2** EndoWrist monopolar and bipolar instruments. (a) Hot Shears (monopolar curved scissors); (b) permanent cautery hook; (c) fenestrated bipolar forceps; (d) Maryland bipolar forceps; (e) PK dissecting forceps; (f) vessel sealer.

Robotic needle drivers available for suturing include the large needle driver and mega needle driver (see Figure 81.4a). The surgeon may choose to use an EndoWrist grasping instrument, such as a ProGrasp, in the nondominant hand to economize instrument use. A SutureCut™ needle driver, available in both sizes, allows the console surgeon to cut sutures, but care must be taken not to accidentally cut the suture while handling it during suturing. Black Diamond needle drivers are also available for more precise suturing, such as the vascular anastomosis during robotic kidney transplant. The robotic Hem-o-lok™ clip applier can be useful for clipping vessels, particularly vessels at a challenging angle for the assistant to clip manually (see Figure 81.4b). Robotic clip appliers are available for large or medium–large

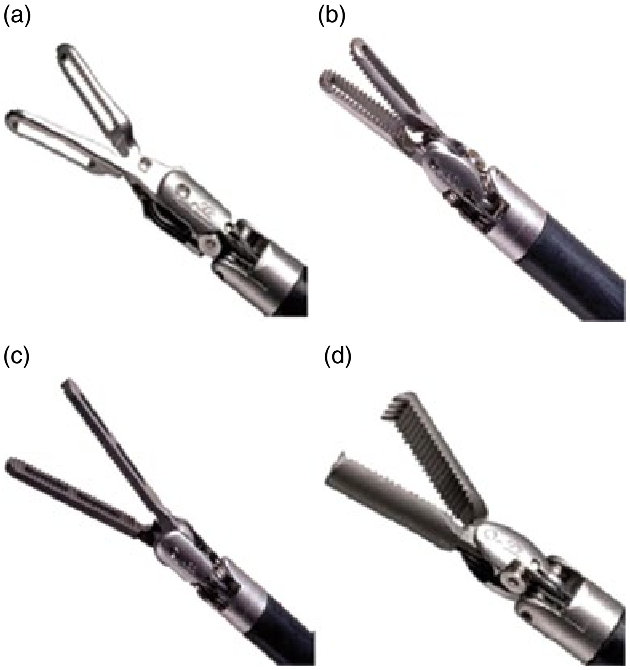

**Figure 81.3** EndoWrist grasper instruments. (a) ProGrasp forceps; (b) Cadiere forceps; (c) double fenestrated grasper; (d) Cobra grasper.

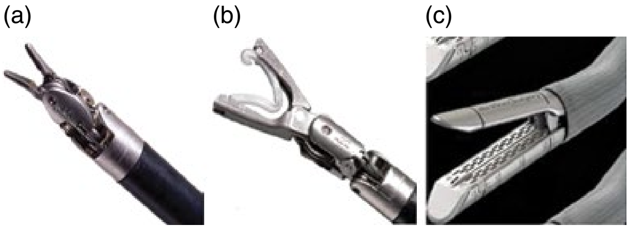

**Figure 81.4** EndoWrist robotic needle drivers, clip appliers, and staplers. (a) Large Hem-o-lok clip applier; (b) large needle driver; (c) robotic stapler.

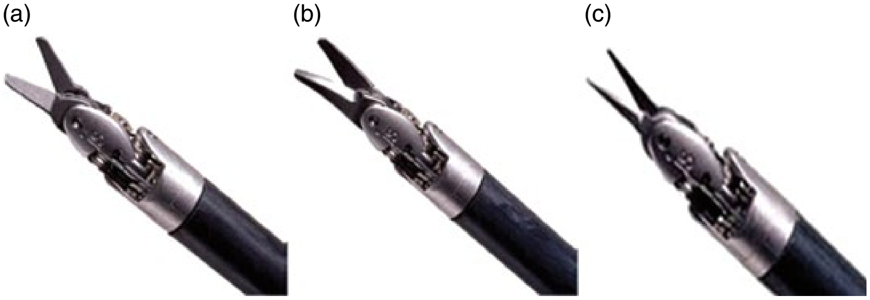

**Figure 81.5** Robotic athermal scissors. (a) Round-tip scissors; (b) curved scissors; (c) Potts scissors

Hem-o-lok clips or for small titanium clips. The clip is loaded externally and introduced by the assistant into the robotic port. The robotic clip applier holds a single clip, so having a second robotic clip applier can facilitate faster exchanges. Care must be taken not to inadvertently squeeze the fingers, as this may cause the clip to misfire. The robotic clip applier will accommodate 100 clip firings. The life of most other robotic instruments is 10 cases, after which the system will not allow the operational use of the instrument. An EndoWrist robotic stapler is also available for the da Vinci Xi Surgical System, allowing surgeon control and autonomy over positioning, gripping, clamping, and firing of the stapler through the surgeon console (see Figure 81.4c). The robotic stapler has fully wristed articulation. It can also detect whether the stapler jaws are adequately closed on the tissue for proper firing. EndoWrist staplers are available in size 30, 30curved, and 45 and available loads include white, blue, and green.

Athermal robotic scissors include round-tip scissors, curved scissors, and Potts scissors (see Figure 81.5).

### Third instrument arm

The third instrument arm can be utilized to provide retraction independent of the surgical assistant. The third instrument arm port is placed away from the other da Vinci instrument ports to minimize arm collisions. EndoWrist instruments used with the third instrument arm include the ProGrasp, and the double fenestrated grasper. For robot-assisted kidney surgery, the third-arm instrument can be used to lift the kidney anteriorly by placing it under the ureter [6]. This places the renal hilum on stretch, allowing two-handed dissection of hilar vessels.

## Robotic Ultrasound, Fluorescence Imaging, TilePro, and Robotic Bulldog Clamps

Robotic ultrasound probes have been developed that allow surgeon control of intraoperative ultrasound using a robotic grasper during robotic partial nephrectomy (Figure 81.6) [7]. TilePro is a multi-image video display mode of the da Vinci Surgical System that allows the surgeon to simultaneously view additional images, such as intraoperative ultrasound and preoperative CT images, as a picture-on-picture on the 3D console screen and assistant monitors. TilePro can be used during robot-assisted partial nephrectomy to localize tumors and to delineate margins of resection using intraoperative ultrasound without the need to leave the console to view external images [6]. The surgeon can switch back and forth from TilePro mode and can adjust the size of the image relative to the console view. The Firefly Fluorescence Imaging system may be utilized to assess vessels and tissue perfusion. After indocyanine green (ICG) dye is injected intravenously, the fluorescence mode is activated, causing near-infrared laser-induced fluorescence of the ICG and a corresponding color signal to perfused structures. The surgeon can toggle between white light and fluorescence modes. Robotic bulldog clamps have

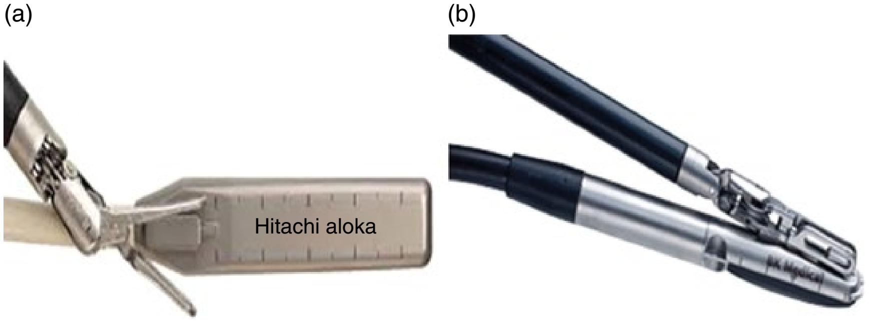

**Figure 81.6** Robotic ultrasound probes. (a) Robotically controlled ultrasound transducer (Hitachi-Aloka Medical America, Inc., Wallingford, CT, USA); (b) drop-in ultrasound transducer (BK Ultrasound, Luton, UK).

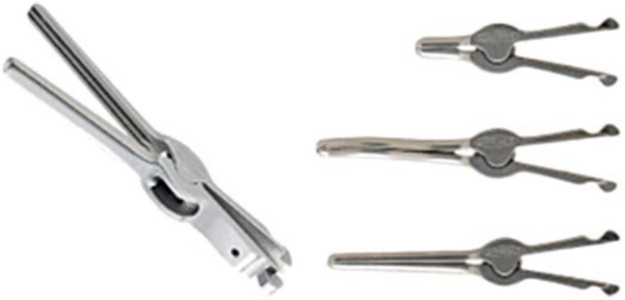

**Figure 81.7** Robotic bulldog clamps (Scanlan® Reliance Bulldog Clamps, Scanlan International, St. Paul, MN, USA).

also been developed that allow surgeon control over clamping of vascular structures (Figure 81.7). The robotic bulldog clamps can be applied using a robotic grasper, such as the ProGrasp, allowing the surgeon to have full articulation when applying and removing the clamp [8].

## Dual console capability

An optional second console available with the da Vinci Surgical System allows two surgeons to collaborate during a procedure. Surgeons can exchange control of the instrument arms and endoscope using the surgeon touchpad, while a built-in intercom system facilitates communication. The addition of a second console offers an environment for training and provides a platform to refine techniques and learn new procedures.

## Integrated table motion

Integrated table motion provides synchronized movement between the da Vinci Xi Surgical System and the operating room table (TruSystem® 7000dv, Trumpf Medical, Saalfeld, Germany), allowing the surgical table to be repositioned with the robotic arms still docked (Figure 81.8). This facilitates intraoperative adjustments to improve gravity exposure and access to target anatomy during multiquadrant surgeries, such as nephroureterectomy. This technology may also reduce the extent and duration of Trendelenburg positioning that a patient must tolerate during a robotically assisted urology procedure.

## Troubleshooting

Several studies have reported that the incidence of mechanical failure or malfunction with robot-assisted urologic surgery is low (0.4–4.6%) [5, 9–15]. Kim et al. reported that the incidence of instrument and mechanical failures was 1.9% [10]. Instrument problems include shaft injuries, broken or dislodged wires, nonrecognition or locking of instruments, unnatural motion because of a problem attaching to an adapter, or inadequate closure of tip. Instrument failure can be easily fixed in most cases by reseating the instrument or changing to a new instrument. Careful examination of instruments should be undertaken by the assistant before insertion. A dry lab experience for the surgical team to practice with the robotic instruments and the robotic interface is strongly recommended [16]. Mechanical failures or malfunctions of the da Vinci system may include the occurrence of recoverable or nonrecoverable faults originating from the surgeon console, patient cart, or vision cart. Maintenance of the system related to faults or damage can result in replacement of components on the surgeon console, patient cart, and vision cart, including replacement of damaged endoscopes. Zorn et al. reported four cases of mechanical failure; all cases were completed by delaying the procedures [11]. In the series of Lavery et al., 34 cases had mechanical failures or malfunctions; they were converted to open or laparoscopic procedure or cancelled [12].

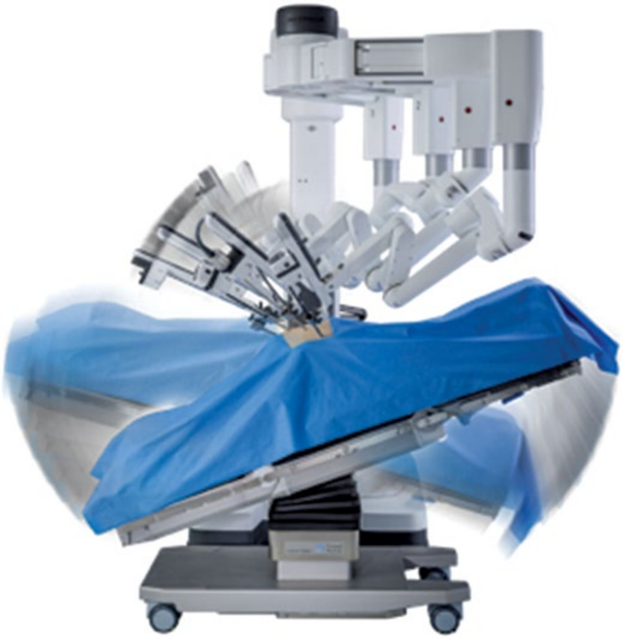

**Figure 81.8** Integrated table motion: combines da Vinci Xi Surgical System (Intuitive Surgical Inc.) and TruSystem 7000dv (Trumpf Medical), allowing ability to reposition operating table with surgical robotic arms docked.

The wider field of view of the da Vinci Xi endoscope may inadvertently result in surgeons bringing the camera closer to the tissue. The autofocus feature also may cause smoke between the camera and target tissue to be more visible. This may lead to increased frequency of smudging or fogging on the camera face. Troubleshooting tips to improve vision may include the use of the digital zoom feature to help bring the endoscope farther away from the target tissue, the use of the AirSeal® valveless insufflation system (Conmed, Utica, NY, USA) to allow for constant smoke evacuation, and the use of a thermos and hot water to clear the end tip camera and minimize temperature differentials along the shaft of the endoscope.

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# 82

# Minimally Invasive Reconstructive Techniques: Suture, Staple, and Clip Technology

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## Introduction

The evolution of laparoscopic and robotic surgery has expanded to accomplish more in reconstructive and complex urological procedures. For patients to get benefit from minimally invasive surgery (MIS) surgeons must first develop and gain proficiency with minimally invasive surgical skills required for these advanced surgeries. The skillset required for these reconstructive surgeries is very different from traditional open surgery; accordingly, both standard laparoscopic and robot-assisted procedures are associated with definite learning curves [1, 2].

Initially, laparoscopic reconstructive urologic procedures such as radical prostatectomy, partial nephrectomy, pyeloplasty, radical cystectomy, and urinary diversion were technically demanding, even in the most experienced hand; however, with the rapid improvement of laparoscopic instruments, and innovation of different clips, staplers, and suturing materials, intracorporeal suturing became much more efficient, minimizing patient morbidity while maintaining success rates and surgical efficiency. With the introduction of the da Vinci® surgical system (Intuitive Surgical, Inc., Sunnyvale, CA, USA) in the last decade, robotic surgery eliminated the early steep learning curve for novices, and at the same time improved the ergonomics of motion for experts, which may have implications for highly complex reconstructive procedures in limited workspaces (e.g. radical prostatectomy) [3].

Proper hemostasis is considered a critical key issue for successful reconstructive MIS. Precise tissue visualization during robotic and laparoscopic surgeries can be attained only in a bloodless field. Bleeding must be adequately controlled from the first attempt because it becomes more difficult to control in subsequent attempts. Prevention of bleeding requires from surgeons the timely and appropriate use of this innovative technology. A variety of major hemostatic modalities have evolved in the field of MIS (Box 82.1).

In this chapter we review in detail the mechanical methods commonly used in hemostasis and frequently applied during reconstructive MIS, namely "sutures, clips, and staplers."

## Sutures

During MIS, advanced surgical skills such as suturing and knot tying are required for many complex reconstructive procedures. Laparoscopic suturing requires skill and dexterity; the surgeon has an extremely restricted space to maneuver the needle and the 2D vision affords limited depth of perception. In addition, the loss of tactile feedback in laparoscopic surgery often represents a barrier to developing a proficiency in using needle drivers in a standardized way. In robotic surgery, tactile feedback is replaced by haptic feedback. Recent improvements in minimally invasive instrumentation have given surgeons and urologists easier methods of suturing and tying.

Tissue reapproximation is an important step during suturing, and many factors are important to make it reproducible, such as adequate port placement site, proper suture type and needle selection, understanding the relationship between the tissue, camera, and ports by the operating surgeon. Moreover, the use of mechanical suturing devices may improve efficiency and accuracy during suturing.

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Companion website: www.wiley.com/go/smith/textbookofendourology

**Box 82.1 Types of hemostatic modalities used in minimally invasive surgery.**

**Mechanical methods**

- Surgical clips
- Staplers
- Pretied suture loops
- Sutures
- Others:
  - Local pressure
  - Increased pneumoperitoneium

**Energy methods**

- Electrical energy
  - Monopolar electrosurgery
  - Bipolar electrosurgery
- Argon beam coagulator
- Ultrasonic energy
- Radiofrequency energy

**Hemostatic materials**

- Fibrin agents
- Collagen
- Synthetic sealants
- Oxidized regenerated cellulose
- Gelatin
- Flowable gelatin/thrombin

## Characteristics of suture materials

The choice of suture is determined by a balance between the type of surgery, the characteristics of different anatomical layers that requires reconstruction, and the characteristics of available suture materials. Certain types of suturing materials can be particularly difficult to work with due to their stiffness and tendency to resist deformation, and forming the slipknots to close wounds and surgical incisions requires great skill. The characteristics of various suture materials are summarized in Box 82.2. Recently, an absorbable unidirectional barbed suture (V-Loc™180, Covidien, Mansfield, MA, USA) (Figure 82.1) has been introduced and has gained popularity in reconstruction of the urethrovesical anastomosis during radical prostatectomy. The unidirectional barbed suture has many advantages: it makes the anastomosis easier in a shorter time period compared to the nonbarbed monofilament suture, it improves tissue handling and decreases the tension placed by the assistant on the running suture during the anastomosis while re-approximating the urethra and bladder neck, it prevents slippage once the bladder neck and urethral tissue are re-approximated, and the tissue stays in place and does not migrate. In addition, it eliminates the risk of erosion of the Lapra-Ty® clips used to secure the posterior urethral reconstruction [4, 5].

## Suture length

The length of the suture used during MIS varies and depends on its type and application. For extracorporeal knot tying, maintaining a long suture length (80–120 cm) is required to allow passage of the suture ends outside the trocar. On the other hand, intracorporeal knot tying requires a shorter length. For example, 8–10 cm length is adequate for simple interrupted sutures. For running sutures an extra 10–12 mm suture length is needed for each additional stitch. Running locking sutures require additional 20–25 mm length per stitch. Adequate length should be maintained for knot tying at the end of suturing to avoid stress on the reconstructed tissue [6].

## Needle description

The surgical needle has three major parts: the tip (or needle point), the needle itself (body), and the swage (needle back where the suture is attached). The diameter (the distance between the needle point and the swage) is known as the chord length. The needle may be curved, with a radius of between 1/4 and 5/8 of a circle, or straight. The tip may be triangular with either conventional cutting (sharp edge on the inner arc) or reverse cutting (sharp edge on the outer arc). The latter has less chance of tissue tearing during suturing. The needle body may be flattened to facilitate grasping it and to reduce twisting during suturing.

When using a curved needle, it is best to grasp it halfway along the needle arc for better suture control. Likewise, when using a straight needle, placement of the needle holder in the middle allows for more precise needle placement and suturing. Successful needle holding requires alignment of both the tissue and needle.

## Needle entry

Successful needle entry into the abdominal space is the first step of suturing. The commonest entry route is through the trocar lumen, which requires adequate knowledge of needle sizes, shapes, and different trocar diameters. Grasping the needle 2 cm proximal to its swage facilitates its passage together with the needle driver into the abdominal cavity through the trocar, and minimizes risk of trocar valve mechanism damage.

Needle entry through the abdominal wall is an uncommonly used route. This technique is used particularly when a stay suture is required for temporary traction during certain reconstructive urologic surgery, such as

**Box 82.2 Suture material characteristics and properties.**

### Absorbable vs. nonabsorbable

*Absorbable sutures*

Examples: surgical gut, polyglactin 910 (Vicryl, Polysorb®), poliglecaprone 25 (Monocryl®), polydioxanone (PDS II®), polytrimethylene carbonate (Maxon®), and glycomer 631 (Biosyn®).

Absorbable sutures lose most of their tensile strength within 60 days. They are usually used as deep sutures in laparoscopic and robotic surgery (e.g. partial nephrectomy, myomectomy or intestinal anastomosis).

*Nonabsorbable sutures*

Examples: nylon (Ethilon®, Dermalon®, Surgilon®, Nurolon®, Nylene®), polybutester (Novafil®), polypropylene (Prolene®, Surgilene®, Surgipro®), silk (Dysilk®), polyester (Dacron®, Mersilene®, Ethibond®), and GORE-TEX® suture.

Nonabsorbable sutures are used for reconstructive surgery (e.g. sacrocolpopexy or Burch coloposuspension), where manual removal of suture postoperatively is not required.

### Multifilament vs. monofilament

Multifilament sutures are handled more easily and tie well in laparoscopic and robotic surgery. However, they carry an increased risk of infection. Monofilament sutures are more difficult to handle and to knot securely, but have a lower infection risk.

### Tensile strength

Tensile strength depends on the size (thickness) of the suture in use. A smaller suture with adequate tensile strength is preferred by surgeons since it decreases foreign body load on the tissue. For example, 3-0 suture is a thick, strong suture used for fine surgery in laparoscopic surgery (e.g. renorrhaphy during partial nephrectomy or vesicourethral anastomosis during radical prostatectomy), while 6-0 is a thinner and weaker suture which is used for ultrafine surgery (e.g. fallopian tube anastomosis).

### Plasticity and elasticity

Plasticity is defined as the ability to retain strength and length after stretch, while elasticity is the ability to regain original length after stretch. Laparoscopic instruments may cause tissue damage because lack of tactile feedback, therefore surgeons should respect suturing as much as they can in order to reduce postoperative edema without tissue cutting and maintain epidermal approximation after edema resolution.

### Ease of handling and knot security

Ease of handling and knot security are determined by a number of related properties:

- Sutures with low coefficient of friction usually slide well through the tissue, but the knot may unravel easily
- Sutures with high memory will return easily to their original position and are difficult to use. Prolene suture is strong, difficult to tie, and has lower knot security
- High pliable sutures are more easily bent and can be handled well with good knot security during laparoscopic surgery (e.g. Vicryl)

### Tissue reactivity

The degree of tissue inflammatory depends on the suture type. It is high for natural sutures, such as silk and catgut, and low for synthetic sutures, such as nylon.

pyeloplasty. Straight needles pass through the abdominal wall, then the target tissue, and finally through the abdominal wall again and are clamped outside the abdominal cavity to facilitate traction and countertraction. The application of this technique obviates the need for extra trocar insertion for retraction purposes during surgery.

## Suturing instruments

### Laparoscopic needle drivers

A variety of laparoscopic needle drivers are available in several different configurations and can be used based on surgeon preference or type of surgery. Needle driver jaws are divided into four main categories: straight, curved right, curved left, and self-righting. Recently, needle drivers with an articulating tip have become available; these can be controlled by angling the instrument's handle. Theoretically, such devices might offer greater maneuverability and efficiency when compared to nonarticulating types, but they have a steeper learning curve [7]. Needle control and the performance of precise freehand laparoscopic suturing is determined by the needle stability within the driver. An ideal needle driver is characterized by the following properties: it is light with an easy unlocking mechanism, and provides firm grip when driven through the tissues in a direct path [8].

### Robotic needle drivers

The various features of robotic surgical systems, such as stereoscopic 3D vision, magnified view, wristed instruments, and tremor filtration, are presumed to improve

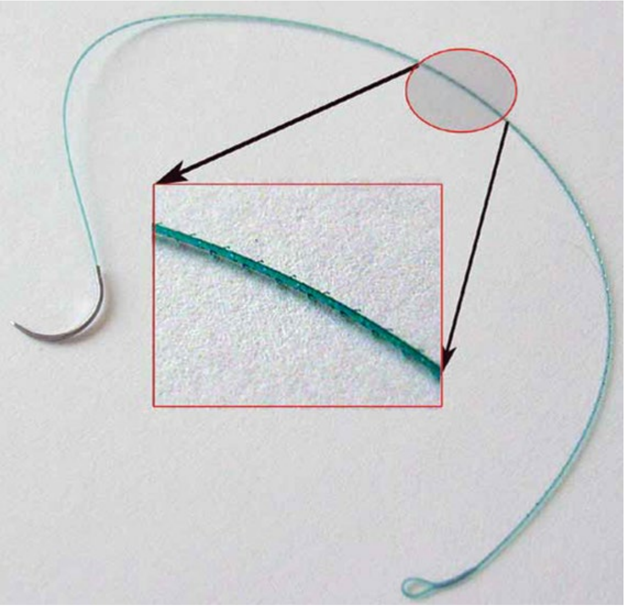

**Figure 82.1** V-Loc™ 180 suture.

performance in laparoscopic tasks. The increase in degrees of freedom for the instrument's tip (seven degrees of freedom) and 90° of articulation which are used inside the human body has led to better instrument tip control in a more natural and fluid flight path (Figure 82.2). The net result is increased dexterity with easier and more accurate suturing in a minimally invasive fashion. Various types of robotic needle drivers are available, including "fine micro-forceps used for suturing the fine structures during cardiovascular surgery and during nerve anastomosis, and a mega-needle driver used for suturing of larger and thicker tissues" (Figure 82.2). The SutureCut™ needle driver is a new needle driver provided with an integral cutting blade for efficient cutting of suture after knot tying.

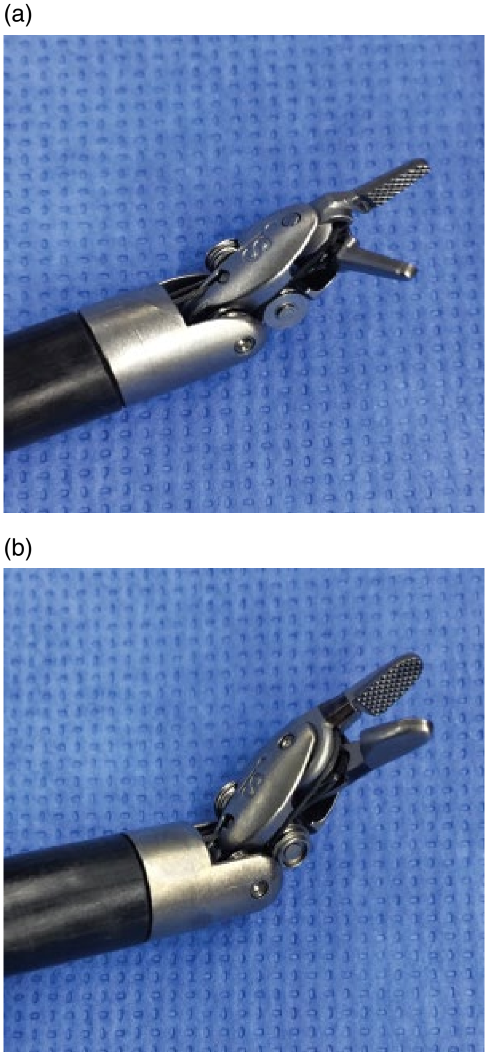

**Figure 82.2** Two types of robotic needle drivers from Intuitive Surgical, Inc.: (a) fine micro-forceps and (b) mega-needle driver.

## Classifications of knots

A variety of knot types are used in laparoscopy. The most common ones are listed in Box 82.3.

### The half knot

For this knot both ends of the suture must be pulled in opposite directions in the same plane with uniform tension. It is incomplete, unreliable, and has a tendency to untie.

### The slipknot

For this knot each thread has a different role; one remains passive and inactive during the tying process, while the other is the active thread which forms the knot by wrapping around the passive one. Similar to the half knot, the

**Box 82.3 Classification of knots used in minimally invasive surgery.**

**Basic knots**

- Half knot: both ends must be pulled in opposite directions in the same plane with uniform tension
- Slipknot: one thread remains passive, and the active thread forms the knot by wrapping around it

**Complete knots**

- Square knot: sequences of two identical half knots
- Surgical knot: blocking sequences of half knots
- Slipknot: blocking sequences of slipknots

slipknot is incomplete and unreliable; it is also an asymmetric knot that cannot maintain approximation of wound edges.

### Blocking sequences

This is a series of half knots and/or slipknots which provide maximum grip to the knot. Both the half knot and the slipknot are considered the cornerstones of the knot (e.g. square, surgical, or slip), which is formed from blocking sequences of two or more slipknots and/or half knots.

## Classification of suturing techniques

Suturing techniques during laparoscopic suturing are divided into two types: intracorporeal and extracorporeal suturing.

### Intracorporeal technique

The intracorporeal knot is a challenging technique, especially for junior laparoscopists, and generally has a steep learning curve. During intracorporeal suturing, the knot is made inside the abdominal cavity using two instruments – either two needle drivers or one needle driver and one assistance forceps, depending on surgeon preference. For easy interrupted suturing, it is vital to keep the tail at the terminal end relatively short before tying a knot. This is because a long tail suture may be difficult to locate if adhered to the abdominal viscera. When this occurs, it requires further cinching movements to bring the knot down to the target tissue, which makes knot tying more difficult at the other end of the suture line. Meanwhile, the running is difficult during the tying of the second knot because of the short remaining suture length available while maintaining constant tension on the first knot. An example of a commonly used intracorporeal knot is the square knot. In a certain circumstances it becomes very useful for the surgeon to know how to convert a square knot into a sliding knot when undue tension is applied to the target tissue. After placing two half hitches in the suture, no further cinching down to the tissue is needed. Instead, the free suture end is grasped and tensioned, converting the square to a slipknot, while pushing the knots towards the target tissue with the free instrument. In order to secure the knot properly, additional half hitches may be applied.

### Extracorporeal technique

During extracorporeal suturing, the knot is made outside the abdominal cavity, then it is pushed intracorporeally using a knot pusher, such as slipknot or Roeder's knot pusher. Various types of extracorporeal knots are available: nonsliding "static" knots (e.g. square knot, half hitches, and revo knot) and sliding knots (e.g. hangman's knot, Roeder knot, Lieurance Modified Roeder knot, Meltzer's knot, Tennessee slider, Tayside's knot, Weston slipknot).

The general drawbacks of the extracorporeal technique are as follows:

- Unlike the intracorporeal knots, it places undue tension on the tissue during tying of the knots which may become macerated and tear the delicate tissues apart.
- Loss of pneumoperitoneum may occur, which can be alleviated by placement of a finger over the trocar mouth during the tying of the knot.

To our knowledge, the square knot and the Roeder's knot are the most common types of extracorporeal knots. They are described below.

#### *Square knot*

This is formed of alternating half knots and then cinched using the knot pusher by advancing it through the trocar down to the tissue. A surgical knot is placed to maintain adequate tension locally at the tissue level while the second half knot is being performed. Tension is maintained on the free ends of the suture, while advancing the knot pusher. To ensure a true square knot the alternating half knots need to be in opposite directions.

#### *The Roeder slipknot*

This was the first knot described in laparoscopic surgery. Roeder's knot is easy to assemble and place, secure, and is a cost-effective alternative to intracorporeal suturing and staples during laparoscopic surgery. Its advantage over the square knot is that the entire knot is entirely formed before advancing it into the intracorporeal space. It may be useful in the ligation of somewhat bulky tissue (e.g. the dorsal venous complex) owing to its slip feature. To form the knot, one short limb (the post) and one long limb (the loop) are made, and then a half hitch is placed. The loop is thrown around the post several times depending on the suture material used (braided and gut-based sutures require 3–5 loops while monofilament sutures require 5–7 loops). The loop is then thrown around both limbs and past the tail of the loop limb between the last two loops. Finally, the loop is thrown only around the post limb. The knot is tensioned and pushed into the joint with a knot pusher on the post limb. Once the initial knot is in position, additional half hitches may be placed for security.

## Knot-tying devices

Knot-tying devices may be used to secure the ends of both running and interrupted sutures.

### The Lapra-Ty clip

The Lapra-Ty® (Ethicon, Cincinnati, OH, USA) is an absorbable one-piece clip molded from the polymer poly(p-dioxanone) (Figure 82.3a). It is delivered by a reusable 10 mm clip applier (33 cm or 45 cm length). Clips are designed as anchors and secure each end of a single strand of 2-0, 3-0, or 4-0 coated Vicryl® (polyglactin 910) suture for soft tissue approximation for a period of up to 14 days. It eliminates the need for intracorporeal knot-tying and frees the bedside assistant from keeping traction on one side while making the opposite half of the anastomosis. The Lapra-Ty clip provides a stable tension on the suture and allows for creation of a safe, watertight anastomosis (e.g. during vesicourethral anastomosis of radical prostatectomy) (Figure 82.3b). Suture lines tied with a Lapra-Ty clip can be further cinched by pulling the suture and applying an additional clip under the previously placed one. This provides a greater flexibility to the surgeon in securing suture lines to the desired level of tension [9]. Another advantage of the Lapra-Ty clip is its usefulness in shortening the time needed to complete time-sensitive tasks such as renorrhaphy during partial nephrectomy (Figure 82.3c). In addition, in the case of a short remaining suture length making it difficult to tie the knot, Lapra-Ty could be applied easily. It should be borne in mind that because of a concern regarding the risk of developing an inflammatory reaction, it is better to apply it on the final knot of running sutures.

### The Ti-Knot TK5

The Ti-Knot TK5® (LSI Solutions, Rochester, NY, USA) is another “knot-tying” device. It delivers titanium knot “non-reactive material” to mechanically fasten a suture and automatically cuts away excess suture in one step. It requires an extracorporeal loading of the suture into the device, and both ends of the suture must be maintained at length to allow the instrument to be loaded extracorporeally. Once loaded, the device is introduced intracorporeally, the desired tension is achieved, and a titanium knot is deployed, which locks the suture in place. The Ti-Knot titanium knot can be applied safely during laparoscopic ligation and control of the dorsal vein complex [10] and renal arteries [11]. However, the additional costs related to the use of this disposable device preclude its widespread use.

## Ancillary suturing devices

Since laparoscopic suturing is a technically demanding task, additional instruments have been developed to facilitate suturing.

### The Endo Stitch

The Endo Stitch™ (US Surgical, Norwalk, CT, USA) suturing device was developed to facilitate suture

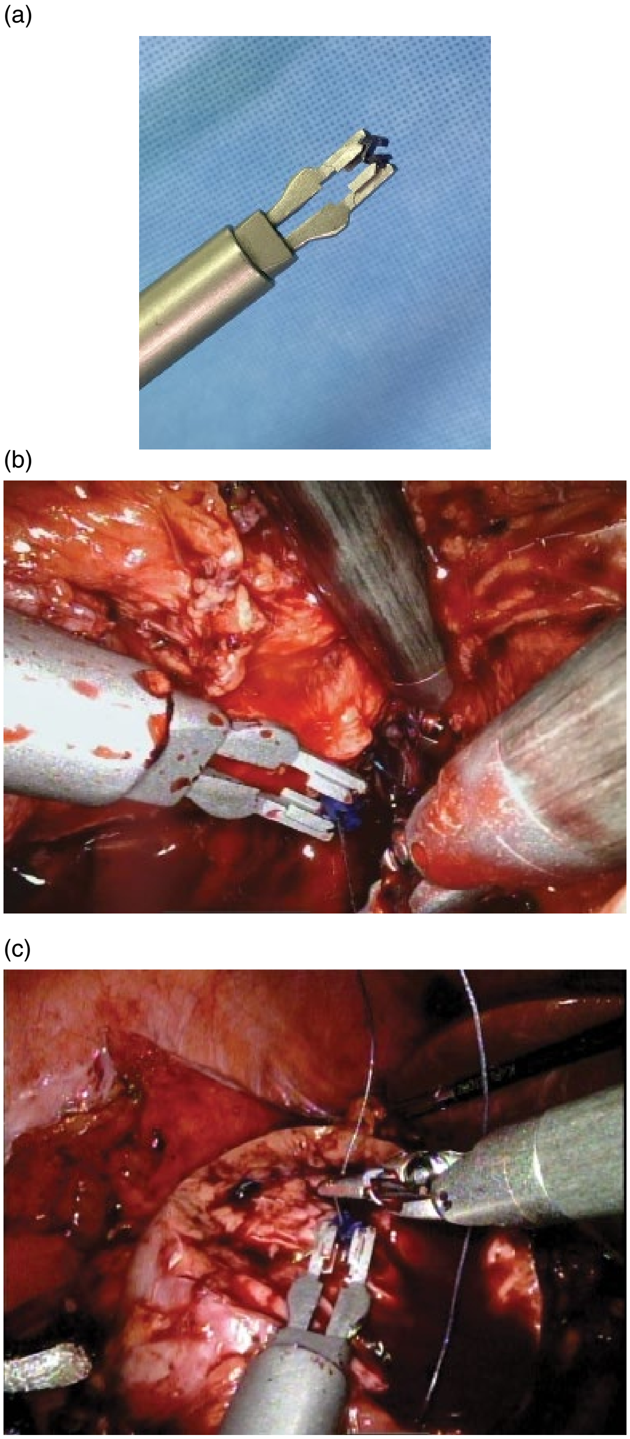

**Figure 82.3** (a) The Lapra-Ty® (Ethicon) and its metal applicator. (b) Application of Lapra-Ty clip at the terminal end of a running 3-0 barbed suture (V-Loc 180) after complete vesicourethral anastomosis during Retzius-sparing robot-assisted radical prostatectomy. (c) Application of Lapra-Ty clip at the terminal end of a running 3-0 Vicryl suture for renorrhaphy during right-side robot-assisted partial nephrectomy.

placement and knotting of advanced reconstructive laparoscopic procedures (e.g. laparoscopic dismembered pyeloplasty and bladder neck suspension) by passing a small needle with its secured suture back and forth between its jaws. After each pass, the needle is locked temporarily in place until the instrument handle is squeezed again to transfer it to the other arm. A 10 mm port is required for its use. It reduces the amount of time needed for placement of stitches and knot tying compared to conventional suturing [12, 13]. It has some disadvantages: its short needle cannot pass through thick tissue so cannot be used for reconstructive surgery requiring large bites, such as renorrhaphy during partial nephrectomy; in addition, it increases the cost of the case as it is disposable and needs reloading.

#### The Suture Assistant

The Suture Assistant® (Ethicon) and Reload Units are used in minimally invasive surgical applications. The Suture Assistant is a 5 mm sterile, single-patient-use instrument designed to secure suture knots intracorporeally. It is disposable and uses dedicated reloads.

#### The Sew-Right SR5

The Sew-Right® SR5® (LSI Solutions, Rochester, NY, USA) is a reloadable 5 mm suturing device that uses two built-in needles to place a simple suture precisely through even a relatively thick tissue. Its needle passes parallel to the instrument shaft. With a single squeeze of the lever against the handle, the first needle passes through the tissue. The needle automatically captures the suture and pulls it back through the tissue to complete the driving of the suture. The second needle is then selected to take a second bite. Once the suture is complete, the instrument is disengaged from the tissue, and a titanium knot is passed onto the suture to secure it. It is a disposable instrument and only a single simple suture is placed every load.

#### The QuikStitch

The QuikStitch® (Pare Surgical, Englewood, CO, USA) is a mechanically assisted suture device of various sizes 3, 5, 10, and 12 mm, where the needle driver passes through a spool containing a pretied knot. Both the device and needle drivers are reusable, making it commercially more appealing than some other designs. Different needle shapes (e.g. straight or curved) and suture types (e.g. absorbable and nonabsorbable) are available [14].

## Clips

Because of the technical difficulty in achieving ligation with sutures, clip systems are the preferred mechanical method for sealing blood vessels and ligation of small structures such as ducts during minimally invasive laparoscopic and robotic surgery. Clips are also faster. There are two main types of clips commonly used in our practice: metallic titanium clips and nonmetallic clips (Hem-o-lok).

### Endoscopic clip appliers

Clip appliers are classified into various categories: single-load or multiload, and disposable or reusable "multiple uses" (Figures 82.4 and 82.5). Both types of applier can carry various types of metallic or nonmetallic clips.

#### Single-load "reusable" clip applier

The single-load reusable clip applier has been the standard clip applier used in open and laparoscopic procedures. High-quality reusable clip appliers are available from several manufacturers. They have the advantage of 360° rotational ability and low cost, but are not without disadvantages:

- They are slower because the instrument must be removed and reloaded for each clip application, which is an important limitation in emergency situations.
- There is a tendency for the loaded clips to dislodge from the jaws when passing into a trocar or through the abdominal cavity.

#### Multiple-load "disposable" clip applier

The majority of clip appliers nowadays are multiloaded and disposable, carrying from 15–30 clips per unit. They are available in many models. This type of clip applier can save time and be helpful during emergency when clipping a bleeding vessel because of its ability to fire multiple clips without exiting the abdominal cavity to reload. Other characteristics include the following:

- They eliminate the risk of dislodging a clip from the applier's jaws while being passed through the trocar valve.
- Closure of the clips occurs from distal to proximal (Figure 82.4c). This ensures that the desired vessel or structure is contained within the clip, and prevents it from being pushed forward and out of the opposing arms of the engaging clip.
- The applier shaft gives 360° rotational capability (Figure 82.4a). This important feature allows for ergonomic hand positioning, which facilitates instrument use and improves the accuracy of clip placement.
- Some clip appliers have the ability to reload clips automatically, thus eliminating another step in the clip application. Immediately after a clip is placed, another one is advanced into firing position. This is an advantage over other clips which require manual reloading through partial closure of the firing handle or that have

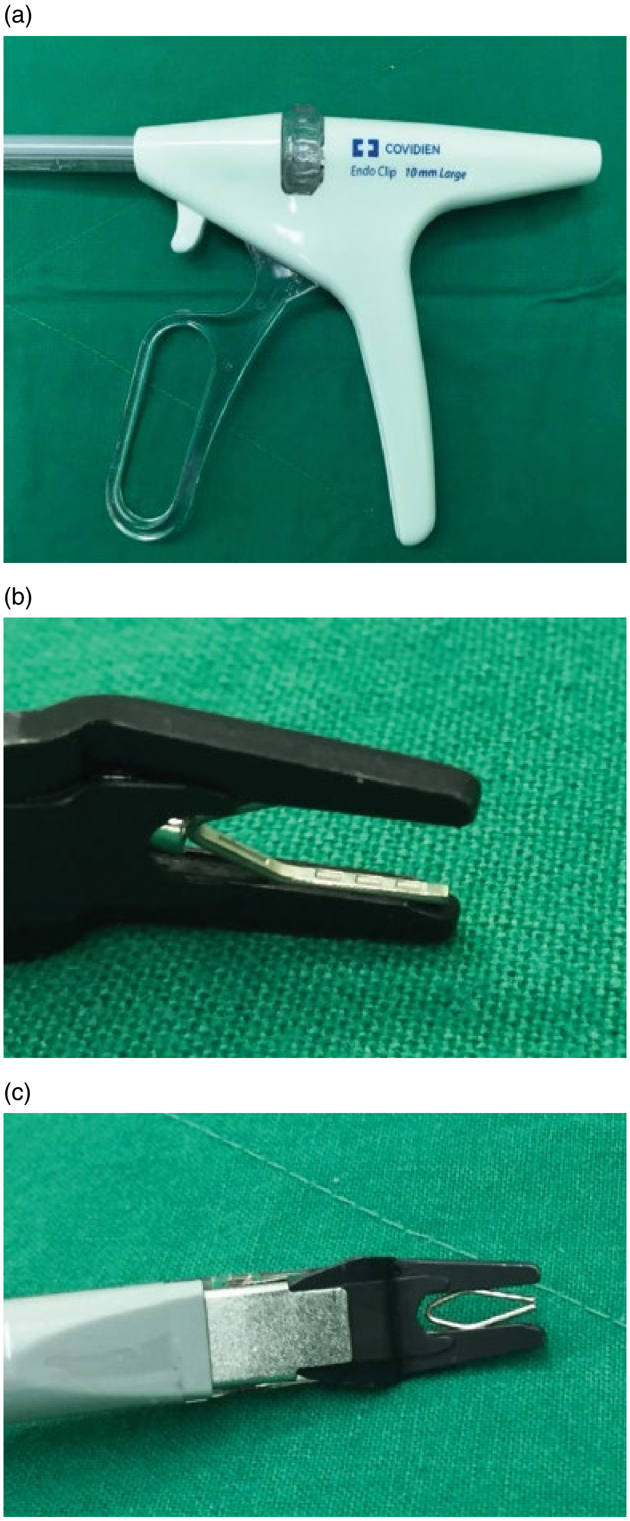

**Figure 82.4** Multiple-load "disposable" clip applier (10 mm Endo Clip™ II, Covidien) with its metallic titanium clips. (a) The applier has 360° rotational ability and is loaded with 10 mm clips. It has a separate trigger that reloads a clip when pulled. (b) The titanium clip has ridges and depressions along its internal surface. (c) Closure of the clip occurs from distal end first.

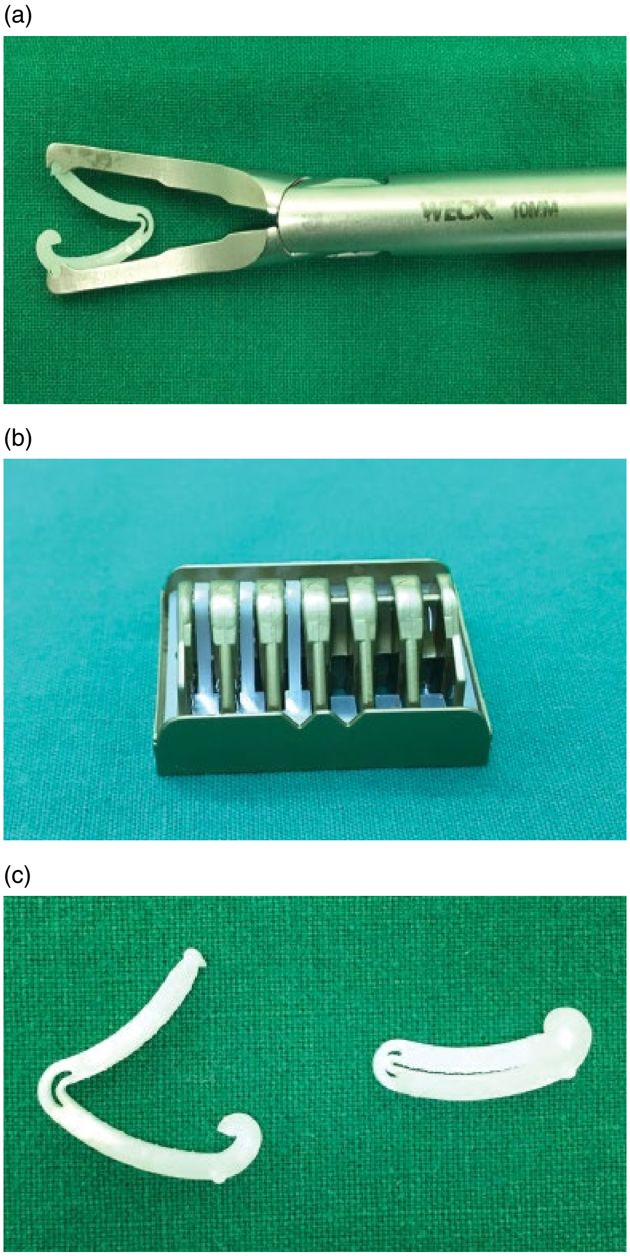

**Figure 82.5** Single-load "reusable" metallic clip applier and the Hem-o-lok® (Weck®, Teleflex Medical, Morrisville, NC, USA). (a) The applier has 360° rotational ability and is loaded with a 10 mm clip. (b) The cartridge contains six clips. (c) The Hem-o-lok™ clip has a lock-engagement mechanism and teeth within its jaws.

a separate trigger that reloads a clip when pulled (Figure 82.4).

- A visual indicator is usually incorporated to show the bedside assistant staff the number of remaining clips after each use.
- To avoid inadvertent injury to a blood vessel or other structure, most appliers are equipped with an automatic lock feature preventing closure of the jaws when the device is out of clips.

- The diameter of the shaft depends on the clip size. Shafts of 5 mm are available for medium clip appliers. For medium–large and large clips, the shaft sizes are 10 mm and 12 mm, respectively.

The automatic reloading clip applier has a potential disadvantage in that the tips of the applier cannot be used as a dissecting instrument without dislodging the loaded clip into the field during dissection.

## Nonmetallic clips

The Hem-o-lok™ (Weck Closure Systems, Research Triangle Park, NC, USA) was introduced in 1999. It is a nonabsorbable radiolucent polymer clip, which has a lock-engagement mechanism and teeth within its jaws (Figure 82.5). There are four sizes of Hem-o-lok clips and appliers (M, ML, L, and XL), ranging from 2 mm to 16 mm. This engaging clip latching mechanism enables the surgeon to feel the transmitted clip closure through the laparoscopic applier via tactile feedback. This design provides better security when the clip is applied to the tissue, and once engaged it is quite difficult to dislodge, even when operator tries to remove them using a purpose-built Hem-o-lok clip remover. The use of Hem-o-lok has been reported to be safe for renal pedicle ligation during laparoscopic renal surgery [15]. Moreover, there are published reports in favor of its application during minimally invasive general surgery procedures such as appendectomy, cholecystectomy, and splenectomy [16–18]. The 5 mm Weck clip can be used during renorrhaphy of partial nephrectomy, using the sliding technique (Figure 82.6).

### *Complications of Hem-o-Lok clips*

Complications are uncommon and only few cases reports have been published. Migration of the clips, although a rare problem, can cause serious complications (e.g. bowel obstruction, bladder or bowel perforation, stone formation and bladder neck contracture) that may necessitate further surgical intervention [19–23].

### *Contraindications*

Hem-o-lok clips are contraindicated for ligation of the renal artery during laparoscopic living-donor nephrectomy. This contraindication has been added to the instruction for use by the manufacturer Teleflex Medical in 2006, after receiving 15 medical device reports of 12 injuries and 3 deaths. Furthermore, an additional 3 kidney donor deaths have been reported since the contraindication was issued [24, 25]. Although there are published journal articles which support the continued use of Hem-o-lok clips for the renal artery ligation during laparoscopic living-donor nephrectomy [26], the US Food and Drug Administration warns healthcare providers regarding this contraindication because of its potential life-threatening complications. The basic principles of the Hem-o-lok and other clip types during their applications for vascular ligation are illustrated in Box 82.4. The failure rates of Hem-o-lok clips may be negligible when considering these principles during surgery [15, 27].

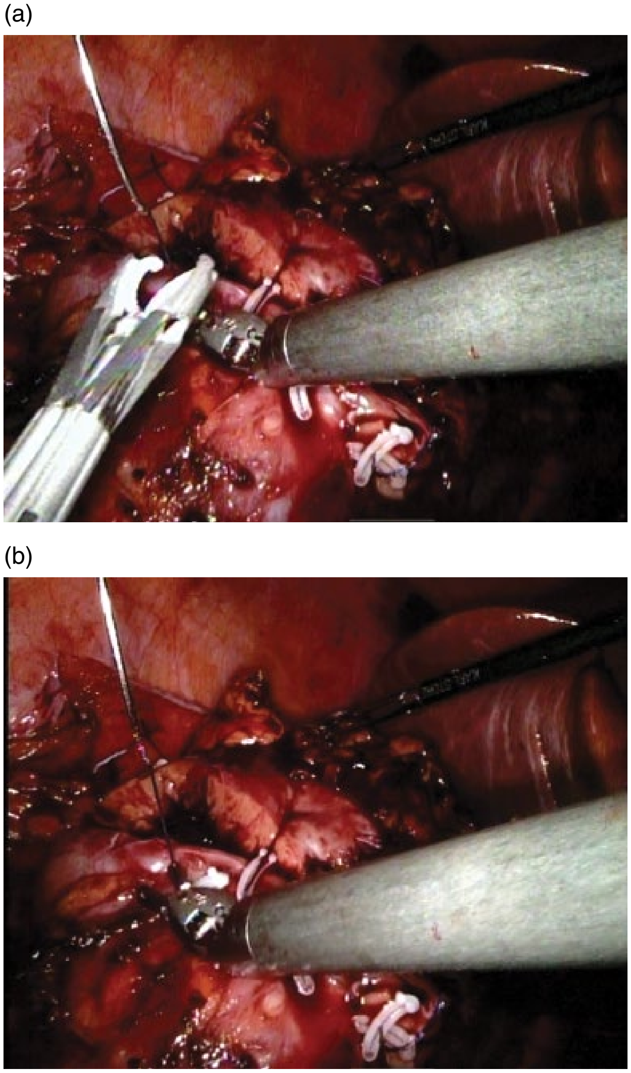

**Figure 82.6** Use of 5 mm (Weck Hem-o-lok Auto Endo5, Teleflex Medical) in the sliding-clip renorrhaphy technique during robot-assisted partial nephrectomy. (a) Application of the Weck to 3-0 Vicryl suture and (b) cinching the thread through the Weck with the robotic needle driver.

## Metallic clips

Titanium clips are nonabsorbable clips available in both straight and right-angled variations. They are commonly carried on the multiple-load disposable devices.

**Box 82.4 Basic principles of clip application during minimally invasive surgery.**

- Complete circumferential dissection of the targeted vessel or structure to develop a wide space to place clips and to prevent inadvertent clipping of nontarget tissues
- Select proper clip size
- The curved tip of the clip must be visualized around and beyond the vessel, and then slid up or down the vessel into optimal position before firing
- Tactile snap should be felt when the clip is engaged
- Adequate visual stump length should be maintained below the most proximal clip
- At least 2–5 clips seem mandatory for safe control of vessels sized ≥3 mm
- For smaller vessels, typically 1–2 clips are used on both the proximal and distal ends of the area to be divided
- Avoid cross-clipping
- The clip should be applied perpendicular (90°) to the vessel
- Unlike metal clip application, do not squeeze the clip handles too hard
- Avoid keeping the applier within the abdomen when not in use
- The same angle should be maintained to avoid pulling of clips during removal of applier
- Ensure that the clip does not catch on the loading mechanism to avoid placing undue shear force on the target vessel
- The applied clip may be pulled back and out of position if undue traction is inadvertently transferred to the clip
- The tips are sharp and may cause laceration of nearby vessels (e.g. renal vein)
- Before transection of vessels, check the ligation site to ensure security and proper closure
- During transection of vessels, partial division is performed initially before complete transaction to ensure proper hemostasis
- Avoid using electrocautery to divide the vessels in order to avoid late tissue necrosis and clip failure
- If a clip is misplaced, Maryland or DeBakey forceps may be used to slowly remove it by backing it straight off the clipped vessel or tissue

Modified from Ponsky et al. [15].

Titanium clips are available in various sizes ranging from 5 to 12 mm and have ridges and depressions along the internal surface that is in contact with the tissue (Figure 82.7). This pattern decreases the likelihood of them slipping off due to either subsequent nearby tissue dissection following ligation or increased vascular pressure within the clamped vessel.

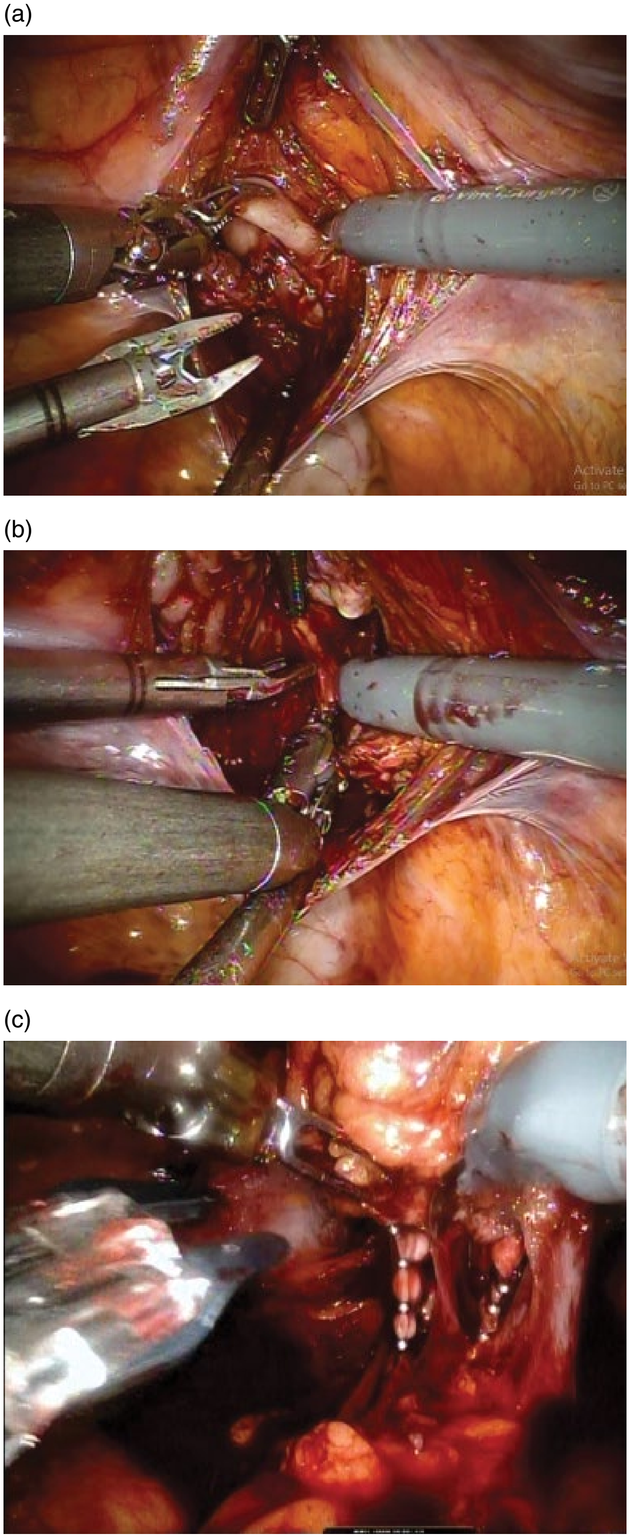

**Figure 82.7** Use of 5 mm titanium clip (LIGAMAX™ 5 EL5ML, Ethicon) during Retzius-sparing robot-assisted radical prostatectomy. (a) Ligation of the right vas deferens before its division and (b) securing the right neurovascular bundles during nerve-sparing step. (c) Application of multiple 10 mm titanium clips (Endo Clip II) during robot-assisted partial nephrectomy for clamping the main and accessory renal arteries.

Titanium clips are most commonly used to clip small-to-moderate sized structures, although they may be used to clip vessels of any size. For example, multiple titanium clips may be used to clip large vessels such as the main renal artery during laparoscopic or robotic nephrectomy when the stapler is not available or cannot be applied (Figure 82.7c).

### Tissue reaction to endoscopic surgical clips

The foreign body reaction profiles of clips used in securing vessels and sutures depend on the materials they are made of. Foreign body reactions correlate to the duration of suture absorption, developing at the end of the absorption processes [28]. Although Hem-o-lok and titanium clips are nonabsorbable materials, they have a low level of foreign body reaction. This was studied in rats, comparing tissue reaction to absorbable endoloop, nonabsorbable titanium staples, and polymer Hem-o-lok clips after laparoscopic appendectomy. There were no significant differences in histopathological changes observed on the 14th postoperative day across the three groups. On the 28th postoperative day, it was found that mild and moderate inflammation was more frequent in the endoloop than in the titanium stapler and Hem-o-lok groups [29].

Klein et al. [30] reported that there were no significant differences in fibrous tissue formation at any time between the absorbable polymeric surgical and titanium clips in the rat model.

## Staplers

Surgical staplers are widely used in various urological surgeries, such as radical nephrectomy, nephroureterctomy, radical cyctectomy, and urinary diversion. They are primarily used for medium and large-sized vessel ligation and division (e.g. renal hilum, bladder pedicle, or bowel mesentry), or reapproximation of visceral structures (e.g. small intestine or bladder) for anastomotic purposes. These instruments are vital to prevent major hemostatic complications.

### Characteristics and mechanism of stapler action

Staplers allow for rapid tissue ligation with or without division by deploying metallic staples arranged in several parallel rows. The metallic staples are laid in a brick-like intercalated pattern which allows them to overlap from one row to the next.

Endoscopic linear cutting devices (Endo GIA™, Covidien) typically use two sets of three parallel rows of hemostatic staples on each side and produce a linear incision of the ligated tissue between them.

The staple sizes are different in the inner and outer rows. The choice of size is based on the type of operation. For example, vascular or thin load sizes of approximately 2 mm or 2.5 mm are used for vascular applications, while large load sizes of approximately 3.5 mm are used for intestinal applications.

Each staple size has its own cartridge color (e.g. gray for 2 mm staple size, tan color for 2.5 mm, purple for 3.5 mm, and black for 4.5 mm). The staples also have different cutting lengths (30, 45, and 60 mm) which are used according to the length of tissue that will be divided.

Before firing and tissue division, the tissue is atraumatically crushed between the stapler and its opposing anvil. A rotational ability of 360° is present in all staplers with either a straight or articulating head. The articulating head offers a wide range of mobility and angulation before application on the tissue, but articulating staplers are more expensive. Noncutting staplers use fewer rows (three or four) of staples.

### Principles of endoscopic stapler application

Several precautions must be taken into consideration before using a laparoscopic stapling device. These are outlined in Box 82.5 and Figure 82.8.

### Complications of endoscopic stapler

In general, the primary stapler malfunction rate ranges from 0.3% to 0.5% [31–33]. If the jaws do not close easily because there is thick surrounding tissue around the target pedicle, there is an increased risk of incomplete ligation and subsequent bleeding. The complication rate associated with using the Endo GIA to ligate the renal vein has been reported to be between 1% and 1.7% and leads to morbidity in 45% of cases, a conversion rate of 20–27%, and need for transfusion in 15% [32, 33]. However, the majority of Endo GIA complications are likely attributed to poor instrument handling or application of an incorrect stapler width rather than equipment failure. At least 3 cm of the vein must be dissected to reduce the risk of complications and to enable accurate stapler position prior to vein ligation. On the right renal vein this can be difficult to achieve because of its short length. For the left renal vein, care should be taken to avoid any clips used before applying the stapler, because if the clip gets trapped between the stapler's jaws it may lead to Endo GIA malfunction and renal vein division without applying the staples. The subsequent outcome is disastrous.

See accompanying Video 82.1.

**Box 82.5 Basic principles of stapler application during minimally invasive surgery.**

- A 12 mm port size is required to pass it safely into the abdomen. For thick and large 4.8 mm staples a 15 mm port size is needed
- During introduction and withdrawal of the stapler, the jaws should be closed to prevent inadvertent trocar dislodgement
- All staplers are incorporated with a safety mechanism to avoid premature stapler deployment or blade cutting. The safety button must be disengaged prior to firing
- The target tissue must be properly dissected from the surrounding connective tissue to a suitable thickness
- The stapler's arms should to be placed accurately, with both tips visible, and closed easily without undue pressure
- The use of a noncutting stapler (e.g. endoscopic TA device) has been advocated to minimize the risk of stapler misfire. Then, the target pedicle can be divided after vessel ligation
- During firing, any torque of the stapler must be avoided. Serious complications (e.g. incomplete ligation or avulsion of the target vessel) may result
- After firing, open the jaws slowly before withdrawing the stapler. The division line should be inspected to ensure proper hemostasis
- In some instances, additional stapler reload or metallic clip application may be required to complete the vessel ligation
- During a second stapler reload, the inclusion of a previously placed titanium clip into the jaws must be avoided, as this will compromise both staple deployment and cutting mechanism
- Use of clips should be minimized on the target area where a stapler use is anticipated to avoid difficulty in maneuvering the stapler

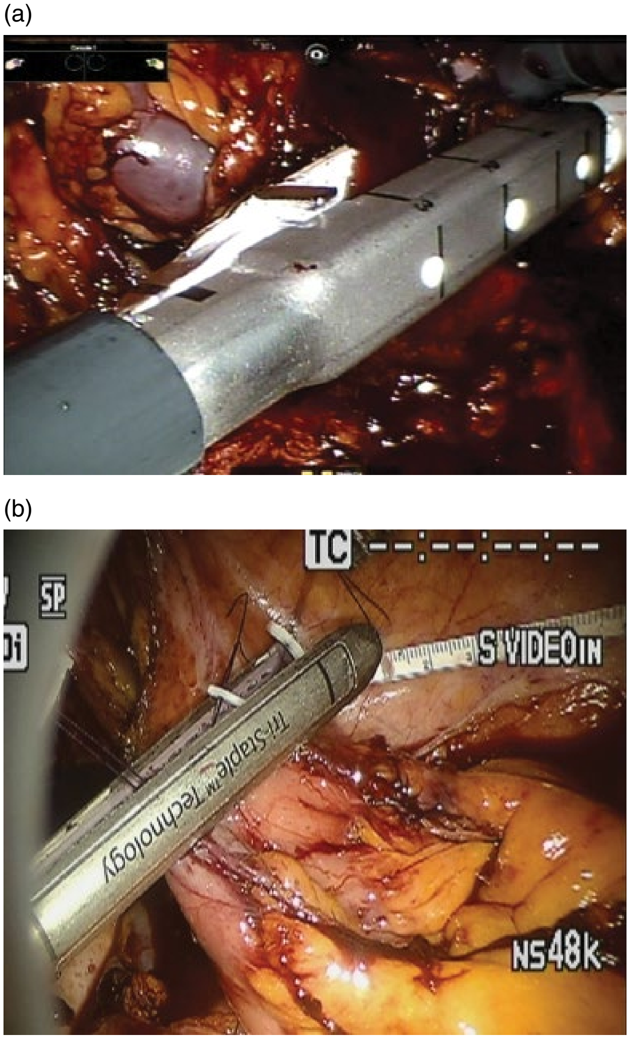

**Figure 82.8** (a) Application of 45 mm–2.5 mm Multifire Endo GIA™, Covidien) stapler device for ligation and division of the renal vein during robot-assisted nephroureterectomy. For ideal and safe vascular division the target tissue must be properly dissected from the renal vein and both tips should be visible before jaw closure, as illustrated. (b) Intestinal reanastomosis during ileal reconstruction of ileal conduit.

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# 83

# Transperitoneal Access and Trocar Placement

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## Introduction and general considerations

Pure laparoscopy and robotic surgery are minimally invasive approaches to access the abdominal cavity for diagnostic or therapeutic purposes, using dedicated instruments. At present, the transperitoneal approach has become widespread and more popular than the retroperitoneal approach due to the familiar intraperitoneal anatomy and the larger available working space. Any transperitoneal laparoscopic or robotic procedure starts with the establishment of a pneumoperitoneum, followed by trocar placement. The choosing of the optimal site on the abdominal wall is the first step in transperitoneal access. In general, the initial site is used to introduce the video-laparoscope. The number, size, and arrangement of the other trocars depend on the type of procedure, patient's body habitus and surgeon's experience. Furthermore, in choosing the entry site it is mandatory to consider previous surgical scars and anatomic anomalies, in order to avoid the risk of injuries. In this chapter, we describe the current "state of the art" regarding pure laparoscopic and robotic transperitoneal access and trocar placement in the most common urological procedures. Advantages, limits, and complications related to transperitoneal access and trocar placement will also be described.

## Anterior abdominal anatomy

Knowledge of the abdominal wall is fundamental to any open or laparoscopic/robotic procedure. The abdominal skin is backed by Camper's fascia, a loose layer of fatty tissue varying in thickness depending on the patient's nutritional status. In this layer superficial circumflex iliac, external pudendal, and superficial inferior epigastric vessels branch from the femoral vessels. The abdominal wall is composed of five paired muscles: two vertical muscles (rectus abdominis and pyramidalis), and three layered, flat muscles (external abdominal oblique, internal abdominal oblique, and transversus abdominis). These muscles and their fascial attachments form a protective layer that supports the anterolateral abdominal wall (Figure 83.1) [1]. Superior epigastric artery and vein (direct continuations of the internal thoracic vessels) provide blood supply to the superior half of these muscles. The inferior epigastric artery and vein, which arise from the external iliac vessels, approximately 1 cm below the inguinal ligament, supply the inferior portion of the rectus muscles and run superiorly until the anastomosis with the superior epigastric vessels. Furthermore, lower intercostal vessels provide additional vascularization [1] (Figure 83.1). Underneath the muscle layers, the transversalis fascia and the anterior layer of the peritoneum are found before entering the intraperitoneal space (Figure 83.1).

### Access to peritoneal cavity and creation of pneumoperitoneum

The transperitoneal approach requires the establishment of a successful pneumoperitoneum. The first step is to optimize entry technique in order to avoid injuries in the abdominal cavity [2]. Three techniques are described: the Veress needle technique, open (Hasson) technique, and direct optical access. The choice of the best method of transperitoneal access is still debated in terms of safety, and there is insufficient evidence to recommend one entry technique over another, although the open access and the direct visual trocar entry appear to have lower minor complications and faster access when compared to the Veress needle entry [3–5].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

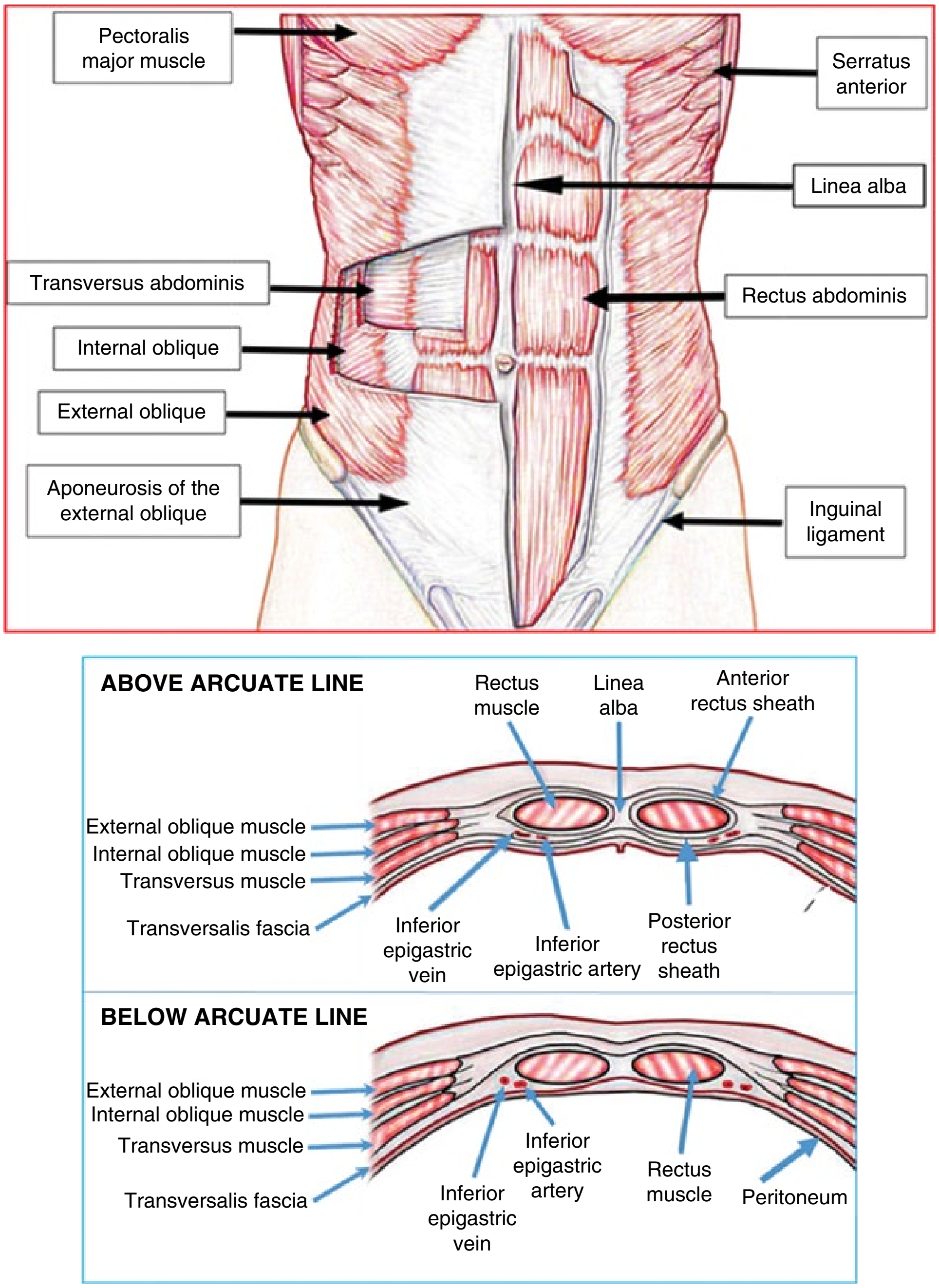
Pectoralis major muscle
Serratus anterior
Linea alba
Transversus abdominis
Rectus abdominis
Internal oblique
External oblique
Aponeurosis of the external oblique
Inguinal ligament
ABOVE ARCUATE LINE
Rectus muscle
Linea alba
Anterior rectus sheath
External oblique muscle
Internal oblique muscle
Transversus muscle
Transversalis fascia
Inferior epigastric vein
Inferior epigastric artery
Posterior rectus sheath
BELOW ARCUATE LINE
External oblique muscle
Internal oblique muscle
Transversus muscle
Transversalis fascia
Inferior epigastric vein
Inferior epigastric artery
Rectus muscle
Peritoneum

**Figure 83.1** Anterolateral abdominal wall. *Source:* From Fundaciò Puigvert, Spain.

## Closed entry technique

A common approach to enter the abdominal cavity and create the pneumoperitoneum is by using a Veress needle. This needle is composed of an inner blunt-tipped obturator and an outer sharp-tipped sheath. This design protects the intra-abdominal structures thanks to the advancement of the inner sheath after the outer sheath encounters an area of decreased resistance (peritoneal cavity). Commonly, access with a Veress needle is obtained in the periumbilical area, and far from previous surgical scars (Figure 83.2a). The needle is inserted, tenting the abdominal wall upward (Figure 83.2a). The rationale for lifting the abdominal wall is to increase the abdominal wall tension against which to push the Veress needle and to increase the distance between the bowel and the major retroperitoneal vessels. The Veress needle is held between the thumb and index finger. In the majority of cases, two clicks can be heard, which correspond to the two areas of

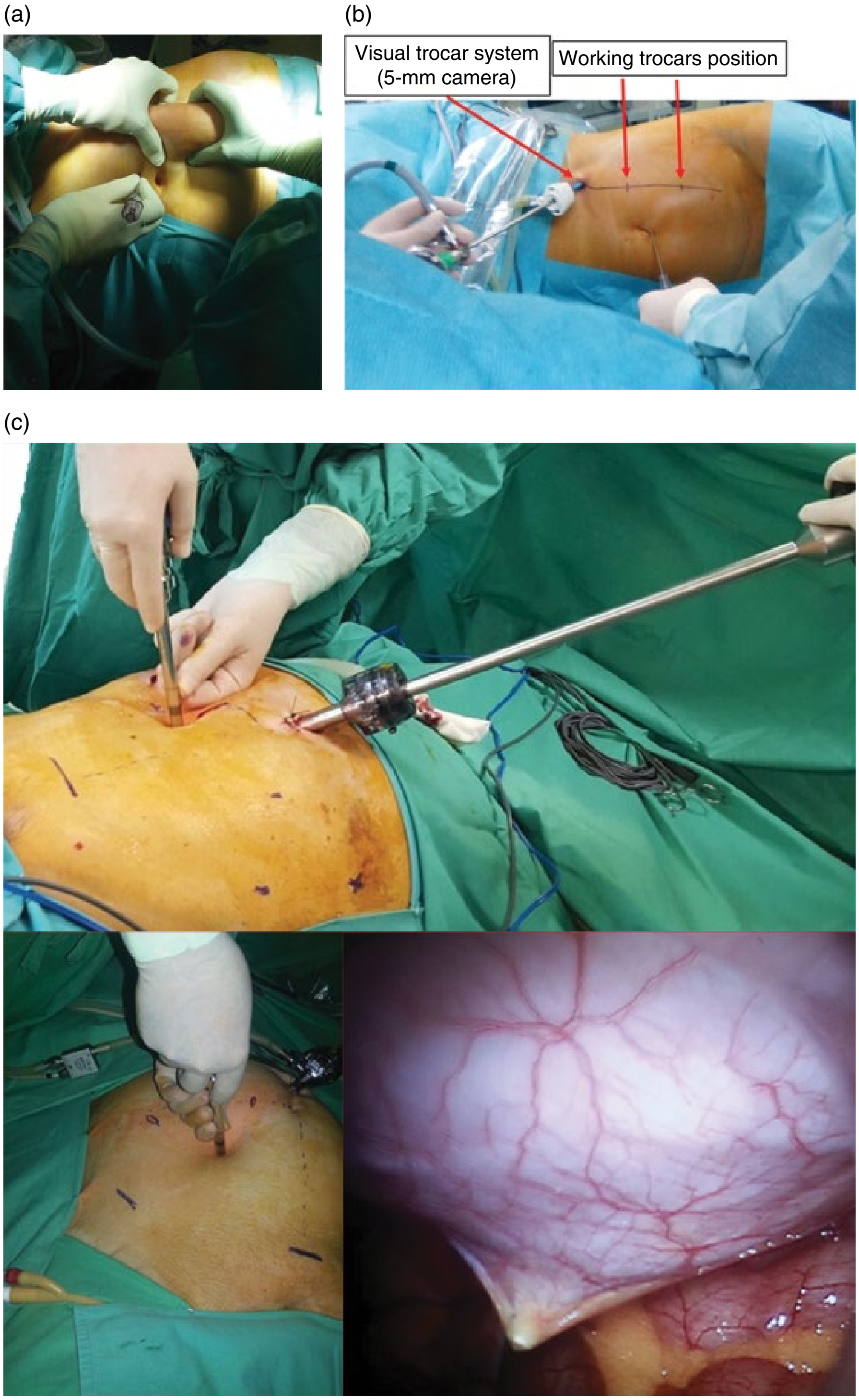

**Figure 83.2** (a) The Veress needle access in periumbilical area, tenting the abdominal wall upward. (b) Initial trocar placement one fingerbreadth inferior to the costal margin, using a visual trocar system with a 5 mm camera and 0° lens (the lens is immediately changed to a 30° one in order to place working trocars and perform the procedure). (c) Second trocar placement at a 90° angle to the abdominal wall and pushed inside until the tip of the trocar can be seen with the laparoscope. *Source:* From Fundaciò Puigvert, Spain.

maximum resistance encountered as the needle passes through the two abdominal wall fascia layers: muscle fascia and peritoneum. Correct placement of the needle into the peritoneal cavity must be quickly verified with the drop test, which consist of injecting 3–5 ml of saline into the Veress needle. In case of correct intraperitoneal placement, the saline is sucked inside the needle due to the negative intraperitoneal pressure. It is also important to aspirate the saline back to verify that no blood, bowel contents, or urine are present. If the first entry attempt fails, a second attempt is performed before choosing an alternative entry site.

An initial gas pressure below 9 mmHg reflects the correct intraperitoneal Veress needle placement [6]. It is important to avoid any movements of the needle after its placement in the abdominal cavity. When the Veress needle is correctly positioned, the insufflation of $CO_2$ gas can start. The initial intra-abdominal insufflation pressure is normally set at 12–15 mmHg, with 3–6 liters of $CO_2$ per minute. Once adequate intraperitoneal pressure is achieved, the first trocar can be placed (Figure 83.2b). Video-endoscopic inspection is performed immediately after to verify the intraperitoneal trocar placement and to check for potential intraperitoneal injuries.

### Open entry technique

The open entry technique was first described by Hasson in 1974 [7] and provides direct access to the peritoneal cavity. A mini-laparotomy (1.5–2 cm) at the umbilical area or pararectal line is usually performed. The fascia is exposed with narrow retractors and incised. The peritoneum is identified by sharp dissection of the muscles, tented up, and incised under vision. At this point, the peritoneal cavity adjacent to the incision should be explored with a finger to ensure absence of adhesions. The Hasson trocar is placed immediately after and pneumoperitoneum is initiated. This port consists of a blunt trocar, a cannula with an adjustable conical sleeve, and suture-holding arms for fixation.

### Direct optical access

The direct optical access is an alternative to the Veress needle. Optical trocar access is considered by many the safest entry method and is associated with a low incidence of intraoperative complications [8]. Nevertheless, in the obese population a randomized controlled trial showed that the Veress needle insertion technique is safer than direct trocar insertion using a nonoptical bladed trocar [9].

A 5 or 10 mm laparoscope is placed directly into the visual trocar sheath. The trocar is then pushed with a twisting motion stepwise into the peritoneal cavity, visualizing each abdominal wall layer during the trocar movement. Under the continuous gentle rotation of the optic trocar, the sequential layers of subcutaneous fat, anterior rectus sheath, pre-peritoneal fat, and peritoneum are visualized [10]. Once inside, the $CO_2$ is connected and pneumoperitoneum is obtained.

## Principles of trocar placement

The camera and working trocar arrangements depend on the type of surgical procedure and the surgeon's individual preference or experience. Commonly, triangulation is considered a basic principle of laparoscopic port placement, and for this reason the trocar arrangement is described as using a four-point diamond configuration, in which the operative site is enclosed within the diamond, with the camera placed between two working trocars [11]. For upper tract transperitoneal surgery, the camera is often placed in the periumbilical area with the other trocars positioned according to the exact procedure, the location of the disease, and the body habitus of the patient [12]. For renal and adrenal laparoscopic surgery performed in obese patients, port placement is further modified by shifting it laterally. Once the aiming point has been located, second trocars are placed at a 90° angle to the abdominal wall and pushed inside until the tip of the trocar can be visualized with the laparoscope, in order to avoid intraperitoneal injuries (Figure 83.2c).

Laparoscopic transperitoneal reconstructive surgery in which laparoscopic suturing is needed still represents a challenge, mostly due to spatial limitation, fixed trocar positions, and restricted instrument movements. In order to optimize laparoscopic suturing, Frede et al. [13] found that an isosceles triangle trocar arrangement is needed, and the angle between laparoscopic instruments should be adjusted to between 25° and 45°. Even if this positioning is intuitive and replicates human anatomy with an arm on either side of the point of view, this arrangement often fails to be ergonomic, due to interactions between the assistant holding the camera and the surgeon.

In order to reduce this arm conflict between the surgeon and camera holder, and obtain a better ergonomic working position for both, Harper et al. [14] were the first to describe a linear port configuration suitable for all urological transperitoneal laparoscopic renal and adrenal surgery. After creating the pneumoperitoneum with a Veress needle, the first and uppermost port is placed one fingerbreadth below the costal margin, using a visual trocar. The camera is introduced through this trocar. The middle (second trocar) and inferior trocars (third trocar) are placed approximately four fingerbreadths apart. The lowest inferior trocar is approximately at the level of the umbilicus, rarely lower. A fourth port is often placed off the tip of the 11th or 12th rib and used for retraction (Figure 83.3).

For right-sided cases, the first trocar is placed two fingerbreadths lower than the left side (because of the liver) and a trocar for liver retraction is also placed in the midline, right below the xiphoid sternum. Considering this trocar arrangement, both working ports are to one side of the camera and the surgeon's point of view remains intuitive.

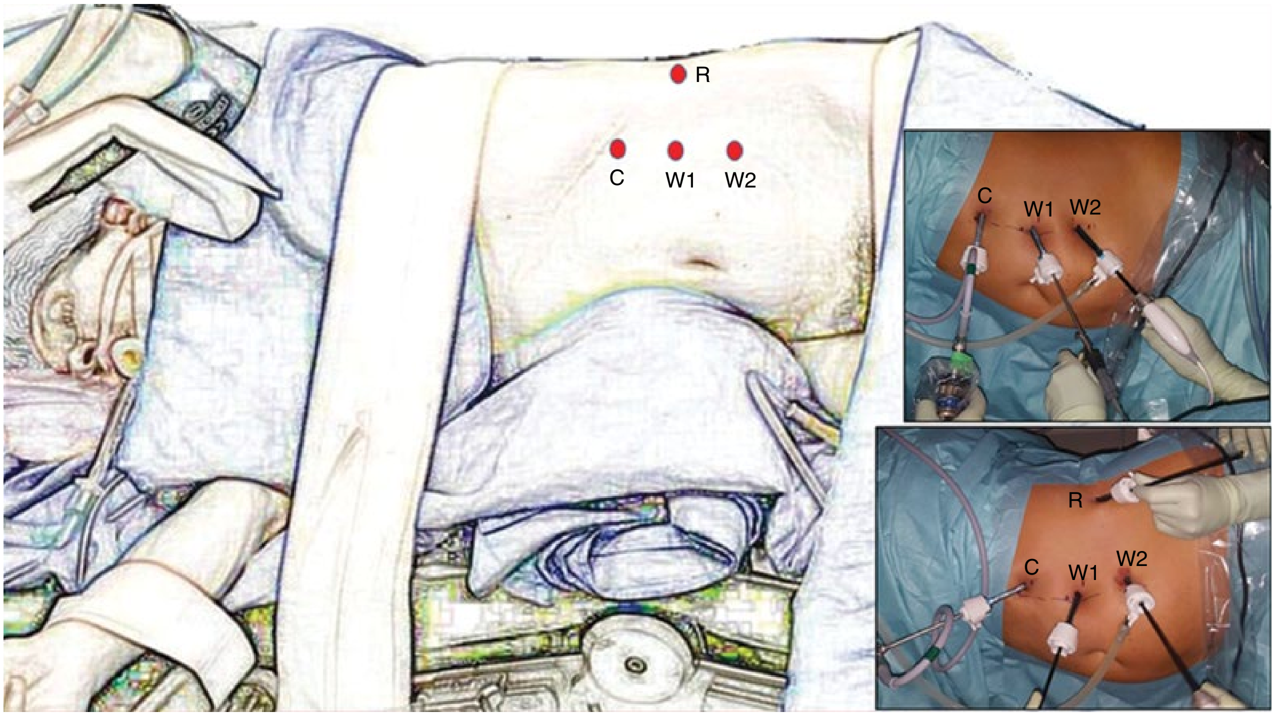

**Figure 83.3** Linear port configuration for left side upper tract surgery using three 5 mm trocars along left pararectal line and a fourth 5 mm port placed off the tip of the 11th or 12th rib for retraction. C, camera; W1 and W2, working ports; R, retractor). *Source:* From Fundaciò Puigvert, Spain.

Furthermore, the authors [14] described the use of a 30° lens that is usually oriented in line with the surgeon's angle of view. Linear port placement along the pararectal line is well suited also in cases of performing sutures (pyeloplasties and partial nephrectomy renorrhaphy), positioning the camera temporarily through the middle trocar. This generates a helpful separation of the laparoscopic instruments, making suturing and knot tying quicker and easier [14].

### Choice of the trocar and laparoendoscopic single-site surgery

The choice of trocar size depends on the instruments needed for the procedure. Generally, in laparoscopic surgery, trocars from 3 to 12 mm can be used. When larger instruments such as entrapment devices or endoscopic ultrasound probes are needed [14], larger trocars are available as big as 15 mm. Trocar length is usually the standard 10 cm, although longer trocars (15 cm) are available for obese patients.

Recently, in a multicenter prospective study, Breda et al. [15] evaluated the role of mini-laparoscopy, using 3 mm instruments and a laparoscope, in renal and adrenal surgery. The same mini-laparoscopic approach was also proposed in live donor nephrectomy as an attractive alternative to the standard laparoscopy [16]. The authors found that the operative time was possibly longer than that in a standard laparoscopy, but clinical and safety outcomes were not compromised. Furthermore, mini-laparoscopy provided excellent pain control and cosmetic results by minimizing the incision site [15].

As far as the type of trocar to use is concerned, many are available, including bladed, bladeless/blunt, and radially dilating trocars. According to the literature, bladeless/blunt and radially dilating trocars are preferred to the bladed ones due to a lower incidence of bleeding, hernia, and pain. Furthermore, by using radially dilating devices, fascial closure can be avoided [17–20].

Finally, laparoendoscopic single-site (LESS) surgery was introduced in urology in order to decrease morbidity and improve recovery times and cosmetic results [21]. The umbilicus is the most frequently used access site, with a 4–5 cm periumbilical incision. There are multiple LESS devices available, the majority of which include a multichannel port [22].

## Complications related to trocar placement and transperitoneal access

### Trocar-related complications

Trocar-related complications such as trocar site bleeding, herniation, infection, and postoperative pain may be related to the type and size of trocars [17]. Abdominal wall vessel injury (usually the epigastric vessels) can be managed with direct coagulation through a second trocar placement. If direct coagulation fails, a Carter–Thomason closure device may provide a figure-of-eight absorbable suture in order to control the bleeding. The risk of hernia occurrence in the entry site increases with the trocar size used, although fascial closure is performed [23]. The data reported by Kadar et al. showed an increasing port site hernia rate of 3.1% using 12 mm trocars compared with 5/10 mm ports. The same authors also recommended closure of the fascia after laparoscopic procedures using larger than 5 mm trocars [24]. The majority of these hernias occurred within the first two weeks, with a range between a few hours and 1 year [25] and the most frequent site of occurrence is the umbilical scar [23]. Shalhav et al. [26] found that by using blunt trocars rather than sharp trocars the risk of hernia formation could be limited due to the mechanism of insertion. A blunt trocar penetrates the abdominal wall layers by splitting fibers, allowing a nontraumatic separation of the tissues and a spontaneous muscle reapproximation after trocar removal.

Although infrequent, port site infection is one of the most bothersome complications in laparoscopic and robotic surgery, increasing patient morbidity. Infections are more common at the umbilical port [27]. In this site, the infection may be related to the specimen extraction technique. For this reason, Sasmal et al. underlined the importance of irrigating and cleaning the port site before closure and removing the specimen in an endobag [27]. Furthermore, the risk of port site infections increases in cases of diabetes, malnutrition, a history of nicotine or steroid use, a long pre- and postoperative hospital stay, and blood transfusion [28].

Postoperative pain has been consistently evaluated. Cristaudi et al. [29] reported on postoperative pain and cosmetic results using 5 mm and larger trocars. Pain assessment was measured with visual analog scale. The authors reported significantly lower pain using 5 mm trocars compared to the larger sizes, in particular in the lower abdomen, and the scar assessment score was significantly lower for the 5 mm trocar. Breda et al. also reported excellent pain control and cosmetic results using 3 mm trocars [15].

### Intra-abdominal complications

Complications related to transperitoneal access include intra-abdominal vascular and visceral injuries. During the creation of the pneumoperitoneum, the most common major vascular injuries are at the level of aorta and inferior vena cava [30]; although rare, these lesions may require a fast open conversion to control bleeding. Two multicenter studies found that the risk of vascular injury is higher in the direct trocar insertion technique than in the open technique [31,32]. Spleen, liver, and bowel injuries are mainly related to blind initial access, either through a trocar or Veress needle [33]. The choice of an entry point away from an abdominal scar (previous surgery) and insufflation at or above the midclavicular line when in the flank position can avoid these injuries.

Although liver injuries rarely represent a problem, splenic injuries frequently require revision, which sometimes ends up with a splenectomy. A bowel injury can be suspected with aspiration of intestinal fluid or in case of irregular abdominal insufflation. Any bowel injury, including serosal abrasions, should be treated at the time of recognition. In case of a small and isolated injury, the area of injury can often be repaired with laparoscopic suturing. Larger injuries may require laparotomy [34]. In the case of a misdiagnosed intraoperative bowel injury, postoperative presenting symptoms may include leukopenia or diarrhea, abdominal pain, or fever. Diagnosis can be confirmed by a computed tomography (CT) scan [35].

## Trocar placement in laparoscopic and robotic transperitoneal procedures

### Adrenalectomy

Using a laparoscopic or robotic technique, several surgical approaches have been proposed, including the anterior and lateral transperitoneal and retroperitoneal, the last being first described by Mercan et al. in 1995 [36]. Although there is no consensus on optimal access, the most commonly preferred approach to the adrenal gland is transperitoneal, since it provides a larger operative field, wider visibility, and more anatomical familiarity for urologists [37–39]. With the patient in a lateral decubitus, the procedure is usually performed using 3–4 ports. The size of the ports depends on the surgeon's preference although a 10/12 and two to three 5 mm trocars are usually the most commonly adopted. The trocars are usually placed in a circular configuration, with the camera port placed in the periumbilical region. The working trocars are arranged in the anterior axillary and midaxillary line, and an additional retractor placed lateral to the working trocars [40]. A different configuration is also described for laparoscopic adrenal surgery, consisting of ports arranged along the ipsilateral costal margin [12, 41] (Figure 83.4a,b). Linear trocar placement along the pararectal line (Figure 83.3) with all 5 mm trocars is also possible for both right and left laparoscopies, only shifting the inferior port laterally in a right-sided adrenalectomy

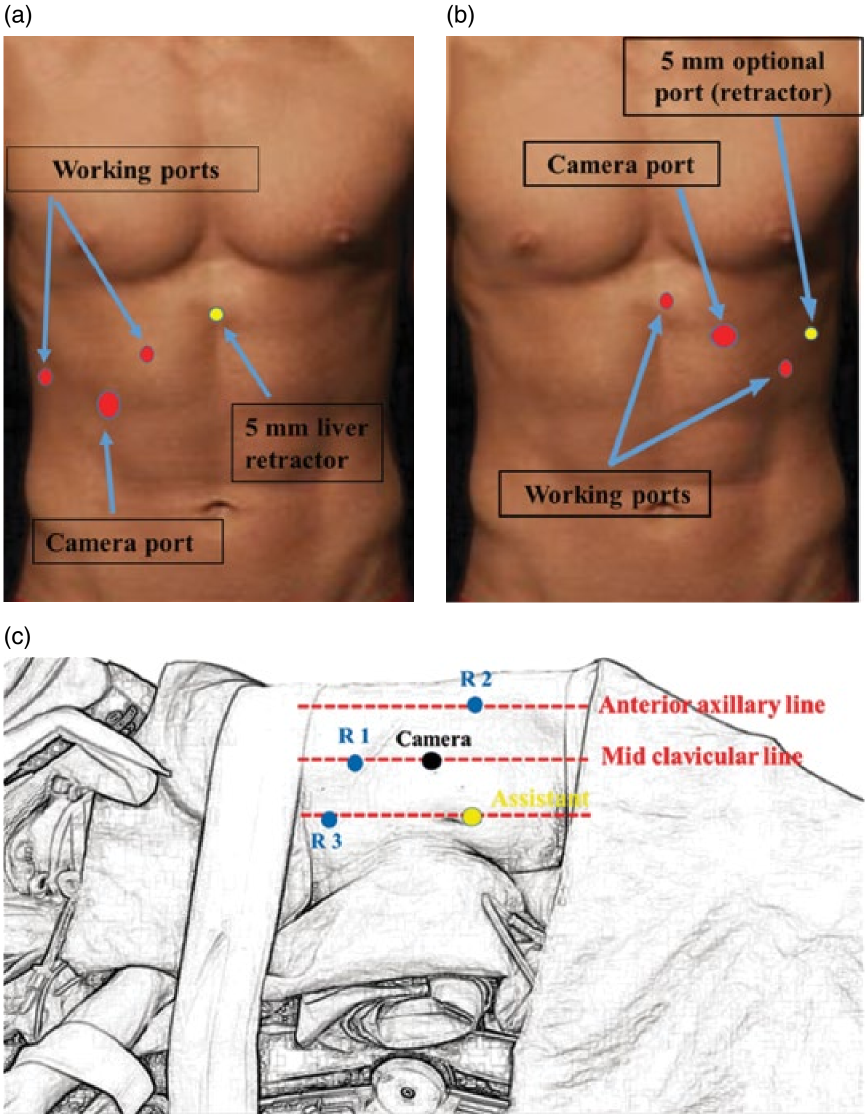

**Figure 83.4** Port placement for transperitoneal laparoscopic adrenalectomy along the costal margin in right side (a) and left side (b). Left robotic adrenalectomy trocar placement (c) using four-armed da Vinci System: one 12 mm camera port, one 12 mm assistant port, and the three 8 mm robotic arm ports (R1, R2, and R3). R, robotic arm port. *Source:* From Fundaciò Puigvert, Spain.

to facilitate the dissection at the inferior vena cava and adrenal vein junction [14]. The robotic trocars arrangement is shown in Figure 83.4c.

## Live donor nephrectomy

The choice of the kidney for live donation remains a dilemma since a right-sided donor nephrectomy is associated with a shorter renal vein (more technically challenging for the anastomosis) [42]. Therefore, laparoscopic left live donor nephrectomy is often performed. The patient is placed in a flank position. The pubic area is included in the field to facilitate suprapubic incision (Pfannenstiel incision) and kidney extraction. The pneumoperitoneum is created [43, 44]. A classical triangular diamond-shaped configuration with the camera port in the middle is traditionally used. In this configuration a 10/12 mm trocar is usually placed lateral to the umbilicus along the pararectal line (alternatively the camera can be inserted at the umbilicus, although we believe this position to be uncomfortable) and two working ports (5 and 12 mm) are inserted at four or five fingerbreadths from the camera bilaterally in a triangular shape configuration (Figure 83.5a). An additional 5 mm trocar can be inserted at the tip of the 11th or 12th rib for lateral retraction.

In our own practice, we usually create the pneumoperitoneum using a Veress needle [14]. We use all 5 mm laparoscopic instruments as well as a linear trocar

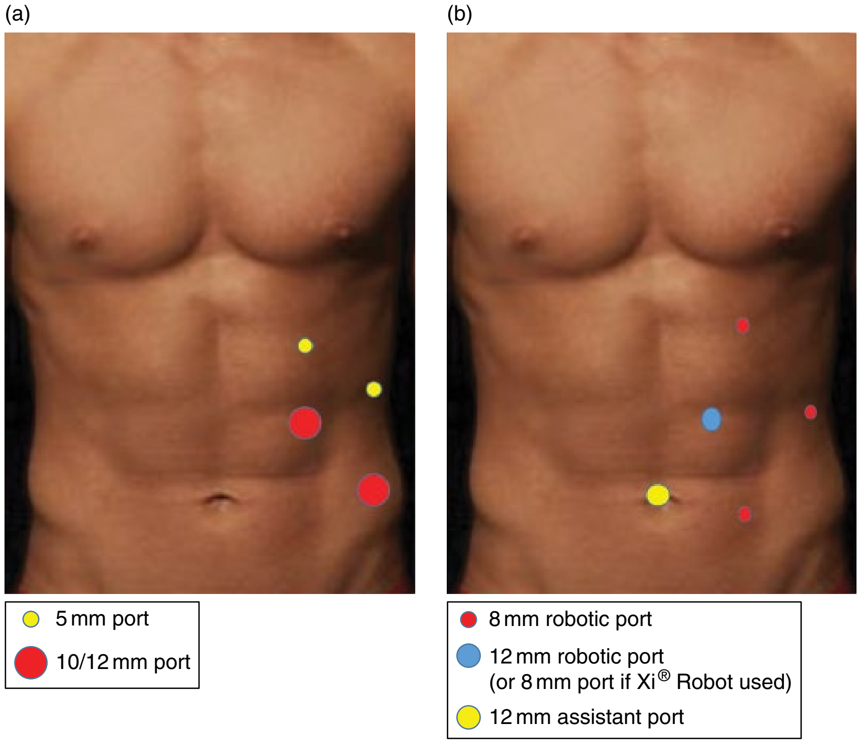

**Figure 83.5** Port placement in laparoscopic (a) and robotic (b) live donor nephrectomy, nephroureterectomy, radical, and partial nephrectomy. *Source:* From Fundaciò Puigvert, Spain.

configuration along the ipsilateral pararectal line, with the camera placed at the most cephalic position. The middle (5 mm second trocar) and inferior trocars (5 mm third trocar) are placed approximately four fingerbreadths apart. A fourth trocar off the tip of the 11th or 12th rib is added as a retractor (Figure 83.6a,b). A Pfannenstiel-like incision is made approximately at the pubic hairline, through which a 15 mm trocar is inserted. Through this port the endovascular stapler may be introduced, as well as the placement of the 15 mm Endo Catch™ bag for kidney extraction (Figure 83.6c). Alternatively, a hand-assisted device can be inserted at the umbilicus for faster kidney extraction [14].

Considering a robotic approach, the patient is positioned in a 45° dorsal position and a 10/12 mm trocar is placed at 3 or 4 cm lateral to it at the pararectal line. Under direct endoscopic vision, two or three robotic ports (8 mm) are placed, as in laparoscopic nephrectomy, with one assistant (10/12 mm) trocar at the level of the umbilicus (Figure 83.5b) [45,46].

## Radical and partial nephrectomy

The patient is positioned in lateral decubitus in both the robotic and laparoscopic approaches. Laparoscopic trocar disposition using a classical triangular configuration was recently reported by Gaunay et al. [47] and is shown in Figure 83.5a. On the right side, an additional trocar can be used for liver retraction, positioned in the epigastrium, just inferior to the xiphoidal process. In obese patients it is recommended to shift this configuration laterally to the rectus muscle in order to reduce the distance from the target tissue [47]. Linear port configuration along the ipsilateral pararectal line is also available for both laparoscopic radical and partial nephrectomy, with the camera placed at the most cephalic position port as described above. When performing a suture, as in a partial nephrectomy, the camera is temporarily placed in the middle trocar, making knot tying quicker and easier [14].

Using a robotic approach for radical and partial nephrectomy, two types of trocar configurations can be used: medial (Figure 83.5b) [48] and lateral [49] camera port placement. In the medial camera port configuration, a 10/12 mm camera port is placed in the periumbilical area using a 0° or 30° angle-down scope with the patient in a full or modified flank patient position, similar to the pure laparoscopic approach. An 8 mm subcostal robotic trocar is positioned in the anterior axillary line. Another 8 mm robotic trocar is situated in the posterior axillary line, about 2 cm above the iliac crest. A 12 mm assistant trocar is placed in the low midline in order to allow the passage of bulldog clamps, sutures, and suction. An additional 12 mm subxiphoid assistant trocar can be positioned for the retraction and the passage of bulldog

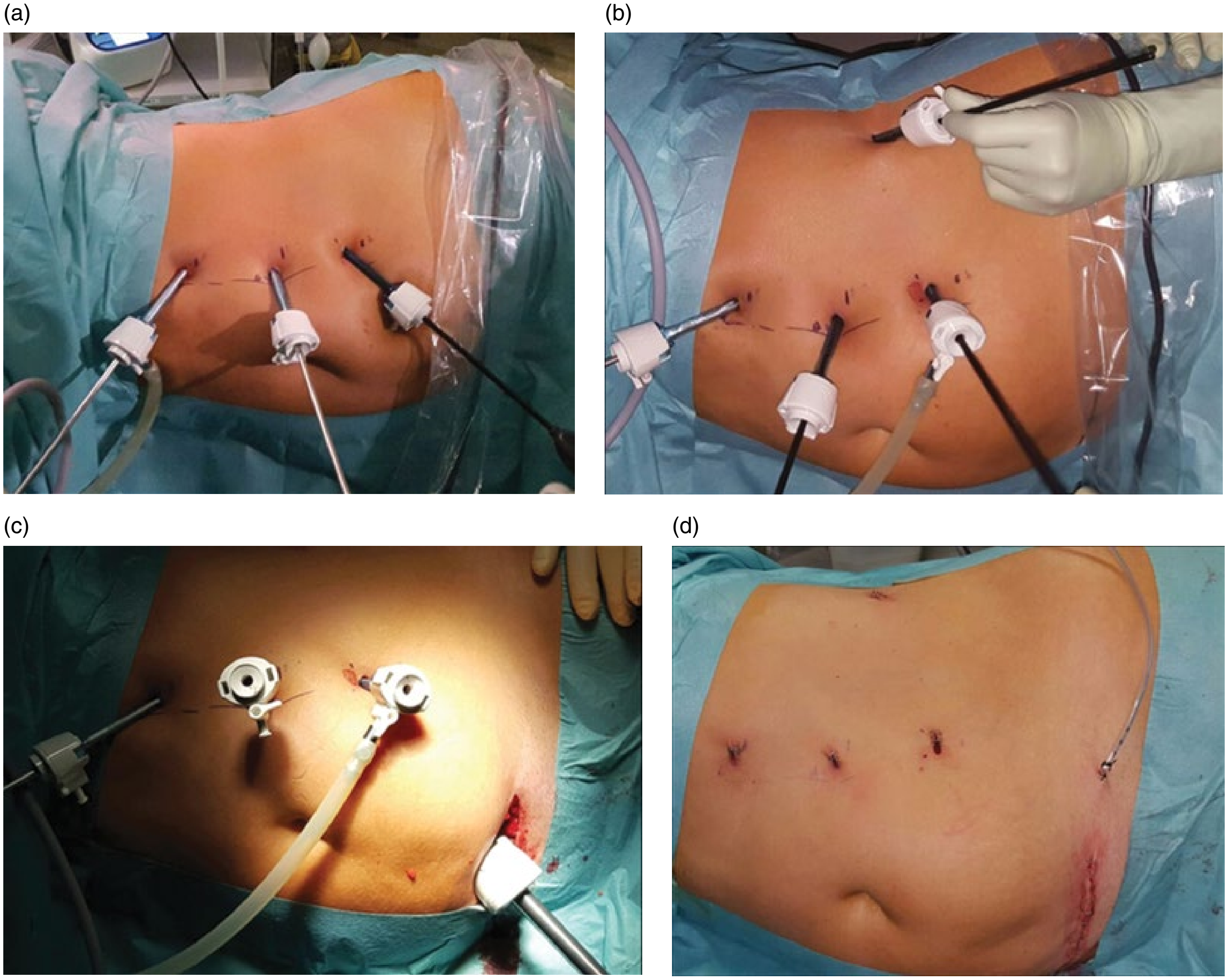

**Figure 83.6** Laparoscopic left live donor nephrectomy. (a) Linear port configuration along the pararectal line (camera holder at the most cephalic position). (b) An additional trocar used as retractor. (c) Through a Pfannenstiel incision a 15 mm trocar is placed to introduce endovascular stapler and the 15 mm Endo Catch bag for kidney extraction. (d) Final view of trocar positions and Pfannenstiel incision. *Source:* From Fundaciò Puigvert, Spain.

clamps from a different angle. The lateral camera port configuration uses a 30° angle-up laparoscope with the patient in the full flank position. In this kind of lateral configuration, a 12 mm camera port is placed a hand's width from the costal margin, between the midclavicular and anterior axillary line. The lateral camera port assessment avoids conflict between working arms and allows hilum dissection without needing help from an assistant for bowel retraction. If the new Xi machine is used a forth arm can be used for lateral retraction.

### Nephroureterectomy with bladder cuff excision

The modified lateral decubitus position is used in both laparoscopic and robotic approaches. Trocar assessment for laparoscopic nephroureterectomy is identical to the trocar configuration used for laparoscopic radical nephrectomy, using an additional 12 mm port suprapubic (in the midline between the umbilicus and the pubis) to perform distal ureter dissection and bladder cuff excision [47]. As in radical and partial nephrectomy, this configuration is shifted laterally in obese patients. Trocar assessment in robot-assisted nephroureterectomy was recently reported by Gaunay et al. [47] (Figure 83.5b). The issue regarding the best method for distal ureter dissection and bladder cuff excision remains controversial and is largely based on surgeon preference for both laparoscopic and robotic approaches [50]. However, the open approach is considered the safest, using the same single incision for specimen extraction and bladder cuff excision [51] and it is the approach that we recommend.

## Ureteral procedures

Several ureteral procedures, including pyeloplasty, ureterolithotomy, and ureterovesical reimplantation, are treated using conventional laparoscopy or a robot-assisted approach [52,53]. Depending on the ureteral tract to be treated, different trocar configurations, using three or four trocars, are possible. A linear port configuration (Figure 83.3) and trigonal or rhomboidal arrangements (Figure 83.7a) can be used for laparoscopic upper tract ureteral procedures. The trocar assessment for a robotic approach is allocated in a V-shape fashion (Figure 83.7b). In the case of low ureteral procedures, the patient is positioned in a supine fashion for both pure laparoscopy and robot-assisted surgery and trocar configuration is as shown in Figure 83.7c. For both laparoscopic and robotic approaches, one periumbilical trocar is placed for the camera (5–10 mm). Furthermore, two ports are placed, at two or three fingerbreadths medially to the anterior superior iliac crest bilaterally. An additional assistant trocar can be inserted in the suprapubic space to provide further help [52,53].

## Bladder surgery and pelvic lymph node dissection

Both laparoscopic [54] and robotic [55] approaches for radical cystectomy were introduced in order to decrease morbidity rate and length of hospitalization. Although many trocar positions have been described [55,56], our recommendation for laparoscopic radical cystectomy and pelvic lymphadenectomy is a five-port configuration (Figure 83.8a). A 10/12 mm trocar is positioned 1–2 cm above the umbilicus. A second 10/12 mm trocar is introduced at 8 cm in a virtual line between the umbilicus and the left iliac crest, followed by a 5 mm trocar at two fingerbreadths from the right iliac crest. Furthermore two additional assistant 5 mm trocars are placed in a similar linear fashion separated 8 cm from each other on the right.

The same port configuration is adopted in the robotic procedure with extracorporeal neobladder reconstruction or ileal conduit, with the addition of a 5 mm trocar for the assistant as shown in Figure 83.8b (with the 8 mm robotic trocars). Collins et al. [57] described radical cystectomy with intracorporeal neobladder diversion using a robotic approach. In this case, the camera port is placed 5 cm above the umbilicus. Two 8 mm robotic ports are placed bilaterally at umbilicus level, lateral to the rectus sheath. A 15 mm trocar is positioned just above and medial to the left superior iliac spine, allowing the use of laparoscopic stapling when the robotic arm is temporarily disconnected. Two 12 mm assistant ports are placed on the right side (Figure 83.8c) [57]. Laparoscopic and robotic trocar assessment for other bladder procedures, including partial cystectomy, diverticulectomy, and augmentation cystoplasty, do not vary from the previous described position for radical cystectomy.

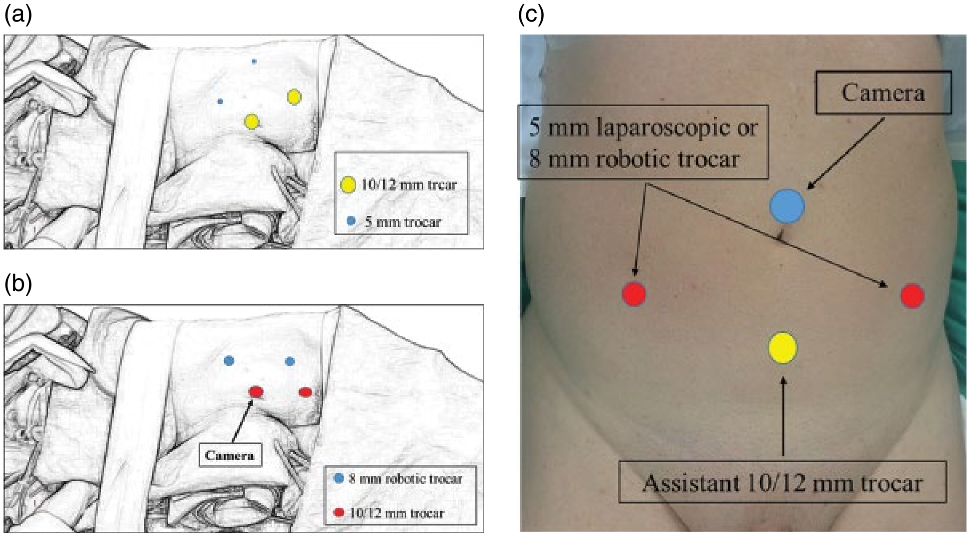

**Figure 83.7** (a) Port placement in laparoscopic upper tract ureteral procedures: 10 mm umbilical trocar, a 5 mm trocar under the edge of the costal arch, and a 12 mm trocar between the umbilicus and pubis. (b) Port placement in robotic upper tract ureteral procedures: two 8 mm trocars (the inferior trocar at 3 cm above the anterior superior iliac spine), a 10–12 mm umbilical trocar (camera), an additional 10–12 mm assistant trocar between the umbilicus and the pubis to provide quicker suture exchange. (c) Laparoscopic and robotic port placement for lower tract ureteral procedures: two ports at 2 cm medially to the anterior superior iliac spine and an additional 10–12 mm assistant trocar in the suprapubic space. *Source:* From Fundaciò Puigvert, Spain.

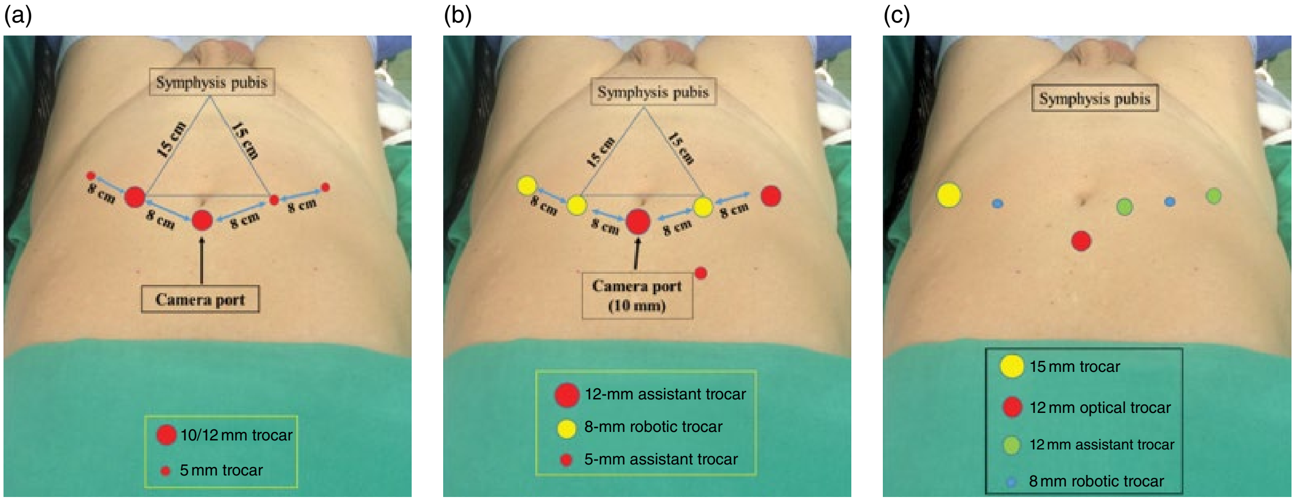
(a)
Symphysis pubis
15 cm
15 cm
8 cm
8 cm
8 cm
8 cm
Camera port
10/12 mm trocar
5 mm trocar
(b)
Symphysis pubis
15 cm
15 cm
8 cm
8 cm
8 cm
8 cm
Camera port (10 mm)
12-mm assistant trocar
8-mm robotic trocar
5-mm assistant trocar
(c)
Symphysis pubis
15 mm trocar
12 mm optical trocar
12 mm assistant trocar
8 mm robotic trocar

**Figure 83.8** (a) Laparoscopic trocar configuration for radical cystectomy with lymph node dissection. Robotic cystectomy with (b) extracorporeal and (c) intracorporeal neobladder reconstruction. *Source:* From Fundaciò Puigvert, Spain.

## Radical prostatectomy

In both laparoscopic and robotic approaches a 10/12 mm port is positioned about 2 cm above the umbilicus for camera introduction. Furthermore, it is important to underline that the laparoscopic and robotic trocar arrangement may vary depending on height, weight, previous surgical scars, and pelvis anatomy. The trocar placement in laparoscopic radical prostatectomy is shown in Figure 83.9a. A 5 mm trocar is inserted four fingerbreadths lateral to the umbilicus in the anterior axillary line on the right side. Another 5 mm trocar is positioned at distance of three or four fingerbreadths from the other in the direction of the anterior iliac crest. On the left side, a 12 mm trocar is placed lateral to umbilicus at 8–9 cm in the anterior axillary line, and a further 5 mm trocar is placed symmetrical to the contralateral one.

Several port positions have been reported for robotic radical prostatectomy, with the optical trocar at the level of or just above the umbilicus [58–60]. The trocar placement in robotic radical prostatectomy is shown in Figure 83.9b. An 8 mm robotic trocar is placed at 10 cm from the umbilicus, both on the right and on the left side along the anterior axillary line at 15–18 cm from the pubic bone. Alternatively, these two trocars can be positioned at 8–10 cm bilaterally

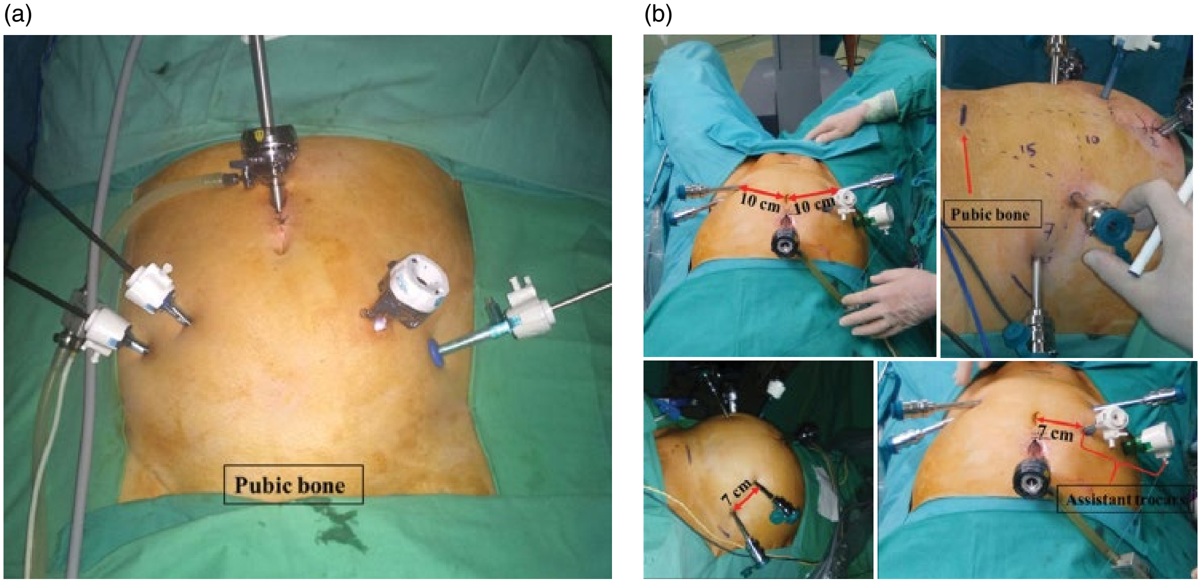
(a)
Pubic bone
(b)
10 cm
10 cm
15
10
Pubic bone
7 cm
7 cm
Assistant trocars

**Figure 83.9** (a) Trocar placement for laparoscopic radical prostatectomy. (b) Trocar placement for robot-assisted laparoscopic radical prostatectomy for four-arm robot. *Source:* From Fundaciò Puigvert, Spain.

in a virtual line between the camera and the superior iliac crest. On the left side, an 8 mm robotic trocar is placed at two fingerbreadths from the iliac crest for the fourth arm. An assistant 5 mm trocar is placed three fingerbreadths on the right side parallel to the umbilicus; a second assistant 12 mm trocar is placed three fingerbreadths from the superior anterior right iliac crest. In cases of a small pelvis, the robotic port configuration can be modified, positioning the most lateral ports on the left side more horizontally, 7 cm apart from the other robotic trocars.

## Conclusions

Although there is no strong evidence from the literature, it appears that the induction of pneumoperitoneum is safer when open access or direct optical access are performed.

Minimizing the trocar size reduces complications and postoperative pain, as well as giving better cosmetic results. Bladeless and radially dilating trocars should be used rather than bladed ports to minimize bleeding and postoperative port site hernias.

Traditionally, in renal and adrenal surgery, laparoscopic port placement relies on a diamond triangular trocar configuration in which the camera is included within the diamond. The linear port configuration has been introduced to standardize and simplify trocar placement for all adrenal, renal, and ureteral procedures.

For pelvic procedures, the optical trocar is maintained at the level of, or just above the umbilicus, with trocar position varying minimally among different procedures.

See accompanying Video 83.1.

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# 84

# Retroperitoneal Access and Trocar Placement

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## Introduction

The first technical part of any urologic laparoscopic or robotic procedure involves obtaining access to either the peritoneum (see Chapter 83) or the retroperitoneal/extraperitoneal space. Access and trocar placement is of critical importance for all minimally invasive abdominal surgery. However, due to the limited working space in retroperitoneoscopic and extraperitoneoscopic surgery, not optimizing access points in these spaces may limit the ability of the surgeon to accomplish the case safely and efficiently. In this chapter we outline the necessary steps for proper patient positioning, primary retroperitoneal access, development of the retroperitoneal space, and secondary trocar placement for both retroperitoneal renal and adrenal surgery as well as pelvic extraperitoneal surgery. In addition, we outline potential inclusion and exclusion criteria to help surgeons select cases ideal for a retroperitoneoscopic renal/adrenal surgery and extraperitoneal laparoscopic and robotic pelvic surgery. Finally, we briefly summarize critical issues related to specimen retrieval and laparoscopic exit at the end of these retroperitoneal and extraperitoneal pelvic access cases.

## Retroperitoneal renal/adrenal access

### Patient evaluation and selection

As with the selection of open surgical approaches, patient characteristics, pathology, and surgeon preference will guide the incision to optimize access for the operation with the goals of avoiding challenging anatomy or scar tissue, improving ease of access to the pathology being addressed, and increasing safety to the patient. Retroperitoneoscopic access to the kidney and adrenal gland mimics a retroperitoneal open flank approach, which can offer several potential advantages over the transperitoneal approach.

Although prior abdominal surgery is not a contraindication to a transperitoneal laparoscopic approach, the number and extent of prior abdominal procedures may render patients more suitable for a retroperitoneal approach to renal or adrenal surgery [1]. Patients with history of peritonitis often have diffuse intra-abdominal adhesions and may benefit from avoiding the peritoneal space. Similarly, patients with abdominal wall or umbilical hernias are at heightened risk of potential bowel injuries when approached via a transperitoneal approach, because bowel and other organs may be contained within the hernia sac. Moreover, abdominal wall reconstruction for complex hernias with mesh can often lead to the development of significant adhesions under the abdominal wall, which can make port placement difficult and limit the working space in a transperitoneal case.

The target organ and the specific site of pathology can also help the surgeon to select a surgical approach. Anatomically, adrenal masses, posteriorly based renal masses, and ureteropelvic junction obstructions can be easily accessed via the retroperitoneoscopic approach and may obviate the need for full renal mobilization, which is often required when addressed via a transperitoneal surgical approach. A retroperitoneoscopic approach can also allow for prompt identification of major vasculature, specifically the renal hilum and the great vessels, circumventing the need for bowel mobilization. Furthermore, approaching the hilum posteriorly can offer direct access to the renal artery, which can allow for expeditious identification and control of the

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arterial supply for either ligation in cases of radical nephrectomy or clamping for partial nephrectomy.

No definitive exclusion criteria exist for retroperitoneal access, although a few cases may present more challenges for retroperitoneoscopic surgery. Cases of dense retroperitoneal inflammatory fibrosis or any prior retroperitoneal surgery should be evaluated on a case-by-base basis to weigh the risks of transperitoneal versus retroperitoneal access, taking into account the surgeon's preference and comfort level [2]. Prior retroperitoneal access for previous renal surgery, including percutaneous stone surgery or tumor ablation, can lead to scarring within the retroperitoneal fat, resulting in the adherence of natural tissue planes and difficulty in developing the retroperitoneal space. Another relative exclusion is management of large renal/adrenal masses or large-volume hydronephrosis, as the working space in the retroperitoneum is limited; in such cases, a transperitoneal laparoscopic approach would afford the surgeon a more generous working space to approach these problems [3].

## Patient positioning

After induction of general endotracheal anesthesia and sterile insertion of a Foley catheter, the patient is repositioned into a full flank position, similar to the approach for an open flank incision. All pressure points are well padded with surgical towels and/or foam padding to prevent a pressure injury or neuropraxia. Securing the patient in this way allows the table to be rotated from right to left intraoperatively. Some centers use a bean bag under the patient for positioning in the flank position, but in our experience, these devices are not necessary if the patient is well-supported posteriorly with a gel roll or blankets.

The table is flexed at the waist level to open the space between the costal margin and the iliac crest. At this point an axillary roll is placed to help prevent compressive nerve plexus injury. Pillows are placed between the legs and lower extremity pressure points are properly padded. The upper extremities are secured, the dependent arm is placed on an armboard outstretched and the upper arm is placed either in an elevated armboard or secured on pillows. Both upper extremities are maintained in a well-padded, neutral position secured away from the surgical field. The patient is secured to the table with 3-inch tape at the level of the chest and at the hips, taking care not to restrict chest wall movement, which could impair the ability of the anesthesia team to adequately ventilate the patient. The exposed flank and abdomen are prepped and draped in preparation for initiating operative access.

The tip of the 12th rib should be identified; we recommended marking this site prior to prepping the abdomen/flank as palpation of the 12th rib can be impaired after preparation and gloving, especially in the obese patient. After sterile preparation and draping, a line is extended from the iliac crest in a cephalad direction, in the midaxillary line intersecting with the marking of the tip of the 12th rib.

## Placement of initial trocar retroperitoneal access

In the midaxillary line, a 15 mm skin incision is made between the tip of the 12th rib and the iliac crest,. Adjustment of the cranial–caudal positioning of this access trocar is dependent upon the pathology prompting surgery, as well as the use of accessory trocars and the use of the da Vinci robotic system (Intuitive Surgical, Sunnyvale, CA, USA). The incision is carried down to the level of the external oblique fascia. A 10–15 mm incision is made in the fascia with Bovie electrocautery. Fine retractors or blunt finger dissection can be used to spread the abdominal wall musculature down to the lumbodorsal fascia. The lumbodorsal fascia is incised with cautery to open a 1 cm access point. The surgeon's index finger is the inserted into the retroperitoneal space and the tip of the finger should be aimed posteriorly, with the goal of palpating the anterior surface of the psoas muscle (Figure 84.1a). Finger dissection along the surface of the psoas muscle, extending cranially and caudally, will develop the avascular space in the retroperitoneum posterior to Gerota's fascia. The lower pole kidney can typically be felt just anterior to the space developed along the psoas muscle.

Once this space is initially developed, a balloon dilating system can be used to further develop this space prior to port placement. Balloon dissection of the potential space posterior to the kidney was first described for retroperitoneoscopy by Gaur et al. in 1993 [4]. The balloon tip of this visual obturator trocar is inserted just posterior to the kidney anterior to the psoas muscle, in the space previously developed bluntly by the surgeon's finger. The balloon is inflated 20 times (~400 ml) under direct visualization using a 0° or 30° lens 10 mm laparoscope, ensuring that the balloon unfolds and expands in a cranial–caudal orientation. A laparoscope inserted into the device allows for appreciation of the adjacent anatomy through the dissecting balloon as the space is developed. The psoas muscle can typically be assessed posteriorly and the kidney and peritoneum which lay anteriorly. Up to an additional 400 ml is insufflated into the balloon (800 ml in total) (Figure 84.1b). The balloon dissecting trocar is deflated and a balloon working trocar typically used for Hasson entry is placed in the same access site for cases of multiport retroperitoneoscopy. Pneumoretroperitoneum is achieved at a pressure of 15 mmHg through this working trocar.

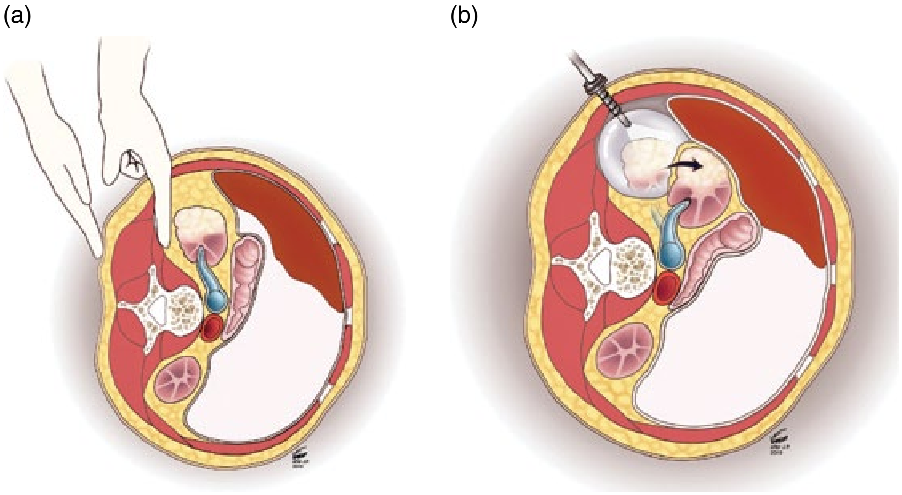

**Figure 84.1** (a) Surgeon's index finger inserted through the lumbodorsal fascia into the retroperitoneal space anterior to the psoas muscle. (b) Balloon dissection of the retroperitoneum. The round-shaped balloon is posterior to the kidney and adrenal gland during pneumodissection. *Source:* Urologybook.com. Reproduced with permission of Urologybook.com.

In cases of laparoendoscopic single-site surgery approached via a retroperitoneal access, the primary access site is developed in a similar fashion with blunt finger dissection, followed by balloon distension of the retroperitoneal space. At this point, the original midaxillary line incision is extended to create a 3–5 cm opening through the skin, abdominal musclulature, and fascial layers to accommodate a multiport single-site access device [5, 6].

## Placement of secondary trocars for retroperitoneoscopic surgery

For cases of conventional multiport retroperitoneoscopic surgery, the primary access trocar is used as a port for laparoscopic visualization during accessory trocar insertion.

The anterior trocar is placed approximately 7–8 cm anterior to the camera trocar site in a line drawn in a cephalad direction from the anterior superior iliac spine. The posterior trocar is placed in a line drawn at the level of the extensor muscles of the back, also at the level of the camera trocar (Figure 84.2). Both accessory trocars are placed under direct laparoscopic visualization.

For the anterior trocar, care is taken to ensure the peritoneum is well shifted anteriorly and the entry space allows direct retroperitoneal access. In some cases, placement of the posterior accessory trocar first will allow for additional peritoneal dissection and mobilization through this posterior working port with a blunt grasping device or laparoscopic Kitner to develop the entry space for the anterior trocar. The posterior trocar may be angled in a slightly more cephalad direction or in some cases the entry may be shifted cranially 1–2 cm,

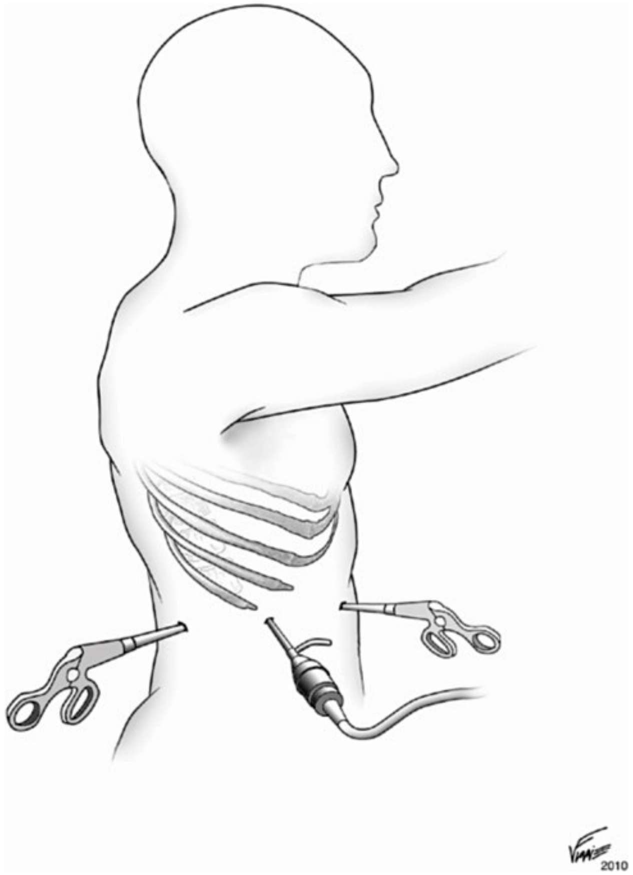

**Figure 84.2** Trocar placement for retroperitoneal renal/adrenal surgery. Patient is positioned in the full flank position. All three trocars line up in a straight line. *Source:* Urologybook.com. Reproduced with permission of Urologybook.com.

which will decrease the amount of torque on the trocar and surgeon fatigue during conventional retroperitoneoscopic cases. Ultimately, the surgical left trocar, camera trocar, and right trocar are all placed in a straight line, perpendicular to the midaxillary line, with slight modification if the posterior trocar is shifted cranially by surgeon preference (Figure 84.2).

In cases of robot-assisted laparoscopy via a retroperitoneal approach, an accessory trocar for bedside assistance can be placed inferior to either of the robotic trocar sites or triangulated inferiorly between the camera and robotic trocar sites (Figure 84.3a,b).

### Limitations of retroperitoneoscopic surgery

Limitations to the retroperitoneal approach to laparoscopic and robot-assisted laparoscopic surgery include the limited anatomic space both internally and externally. Patient anatomic variability may further limit the space between the costal margin and iliac crest and create a challenge for adequate trocar spacing for ease of triangulation. Furthermore, internal space in the retroperitoneum is dependent on the degree of peritoneal mobilization anteriorly with the balloon and manual dissections employed. As mentioned previously, size of the renal or adrenal mass, degree of hydronephrosis, or other pathology or anatomic variation may further limit the utility of the retroperitoneal space. In addition, because of the limited space in the retroperitoneum, camera mobility may be limited due to crossing of working instruments and avoidance of retroperitoneal fat and structures that may smudge the lens and blur visualization during the operation.

## Extraperitoneal pelvic access

### Patient evaluation and selection

Most radical prostatectomies are currently performed via a minimally invasive approach. Other urologic pelvic surgeries that can also be performed in a minimally invasive fashion include simple prostatectomy, radical cystectomy, partial cystectomy, and surgeries of the distal ureter. The majority of minimally invasive urologic pelvic surgery is performed via a transperitoneal approach, which provides increased working space and less instrument conflict. However, there are scenarios where an extraperitoneal approach may provide some distinct advantages. In patients with

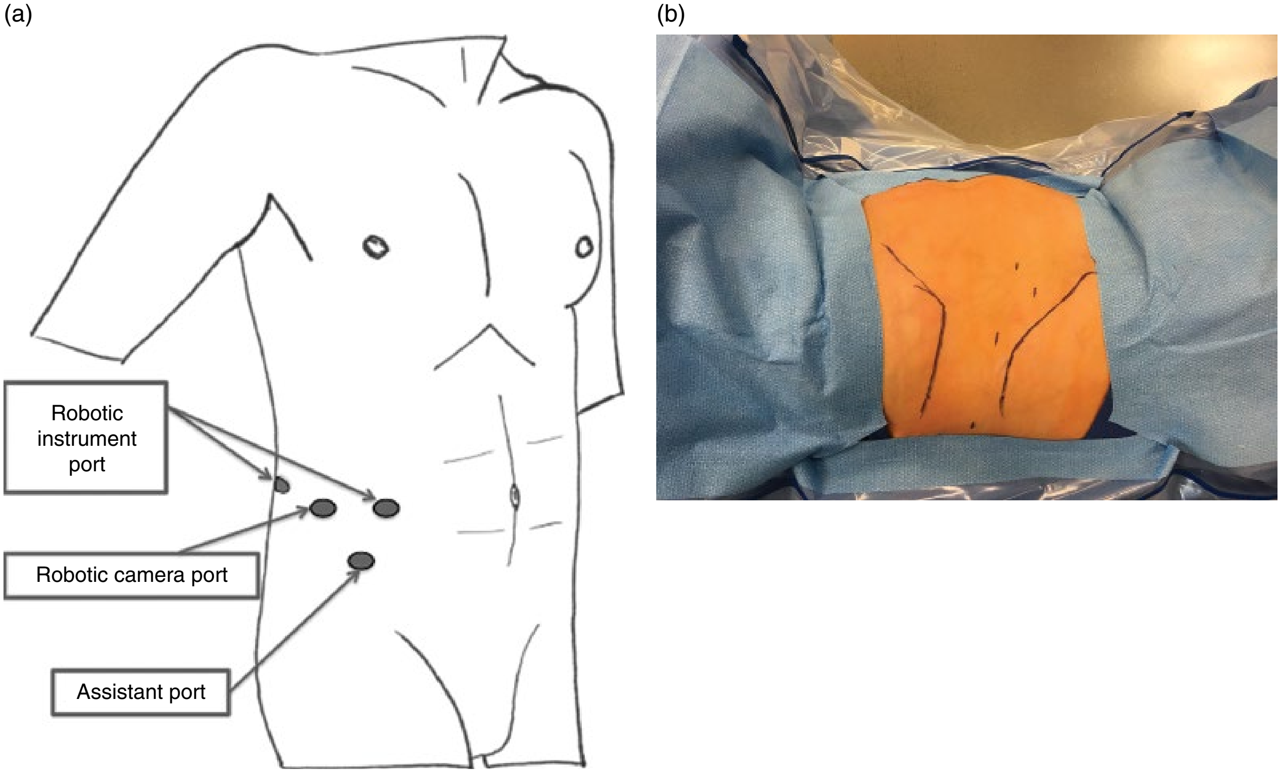

**Figure 84.3** (a) Diagram depicting trocar placement for robot-assisted retroperitoneal renal surgery with midaxillary line camera trocar, anterior and posterior robotic trocars, and inferior bedside assistant trocar. (b) Operating room positioning and markings depicting sites for planned trocar placement for robot-assisted retropertoneoscopic right partial nephrectomy.

previous abdominal surgery, the extraperitoneal approach avoids entry into the peritoneal cavity and obviates the need to perform an adhesiolysis, which could otherwise increase operative time. Although the risk of inadvertent bowel injury when performing minimally invasive urologic pelvic surgery is low overall, the risk increases in patients with previous abdominal surgery, inflammatory bowel disease, or previous peritonitis. Avoiding entry into the peritoneal cavity can reduce the risk of bowel injury in such patients. In transperitoneal pelvic surgery, the patients are often placed in the steep Trendelenburg position to help mobilize the bowel out of the pelvis. This extreme positioning is not required when performing the extraperitoneal approach because the peritoneum prevents the bowel from encroaching upon the pelvis and the surgeon's visual field [7]. Patients who are obese or have restrictive lung disease may not be able to tolerate the steep Trendelenburg position and in such scenarios, the extraperitoneal approach can be utilized to perform the surgery in a minimally invasive fashion. Finally, in the event of postoperative bleeding or urine leak, the hematoma or urinoma would be limited to the extraperitoneal space, which could minimize the development of associated intraperitoneal complications (i.e. ileus, distention, development of peritonitis, etc.). A randomized study comparing the approaches to robotic radical prostatectomy demonstrated no significant differences in any operative parameters analyzed and suggested that patients with prior abdominal operations would be best suited for the extraperitoneal approach [8]. In addition, a meta-analysis comparing extraperitoneal robotic radical prostatectomy and transperitoneal robotic radical prostatectomy showed a trend toward shorter operative times in the extraperitoneal patient cohort with equivalent oncologic outcomes [9].

Disadvantages to this approach include the smaller operative working space, which can increase conflict among working arms, especially if a fourth robotic arm is used. Moreover, there is limited access to the cepalad aspect of the pelvis, which can limit the surgeon's ability to perform an extended pelvic lymphadenectomy or access the ureter above the common iliac vessels. The extraperitoneal approach also results in a higher rate of pelvic lymphocele formation, many of which would otherwise be reabsorbed by the peritoneal cavity if a transperitoneal approach were used [10]. Scarring within the extraperitoneal space will limit the surgeon's ability to develop the working space. Because of this, the extraperitoneal approach should be avoided in patients who have undergone prior extraperitoneal pelvic surgery, such as inguinal hernia repair with mesh or renal transplantation.

## Patient positioning and placement of initial trocar access

After general anesthesia is established, the patient is then positioned for the operation. When the da Vinci Si is being used, the patient is placed in the dorsal lithotomy position to accommodate the robot in between the legs. With the newer da Vinci Xi model, the robot can be docked from the side of the patient and dorsal lithotomy is not required. The patient is adequately secured to the operating room table to allow for the Trendelenburg position; the method of patient securing is left to the surgeon's discretion. The authors have used the Pink Pad XL system (Xodus Medical Inc., New Kensington, PA, USA) with good success. After sterile preparation of the abdomen and genitalia, a Foley catheter is placed to decompress the bladder. The pubic bone is identified and a vertical, infra-umbilical incision of about 15 mm in length is made in the midline. S-retractors are used for retraction and dissection is continued through the subcutaneous tissue to the external fascial layer. Stay sutures of 0 Vicryl are placed in the rectus fascia, caudal and cephalad to the incision site on the fascia. Holding the lower fascia anteriorly, the fascia is incised. The rectus muscle belly is separated in the midline. A transversalis fascia below the arcuate line is identified and incised with scissors or blunt index finger dissection. The surgeon's index finger is then inserted into the preperitoneal space and the space is developed, taking care not to enter the peritoneal cavity superiorly. A kidney-shaped dissecting balloon (Covidien/Medtronic, Minneapolis, MN, USA) is inserted into the space in the direction of the pubic bone (Figure 84.4). The balloon is insufflated 30 times (~600 ml). Under direct laparoscopic visualization with a 10 mm laparoscope passed through the visual obturator of the balloon dissecting trocar, insufflation is continued until the pubic bone is visualized from within the dissecting balloon. After creating the operative space anterior to the bladder, the dissecting balloon is deflated and this trocar is removed. Care is taken to avoid disruption of the inferior epigastric vessels during insufflation which can be visualized with the angled lens laparoscope. A Hasson trocar of the surgeon's choice is then placed to serve as a camera trocar (10–12 mm caliber selected for specific laparoscopic or robot-assisted laparoscopic platforms).

## Placement of secondary trocars

Reflection of the peritoneum in a cephalad and lateral direction is often necessary to allow for placement of additional trocars. Using a 10 mm laparoscope with some gentle pressure, the peritoneum is swept in a cephalad and lateral direction to develop the working space.

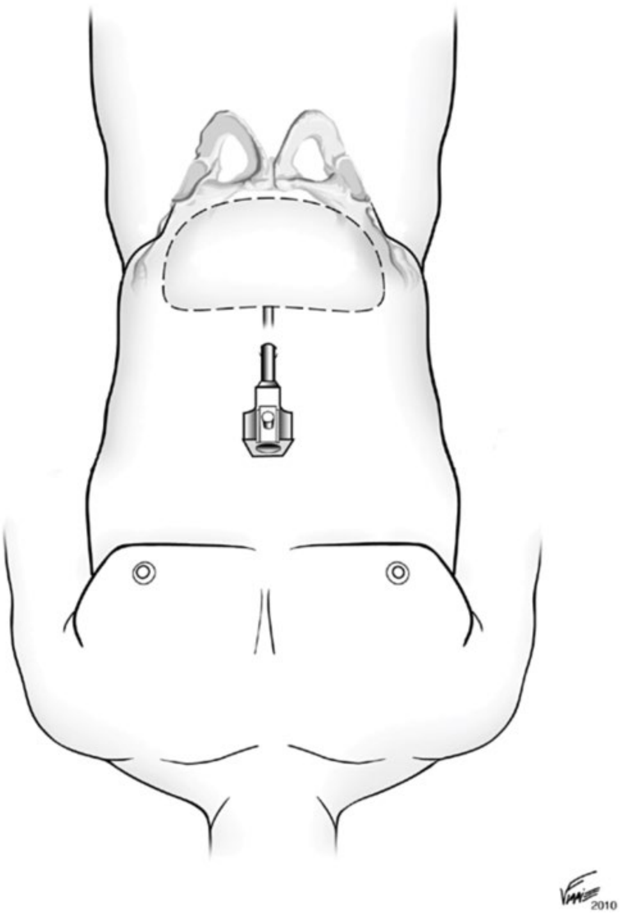

**Figure 84.4** Extraperitoneal balloon dissection for laparoscopic or robotic pelvic surgery. *Source:* Urologybook.com. Reproduced with permission of Urologybook.com.

Inadvertent entry through the peritoneum can occur, which can lead to gas escape into the peritoneal cavity and collapse of the working space. An attempt can be made to close the hole with a suture; alternatively, a small trocar can be placed in the peritoneal cavity to allow for slow decompression of the pneumoperitoneum. If these maneuvers prove ineffective, the surgeon should consider converting to a transperitoneal or an open extraperitoneal approach.

Prospective identification of the pulsations of the iliac vessels and inferior epigastric vessels should be performed to avoid inadvertent injury during dissection of the extraperitoneal space and trocar insertion, respectively. The standard robotic prostatectomy trocars are then placed, arching laterally and inferiorly and spaced approximately 7–8 cm from the camera trocar. A third robotic trocar can be placed lateral and inferior to one of the medial robotic trocars in one lower quadrant, and a bedside assistant accessory trocar can be placed on the contralateral lower quadrant. All robotic and accessory trocars should be placed under direct laparoscopic visualization to ensure safe entry into the preperitoneal space, avoiding critical vascular structures in the pelvis and anterior abdominal wall. Once the trocars are in place, the robot can be docked to the patient and the surgery can commence.

## Laparoscopic exit in retroperitoneal and pelvic extraperitoneal cases

Although great emphasis is placed on initial access for laparoscopic and robot-assisted laparoscopic cases, of equal importance is the exit or removal of trocars at the end of these procedures. It may be challenging for surgeons to follow through with these steps due to fatigue, but it is necessary for them to maintain vigilance at the end of the case. Herein, we describe the important features of exit from retroperitoneal and extraperitoneal surgery.

If an inadvertent entry into the peritoneum is recognized during retroperitoneal surgery, the surgeon should explore this area and ensure no injury to the bowel or other intraperitoneal organs has occurred. This may require expanding the defect in the peritoneal lining to fully visualize and assess the intraperitoneal space. Upon confirming integrity of all structures and hemostasis, the peritoneum can be reapproximated with a running absorbable stitch to re-establish the separation of the peritoneum and retroperitoneum. For extraperitoneal pelvic surgery it is prudent to create a small peritoneal window at the level of the umbilicus at the end of the case to expel pneumoperitoneum that may have accumulated. Often this window can be achieved using a small instrument puncture which does not require peritoneal lining closure.

The surgeon may decrease insufflation pressures to 10 mmHg or less to ensure no bleeding is visualized. It is standard practice to remove all trocars under direct vision. In the event of bleeding from trocar sites, a Carter–Thomason closing device may be used to close the fascia and obtain hemostasis. Large (≥12 mm) trocar sites may be closed with the Carter–Thomason closing device and Vicryl suture in a figure-of-eight fashion. In cases of extirpative surgery, the specimen extraction site should have complete fascial reapproximation to avoid hernia formation. Hernia formation is still a risk in extraperitoneal and retroperitoneal approaches, although this complication is relatively rare compared to transperitoneal laparoscopic procedures.

See accompanying Video 84.1.

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# 85

# Basic Hand-assisted Laparoscopic Techniques

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## Introduction

The introduction of hand-assisted laparoscopic surgery (HALS) has contributed greatly to the widespread adoption of laparoscopy for renal surgery. The adoption of laparoscopic renal surgery was very modest in the first decade following the initial report by Clayman et al. [1]. Why did laparoscopic nephrectomy take so long to catch on, but then subsequently become a standard procedure? This history of laparoscopic nephrectomy contrasts starkly with that of other laparoscopic procedures introduced in the same time period (late 1980s to mid 1990s). Laparoscopic cholecystectomy, laparoscopic pelvic lymph node dissection (until its utility was reduced by prostate specific antigen (PSA) risk profiling), laparoscopic gastric fundoplication, and laparoscopic hysterectomy all achieved widespread use soon after their introduction. Why was laparoscopic nephrectomy different? The primary reason proposed in the mid 1990s was that the necessary operative skills in laparoscopic nephrectomy were too difficult for the average urologist to develop and maintain, given the relative infrequency of nephrectomy in a typical urology practice. Other factors included concern about oncologic efficacy, the inefficiency of increased operative time, and safety of the procedure in case of vascular injury.

Although there likely were many developments that spurred on the widespread acceptance of laparoscopic nephrectomy, HALS was a major factor. HALS addresses many of the perceived problems: it simplifies the procedure technically, which allows even urologists with a low-volume practice to develop and maintain skills; it facilitates wide dissection and intact specimen removal, which may provide some reassurance as to the oncologic efficacy of the procedure (although there is no evidence that HALS provides any different outcome from standard laparoscopic nephrectomy in this regard); it reduces operative time for most surgeons; and it provides more rapid control of vascular injury, reducing the need for conversion to open surgery. Once a critical mass of surgeons started performing laparoscopic nephrectomy, combined with patient demand, its popularity was inevitable.

Following a brief history of hand assistance, this chapter describes the HALS devices that are currently available along with some general principles of their application. The results of HALS are then provided with emphasis on series that compare HALS to other laparoscopic techniques. Finally, the role of HALS in urology is assessed.

## History

As with many innovations in surgery, initial forays into HALS were met with skepticism [2]. In 1993, Boland et al. reported their experience (starting in 1992) with insertion of a gloved hand through a tight fascial incision to allow direct manual organ dissection and removal while maintaining pneumoperitoneum during laparoscopy [3]. Tierney et al. [4] and Tschada and Rassweiler [5] reported laparoscopic radical nephrectomy using this technique in 1994 and 1995, respectively. Commercial devices to facilitate laparoscopic hand assistance were under development by this time [6], and in 1996 Bannenberg et al. [7] reported hand-assisted laparoscopic nephrectomy in a porcine model using a prototype of the first commercial HALS device. Later that same year, Nakada et al. [8] performed the first clinical laparoscopic nephrectomy with a commercial HALS

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device. In 1997, Keeley et al. [9] reported the first HALS nephroureterectomy, and in 1998 Wolf et al. [10] described the first HALS donor nephrectomy. HALS was soon applied to a number of other urologic laparoscopic procedures. The introduction of improved commercial HALS devices that did not require the use of a sleeve further accelerated the acceptance of HALS in urology.

## Devices for hand-assisted laparoscopy

The first commercial HALS devices, such as the Pneumo Sleeve (Dexterity Surgical, Roswell, GA, USA) and the Intromit (Medtech Ltd., Dublin, Ireland), had sleeves that wrapped around the arm and were affixed to the abdomen with adhesive. The HandPort (Smith & Nephew, Andover, MA, USA) also had a sleeve, but the base was held on the abdomen with inflatable compression rather than adhesion. None of these devices remains in production. Lessons learned through their use, however, prompted the development of improved devices that did not require a separate sleeve.

There are two commercial devices for HALS currently available. The Gelport® (Applied Medical, Rancho Santa Margarita, CA, USA; Figure 85.1a) has two components that fit together on the abdomen, affixed by compression and providing gas occlusion with a gel that fits snugly around the surgeon's forearm. The Dextrus™ Access Port (Ethicon Endo-surgery, Cincinnati, OH, USA; Figure 85.1b) replaced the Lap Disc®, which was of similar design. It also has two components and is held within the abdominal incision by compression, but the gas occlusion is achieved with an iris valve that closes around the surgeon's forearm. A final second-generation device, the Omniport (Advanced Surgical Concepts, Wicklow, Ireland), was a cylinder that inflated to provide both abdominal fixation and gas occlusion; it is no longer manufactured.

### Gelport

The Gelport kit contains the Alexis® wound retractor, which is a pair of plastic rings connected by a flexible skirt that holds the abdominal incision open and provides the base for the second component, and the Gelseal® cap, which snaps onto the outer ring of the

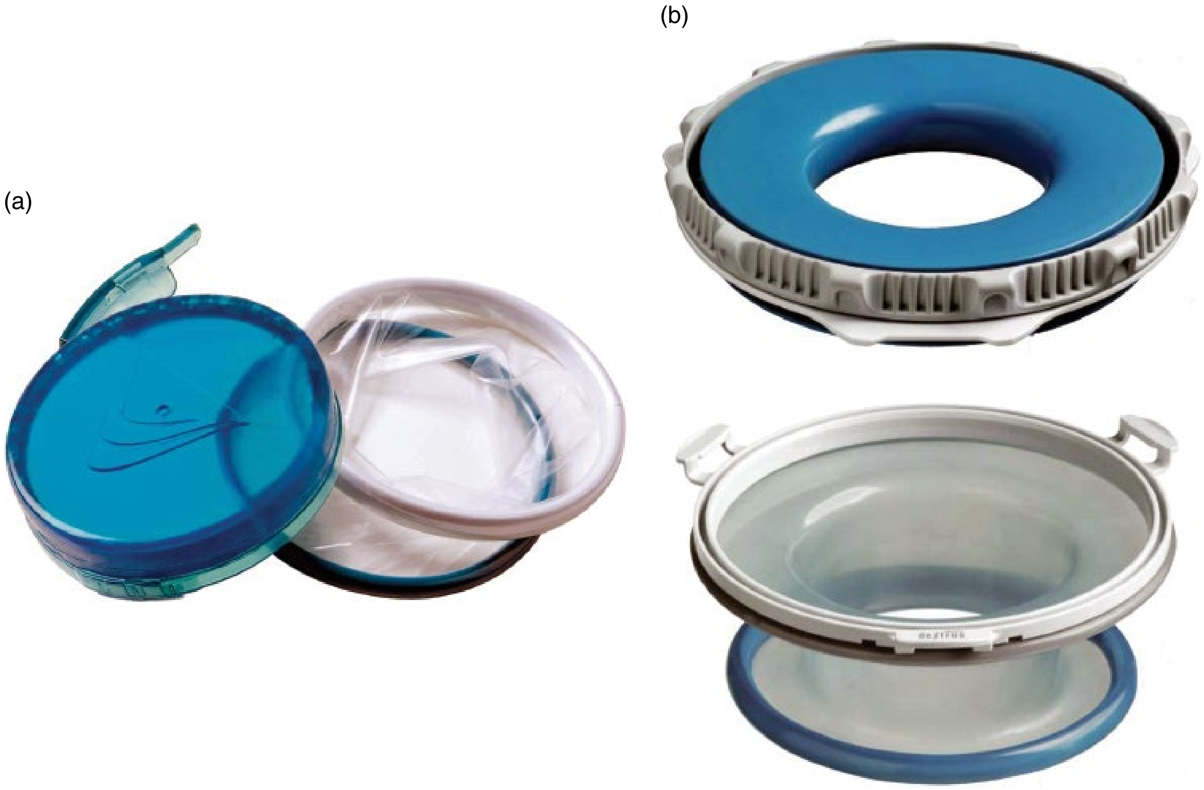

**Figure 85.1** (a) Gelport. *Source:* Applied Medical Resources Corporation, USA. Reproduced with permission of Applied Medical Resources, USA. (b) Dextrus Access Port. *Source:* Ethicon Endo-Surgery, Cincinnati, USA. Reproduced with permission of Ethicon Incorporated, USA.

wound retractor to provide a gas-tight seal through which a hand or laparoscopic ports can be placed. The abdominal incision is made initially, and then the flexible ring of the wound retractor is inserted into the abdomen, leaving the rigid ring outside (Figure 85.2). The outer ring is rotated inward to shorten the skirt and pull the rings tight against the abdominal wall. Once the gel cap is snapped onto the outer ring, the abdomen is gas tight (Figure 85.3). The gel expands enough to allow insertion of a hand through its central slit (Figure 85.4), but also will occlude the incision with nothing passing through it. In addition, ports can be passed through the central slit in the gel, or through a separate stab incision in the gel. An instrument can be passed through the gel alone, or when the hand is in place. See Video 85.1, which demonstrates use of the Gelport kit during a HALS nephrectomy.

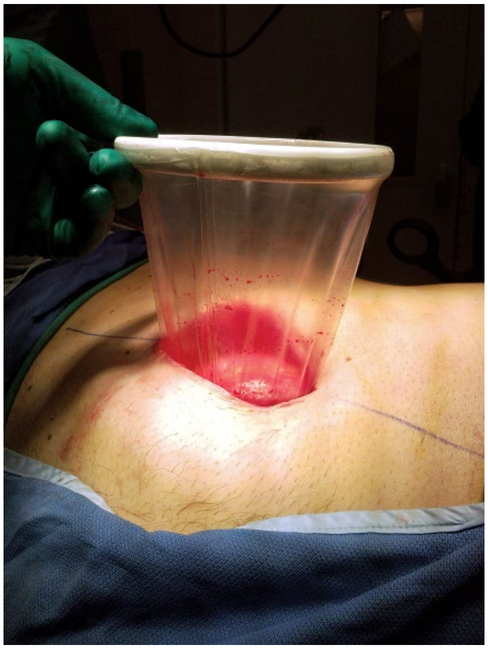

**Figure 85.2** Gelport kit: the flexible ring of the Alexis wound retractor is inserted into the abdomen, leaving the rigid ring outside.

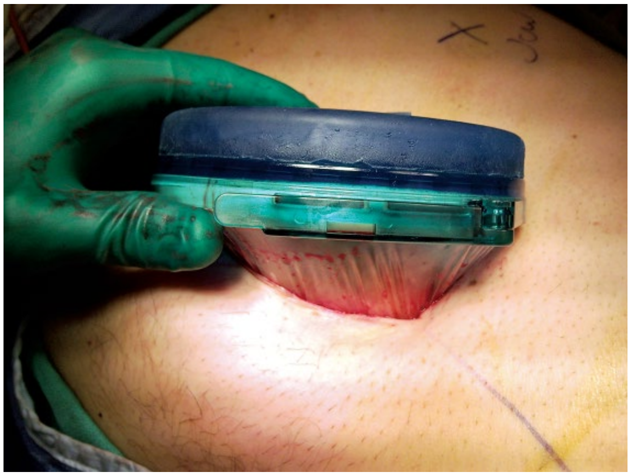

**Figure 85.3** Gelport kit: the gel cap has been attached and maintains pneumoperitoneum even without the hand through the device.

## Dextrus Access Port

The Dextrus Access Port is also a two-piece device. The base is a fixed-length wound retractor composed of an inner flexible ring and an outer rigid ring connected by an elastic skirt that holds the abdominal incision open and provides the base for the second component. The outer cap is a pair of locking rings that snap onto the base and close an iris valve to provide gas occlusion. The fixed-length wound retractor, which is available in three sizes to accommodate abdominal walls of varying thickness, is inserted into the abdominal incision by slipping the flexible inner ring inside the abdomen (Figure 85.5), with the tension from the elastic sheath holding the rigid outer ring stable on the abdominal wall. The outer cap is then snapped onto the wound retractor. For intra-abdominal use, the hand is inserted to the desired depth and the iris valve is tightened around the forearm by turning the outermost ring clockwise and fixing it in place by way of ratcheted teeth (Figure 85.6). Slight inward movements of the forearm can be made, but large movements require that the iris valve be opened a bit. Similarly, pulling back or removing the forearm necessitates tightening the valve to prevent gas leak. The valve can be completely occluded (Figure 85.7) or it can be tightened around a port or laparoscopic instrument.

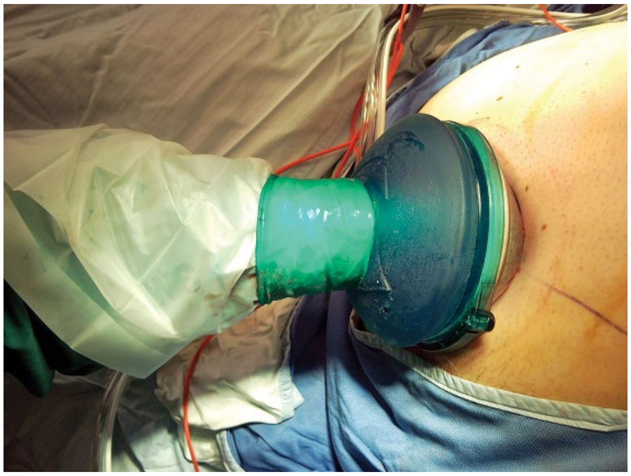

**Figure 85.4** Gelport kit: the intra-abdominal hand is inserted through the central slit of the gel cap.

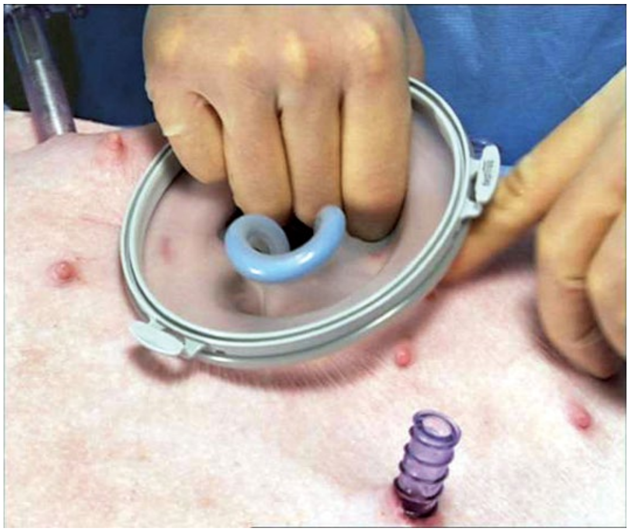

**Figure 85.5** Dextrus Access Port: the wound retractor is inserted into the abdominal incision by slipping the flexible inner ring inside the abdomen. *Source:* Ethicon Endo-Surgery, Cincinnati, USA. Reproduced with permission of Ethicon Incorporated, USA.

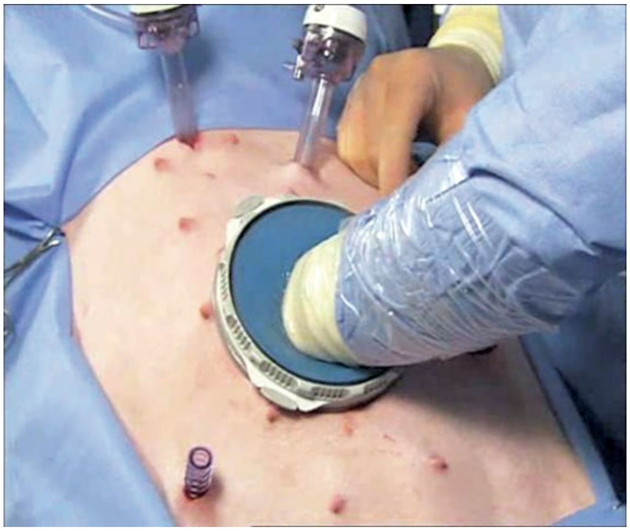

**Figure 85.6** Dextrus Access Port: the iris valve is tightened around the forearm to provide gas occlusion. *Source:* Ethicon Endo-Surgery, Cincinnati, USA. Reproduced with permission of Ethicon Incorporated, USA.

### Adjuncts

Fluid can sometimes track up the intra-abdominal forearm and soak through the surgeon's gown above the glove. Double gloving does not necessarily prevent this and some additional barrier is recommended. We have found the simplest and most effective to be a Steri-Drape™ Small Towel Drape 1000 (3 M Company, St. Paul, MN, USA). The adhesive strip is wrapped around the wrist and the rest of the drape trails down over the forearm, covered by a second glove over the hand and adhesive strip (Figure 85.4). The second glove should be dark to minimize glare. The Dextrus Access Port comes packaged with a plastic wrap that serves the same function. Other surgeons have overcome the fluid problem by using a disposable fluid-impervious gown.

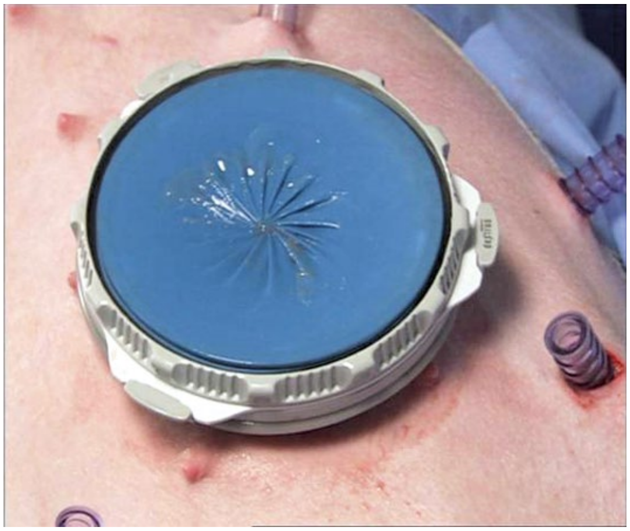

**Figure 85.7** Dextrus Access Port: the iris valve can be completely occluded. *Source:* Ethicon Endo-Surgery, Cincinnati, USA. Reproduced with permission of Ethicon Incorporated, USA.

Surgical instruments can be placed into the abdomen for use by the intra-abdominal hand. Small, open surgical instruments, including Atson forceps and short Satinsky clamps, have been used intra-abdominally during HALS. Of these, the most useful may be hand-held bulldog clamps for temporary vascular occlusion.

## General techniques for hand-assisted laparoscopy

### Choice of position for surgeon, HALS device, and ports

Although the application of HALS to retroperitoneoscopic surgery has been reported, it is not a widely performed technique. This section, pertaining to technique, will not address retroperitoneoscopic HALS, although the few reported series are included in the section on results. See Video 85.1, which demonstrates our technique for nephrectomy using HALS.

Either the primary or the assistant surgeon can use their hand intra-abdominally. When the primary surgeon's hand is intra-abdominal, direct manual dissection is possible. However, the primary surgeon then has only one hand free to manipulate a laparoscopic instrument. If the assistant's hand is in the abdomen, the primary surgeon can use two laparoscopic instruments and the intra-abdominal hand is used primarily for retraction. This distinction is important because it can alter port placement. Figure 85.8 indicates the most common HALS device and port arrangements for HALS renal surgery when the surgeon's hand is intra-abdominal. Figure 85.8a is the most typical arrangement for left-sided renal surgery by a right-handed surgeon. The nondominant (left) hand is placed through the HALS device in the periumbilical midline. This allows simultaneous retraction of bowel and finger dissection of the kidney. The assistant operates the videolaparoscope through a port at the level of the umbilicus, 1–2 cm lateral to the edge of the HALS device (**2** in Figure 85.8a), and an instrument placed through a lateral assisting port (**4** in Figure 85.8a). The surgeon's working port is placed 1–2 cm below the costal margin (**3** in Figure 85.8a), on the line that extends from the videolaparoscope port to the patient's ipsilateral shoulder. There is more variation for right-sided renal surgery by a right-handed surgeon. Some, including these authors, recommend an arrangement that is the mirror image of the left-sided procedure (Figure 85.8b). The right hand is used intra-abdominally, which allows retraction of the liver by the back of the hand while dissecting the kidney. The surgeon's left hand is used to manipulate laparoscopic instruments, which some right-handed surgeons find awkward. The ability to use either hand intra-abdominally is valuable, and if an "ambidextrous" approach is used when starting out with HALS, then it is quickly learned. Some portions of the procedure are facilitated by using a different hand in the abdomen, on either side, so it is helpful to be ready to use either hand intra-abdominally.

An alternative for right nephrectomy by a right-handed surgeon is depicted in Figure 85.8c. Here, the surgeon's left hand is placed through the HALS device and the right hand operates an instrument through the working port (**3** in Figure 85.8c). The assistant operates the videolaparoscope (**2**) and an assisting instrument (**4**). Some place the HALS device obliquely in the ipsilateral lower quadrant when using this approach. A number of HALS device placements have been described, including midline (supra-, peri-, and infra-umbilical), paramedian, subcostal, lower quadrant oblique ("muscle-splitting" Gibson incision), and transverse suprapubic (Pfannenstiel). Each will be associated with slightly different port placements, depending on whether the intra-abdominal hand is the surgeon's or assistant's, and whether the left or right hand is preferred. The general principles that guide device and port placement in HALS are: maximization of effectiveness of the hand, minimization of videolaparoscope obstruction by the hand, and centering the videolaparoscope between instruments rather than working with the hand and instruments all off to one side. Use of a 30° videolaparoscope is very useful during HALS to reduce obstruction of vision by the intra-abdominal hand.

## Tips and tricks

HALS facilitates transfer of skills from open surgery to laparoscopic surgery. Although this is an easier step to make than that from open surgery to standard (non-hand-assisted) laparoscopic surgery, HALS does require a distinct skill set. In this section, some techniques that are different from those used in open surgery and standard laparoscopic surgery are highlighted.

A laparoscopic port can be inserted through both the Gelport and the Dextrus Access Port, and the Gelport will accommodate several ports or a hand and additional ports. This allows inspection of the abdomen laparoscopically before secondary port placement. Ports can be inserted under direct visualization, or a hand can be placed through the HALS device and the ports can be inserted directly onto the intra-abdominal hand (Video 85.1). This maneuver should be performed only with noncutting trocars and only after visual inspection has confirmed the inner abdominal wall to be free of adhesions.

After placing the HALS device and ports, a laparotomy pad is placed into the abdomen. This can be used to soak up fluid and blood, either by itself (when it is not yet saturated) or by compressing it with the hand and using a laparoscopic aspirator to remove fluid through the pad. Some surgeons place a hemostat on the blue tag of the laparotomy pad to prevent its complete placement into the abdomen. We prefer to place the entire pad inside the abdomen to allow its unrestricted use, but we do cut off part of the blue tag and clamp it to the drapes as a visual reminder that a pad is inside the abdomen.

Performing multiple tasks simultaneously with the intra-abdominal hand takes greatest advantage of its presence. Retraction and exposure can be obtained in several directions at once, or the hand can simultaneously retract and dissect. One of the most useful multitasking hand positions is the "C" position (a term coined by Stephen E. Strup MD) for dissection medial to the lower pole of the kidney and at the renal hilum (Figure 85.9). Using the left hand for left renal surgery, or the right hand for right renal surgery, the forearm is placed parallel to the great vessels, palm lateral, wrist flexed 45–90°, index finger lifting the kidney, thumb exerting inferomedial traction on tissue, and the middle fingers extended. This position allows simultaneous retraction of bowel with the back of the hand, elevation of the lower pole, and dissection with the fingers. When the hand is elevating the lower pole, an irrigator–aspirator probe or some other instrument can be placed through an assisting port to help in the dissection.

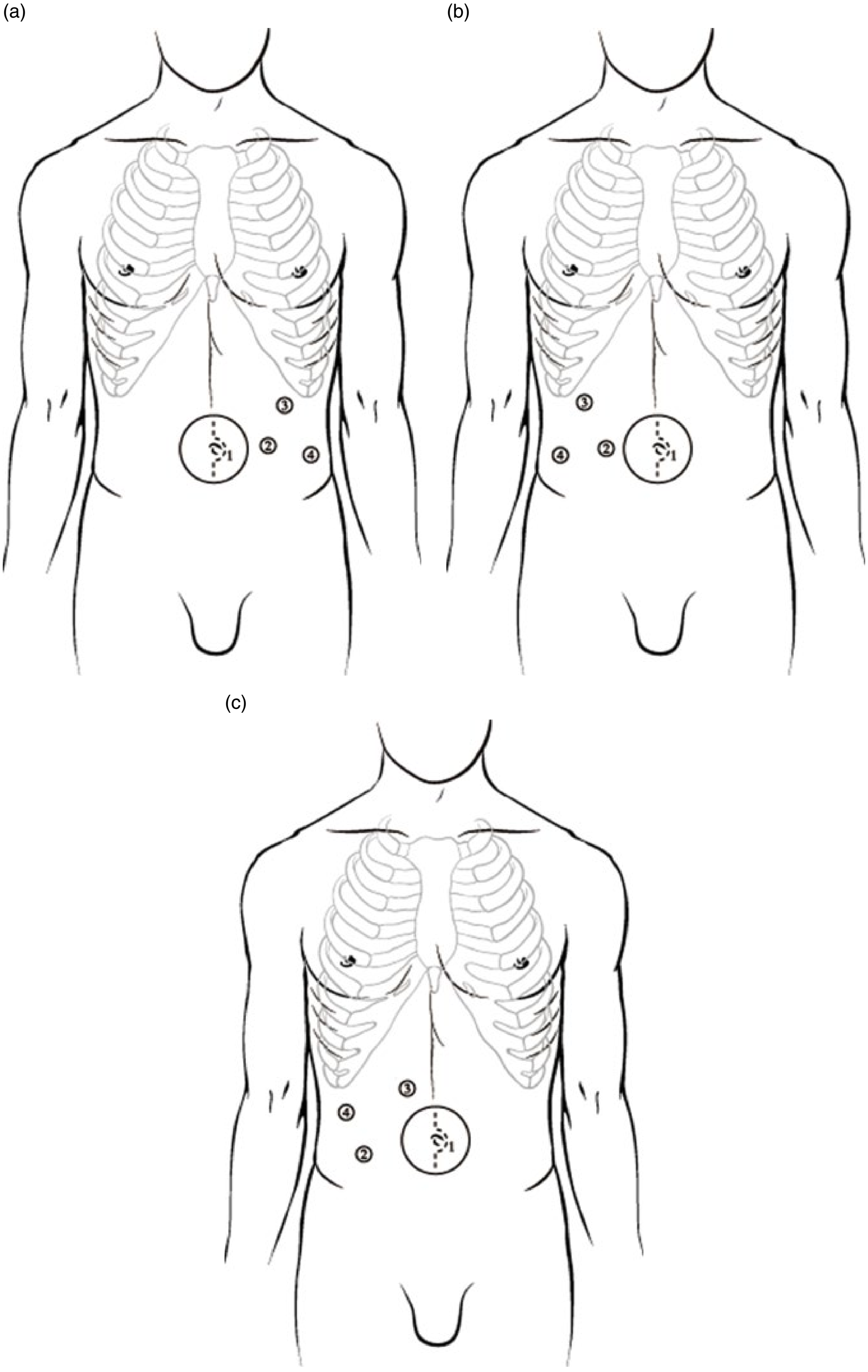

**Figure 85.8** (a) Typical port placement for left hand-assisted laparoscopic surgery (HALS) nephrectomy using the surgeon's left hand in the abdomen. (b) Mirror image, for right HALS nephrectomy using the surgeon's right hand in the abdomen. (c) One alternative for right HALS nephrectomy using the surgeon's left hand in the abdomen. 1, HALS device; 2, videolaparoscope port; 3, working port for surgeon; 4, assisting port.

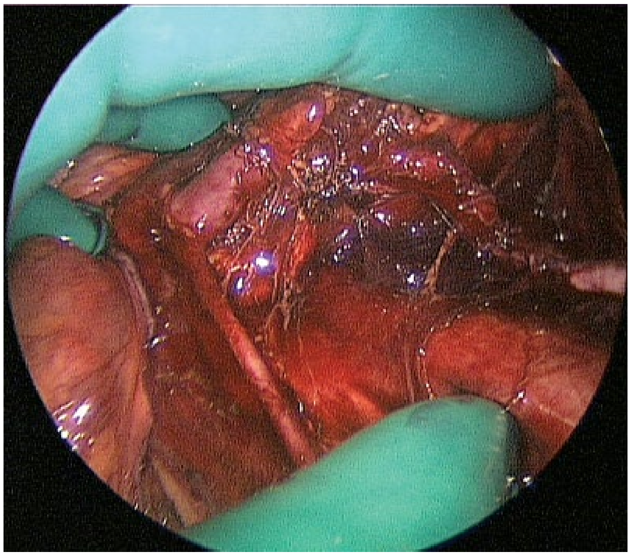

**Figure 85.9** The "C" position. Left hand placed through a midline HALS incision, for left nephrectomy.

When dissecting out the renal hilum, the renal artery and vein can be encircled en bloc with the thumb and forefinger of the intra-abdominal hand. After sharply dissecting tissue cephalad to the renal vein, it is usually easy to bluntly place the index finger cephalad to the renal vein, wiggle it in a posterior direction until the psoas muscle is touched, and then scoop inferiorly to gather up the entire renal hilum. This maneuver is safe as long as a careful touch is used, sensing resistance that indicates an early branch or an accessory vessel. Encircling the hilum in this way provides the ability to rapidly control it in case of vascular injury, and with this added confidence the subsequent hilar dissection can proceed rapidly. This maneuver is less useful if the intention is to remove the adrenal gland with the specimen (on the left side), as it is not safe to perform blunt dissection medial to the adrenal gland.

## Results of hand-assisted laparoscopic surgery

### Series

In urology, HALS is most commonly applied to nephrectomy. The first reported use of HALS in urology was for radical nephrectomy [4], as was the first use of a commercial HALS device in urology [8]. In one of the earliest large series of HALS for radical nephrectomy, Stifelman et al. [11] reported 95 HALS radical nephrectomies for large specimens. The mean operative time was 158 min and the major complication rate was only 4%, with a rate of conversion to open surgery of 3%. The oncologic efficacy of HALS radical nephrectomy has been confirmed in several series with long-term follow-up. Bandi et al. [12] reported 5-year recurrence-free survival of 90% after 65 HALS radical nephrectomies with more than 3-year follow-up. Harano et al. [13] reported a 4-year recurrence-free survival of 88% in a series of 96 patients. At the University of Michigan, the 5-year recurrence-free survival in a series of 108 patients with a mean tumor size of 6.9 cm was 82% [14]. Kawauchi et al. [15] reported a 5-year recurrence-free survival of 92% among 123 patients. Recently, Park et al. [16] provided updated follow-up of the largest series reported to date of HALS radical nephrectomy with long-term follow-up. Their multi-institutional series from 26 centers in Korea involving 197 patients demonstrated a 5-year recurrence-free survival of 95% with a median follow-up of 69 months.

There have been 21 series (containing 10 or more patients) of HALS nephroureterectomy for upper tract urothelial neoplasms (not including series that have been updated by subsequent ones) published through 2015 [17–37]. In the total of 832 patients described in these series, the operative time averaged 253 min, with 7% major and 13% minor complication rates overall (when reported). Conversion to open surgery was required in only 2.1% of cases. The nonvesical recurrence rate was 13% with 24-month mean follow-up. A description of the long-term outcome of HALS nephroureterectomy for urothelial carcinoma from the University of Michigan includes 62 patients with a median follow-up of 77 months: the 5-year cancer-specific survival was 89% for low-grade disease and 72% for high-grade disease [38].

Many of the recently reported series of donor nephrectomy have been with HALS. Among the 14 such series containing 100 or more patients, reporting 2850 patients in total, the mean operative time was 174 min and the mean warm ischemia time 2.7 min [39–52]. The minor and major complication rates were 7.2% and 3.0%, respectively, with a conversion to open surgery in only 0.8% of patients. In the studies that reported convalescence, the mean time to return to nonstrenuous activity levels was 24 days. In the largest series to date, Rajab and Pelletier [53] reported long-term follow-up of nearly 1500 patients. Of patients, only 0.9% experienced graft loss within one month of transplant. A total of 1.4% of patients developed delayed graft function with subsequent recovery of function. 10-year death-censored graft survival was approximately 80%. Of the first 200 HALS donor nephrectomies performed at the University of Michigan, the 1-month, 1-year, and 3-year actuarial graft survival rates are 97%, 95%, and 94%, respectively [42]. On review of 480 consecutive cases of HALS donor nephrectomy, Gabr et al. [54] reported a ureteral complication rate of 3.7%, and noted that ureteral complications were associated with increased donor age and the lack of ureteral stent placement at the time of transplant.

Other reports of HALS for renal surgery include partial nephrectomy [55–59], heminephrectomy (horseshoe kidneys, duplicated upper tracts, etc.) [60–63], bilateral nephrectomy [64–72], and bilateral partial nephrectomy [73]. Bilateral nephrectomy for autosomal dominant polycystic kidney disease is particularly challenging with standard laparoscopic techniques, and is perfectly suited to HALS. Other difficult maneuvers, such as radical nephrectomy with associated excision of renal vein or vena caval thrombus [74–79], and removal of kidneys with xanthogranulomatous pyelonephritis or other inflammatory or unusual conditions [76, 80–85], are facilitated by HALS.

HALS in urology is most commonly applied to renal surgery, but there have been reports of its use for other organs as well. Similar to its use for bilateral nephrectomy, HALS facilitates multiorgan removal for other entities [86–89]. Laparoscopic adrenalectomy is usually well-performed with standard transperitoneal or retroperitoneoscopic techniques, but in cases of large specimens or as an alternative to conversion to open surgery, HALS does have a role in the management of adrenal disease [90–94]. Minimally invasive cystectomy is growing in popularity. Even when using standard or robot-assisted techniques, many surgeons prefer to create at least part of the urinary diversion via a mini-laparotomy. Given this, several groups have reported using this mini-laparotomy incision for a HALS device, and performing the cystectomy or pelvic exenteration with HALS techniques [95–100]. HALS for other procedures, such as ureterolysis [101], retroperitoneal lymph node dissection [102], and resection of local renal cell carcinoma recurrences [103], has been described.

## Comparisons to other techniques

Although HALS has been reported via the retroperitoneoscopic route for renal surgery [20, 28, 31–33, 104–111], this is not a commonly performed technique. Because of this, when assessing the role of HALS in urologic laparoscopy, this chapter considers it to be a transperitoneal approach. Transperitoneal HALS, standard transperitoneal laparoscopy, and standard retroperitoneoscopy all have advantages and disadvantages. In this section, comparisons between the techniques are presented.

Wolf et al. [112] reported the initial comparison of hand-assisted and standard transperitoneal laparoscopic nephrectomy in 1998, using the first hand-assisted ($n = 13$) and standard ($n = 8$) transperitoneal laparoscopic nephrectomies performed at the University of Michigan and the University of Wisconsin. The mean operative time for hand assistance was 90 min shorter than that for standard laparoscopy. This comparison suggests that early in a surgeon's experience, HALS "shortens the learning curve" for transperitoneal nephrectomy. A subsequent report from the University of Michigan made the same comparison after more experience had been gained, and revealed that after an experience of approximately 20 laparoscopic radical nephrectomies, the advantage of HALS over standard laparoscopy in terms of operative time fell to only 30 min [113].

A recent meta-analysis of studies comparing HALS to open and standard laparoscopic approaches for urologic procedures produced similar results to previous publications [114]. This meta-analysis reviewed 62 studies of donor nephrectomy [30], radical nephrectomy [21], and nephroureterectomy [14], which totaled 5446 patients. For donor nephrectomy, HALS was associated with less intraoperative blood loss when compared with open and standard laparoscopic approaches. Length of stay was shorter compared to the open cohort, while operative and warm ischemia times were shorter compared to the standard laparoscopic group. Yuan et al. [115] limited their meta-analysis to donor nephrectomy and included 4 additional years of studies with over 2000 patients total, and found similar results. They noted no increase in donor complications or recipient graft function.

In a randomized trial of HALS versus standard donor nephrectomy (20 in each group), Bargman et al. [116] found that operative time was significantly less with the standard approach (219 vs. 200 min, $P = 0.02$), but that there were no differences in estimated blood loss, warm ischemia time, length of postoperative stay, analgesic use, rate of complications, pain scores on postoperative days 1 and 2, or quality-of-life scores at 1 and 3 months. Of note, all nephrectomies in this series were performed by a surgeon with extensive experience in both HALS and standard laparoscopy, including more than 100 laparoscopic donor nephrectomies and more than 500 other laparoscopic renal operations prior to the study period. This is consistent with the data reported above; with experience, some advantages of HALS over standard laparoscopy (such as reduced operative time) diminish.

There have been two prospective trials involving HALS for radical nephrectomy. Nadler et al. [117] in a comparison of standard transperitoneal, standard retroperitoneal, and HALS (11 in each group; not randomized but prospectively enrolled in alternating fashion) found that operative time was significantly lower in the HALS group, and that hospital stay and time to normal daily activity were significantly shorter in the standard transperitoneal group. Intraoperative blood loss, postoperative narcotic use, and time to oral intake were similar in all three groups. Although there were no differences in early complications, incisional hernias occurred only in the HALS group. In a multi-institutional randomized trial comparing HALS (9 patients) versus standard transperitoneal laparoscopic

(12 patients) radical nephrectomy, Venkatesh et al. [118] found no differences in operative time. Although the meta-analysis by Wadström et al. [114] was not able to compare HALS to standard laparoscopy because of a limited number of studies, they did report improved blood loss and length of stay with HALS when compared to open radical nephrectomy.

As noted above, series of surgeons' early experience with standard laparoscopic and HALS nephrectomy often suggest a lower complication rate with HALS [112, 119], but as experience is gained the overall complication rates of the two approaches become similar. However, the intra-abdominal hand does appear to reduce some specific complications, in particular the need to convert to open surgery. Silberstein and Parsons found this in their meta-analysis [120]. At the University of Michigan, 196 standard laparoscopic radical nephrectomies were compared with 154 HALS radical nephrectomies [121]. There were no conversions to open surgery from HALS but conversion to open surgery occurred in the standard laparoscopic group in 0.8% of nonobese, 3.0% of obese, and 17% of morbidly obese patients. The difference was statistically significant in the latter two groups. In addition, the availability of HALS provides an alternative to conversion from standard laparoscopy to open surgery; converting to HALS from standard laparoscopy may allow the procedure to be completed in a minimally invasive fashion [122, 123].

Conversely, some complications appear to occur more commonly in association with HALS than with standard laparoscopy. Troxel and Das [124] noted a 6% rate of incisional herniation at the HALS site in a series of 50 HALS radical nephrectomies. Terranova et al. [125] reviewed 54 patients undergoing HALS renal surgery, and reported complications related to the HALS incision in 9.3%, including infection, herniation, skin incisional breakdown, fascial dehiscence, and enterocutaneous fistula. Montgomery et al. [126] reviewed 424 consecutive HALS renal procedures and reported similar findings, including infection in 6.8%, incisional hernia in 3.5%, and fascial dehiscence in 0.5% of HALS incisions. Although direct comparative data are limited, some reports suggest an increased wound complication rate with HALS compared to standard laparoscopy. Overall, wound infections and hernias appear to occur less frequently in association with HALS than with open surgery, but more often than in association with standard laparoscopy. In one literature compilation which included 56 reports, there was a significantly greater wound complication rate associated with HALS compared to standard laparoscopy (1.9% vs. 0.2%, $P < 0.05$) [127].

Data comparing the duration and intensity of convalescence after HALS compared to standard laparoscopy are less consistently reported than more objective outcomes, and are subject to bias in retrospective studies. In both of the prospective trials involving HALS for radical nephrectomy described above, there was some measure of a longer and/or more intense recovery period in the HALS patients. Nadler et al. [117] found the hospital stay to be 2.1 days after standard transperitoneal laparoscopy compared to 3.4 days after HALS radical nephrectomy. Narcotic use tended to be less in the former group, but the difference was not significantly different. In their multi-institutional randomized trial comparing standard transperitoneal laparoscopic and HALS radical nephrectomy, Venkatesh et al. [118] found a significantly longer time to return to normal activity and to work in the HALS group, although there were no differences in hospital stay or narcotic use. In a retrospective but large comparison of the two approaches to radical nephrectomy (113 standard laparoscopic, 158 HALS), Matin et al. [128] found longer hospital stay (4 vs. 2 days) and more narcotic use in the HALS group. In another retrospective but large study (147 standard laparoscopic and 108 HALS), Gabr et al. [121] found that hospital stay was longer (by a mean of 0.4 days) and time to return to nonstrenuous activity was greater (by a mean of 3.1 days) in the HALS group.

In addition to patient-related outcomes, HALS appears to have a distinctive surgeon-related impact. Johnston et al. [129], describing a survey of 25 urologists involved in lapararoscopic fellowship programs, reported that HALS was associated with significantly more hand/wrist, forearm, and shoulder pain compared to standard laparoscopy. Conversely, there was significantly more neck pain associated with standard laparoscopy. There was no significant difference between the approaches in terms of lower back pain. Gofrit et al. [130] found similar results in a survey of 73 members of the Endourology Society. HALS was associated with more pain involving the fingers, hand/wrist, and forearm/elbow than standard laparoscopy, while standard laparoscopy was associated with more complaints about neck pain. There were no major differences with regards to shoulder, upper back, and lower back pain. This survey also included questions about robotic surgery. Overall, robotic surgery was associated with the fewest complaints of pain and HALS was associated with the most. The work of Ost et al. [131] suggests one possible mechanism for the increased hand, wrist, and forearm pain with HALS. These investigators used oxygen sensors to measure oxygen saturation in the hand during HALS nephrectomy, and found that a report of hand pain during HALS nephrectomy was associated with hypoxia of the hand, down to 56–88% local oxygen saturation.

Overall, then, published data suggest that HALS is generally faster than standard transperitoneal laparoscopy, but that the difference decreases with increasing surgeon experience. The relative impact of HALS on operative time also appears to vary with the specific procedure. For advanced procedures, HALS appears to reduce the likelihood of conversion to open surgery, and converting to HALS is a good alternative to converting to open surgery when standard laparoscopy cannot be continued. There are important disadvantages of HALS to be acknowledged. The larger incision for HALS is associated with rates of infection and herniation that probably exceed those for standard laparoscopy. The intensity and duration of postsurgical recovery is slightly greater with HALS compared to standard laparoscopy, although the magnitude of the difference between HALS and standard laparoscopy is much less than that between HALS and open surgery. Finally, the surgeon pays a price during HALS in terms of increased upper extremity pain compared to standard or robot-assisted laparoscopy.

## Selective use of hand-assisted laparoscopic surgery

The advantages and disadvantages of HALS are listed in Box 85.1. The relative impact of these considerations differs according to surgeon and procedure. The general situations in which HALS is most useful are listed in Box 85.2. HALS is an excellent choice when intact specimen removal is required, as it takes advantage of the required incision throughout the entire procedure rather than just at the conclusion. Another major consideration is surgeon experience, with laparoscopy in general or with a new procedure. HALS is an excellent way for an inexperienced surgeon to start performing laparoscopy, or for an experienced surgeon to start performing a new procedure. Similarly, a difficult procedure is a good indication for HALS. Large specimens, reoperation, a perihilar mass, or anytime the surgical planes or tissue identification are indistinct can result in a prolonged and complication-prone laparoscopic procedure. HALS can make the difference between conversion to open surgery and completion of the minimally invasive procedure. Finally, for a patient with severe chronic obstructive pulmonary disease or congestive heart failure, in whom a rapid procedure is necessary because of problems owing to hypercapnia or elevated intra-abdominal pressure, HALS can be very useful.

With these considerations in mind, HALS is best selected when there is a clear advantage (in terms of operative time, safety, specimen manipulation, etc.) over standard laparoscopic techniques. The balance between the advantages and disadvantages of HALS is best determined by the individual surgeon and patient using shared decision-making. The best procedures for HALS are advanced extirpative renal procedures. For radical nephrectomy, HALS has most advantage when the specimen is large or the anatomy is difficult. For partial nephrectomy, HALS might facilitate accurate resection, collecting system repair, and/or hemostasis for tumors that are hard to access. For straightforward radical nephrectomies, and for partial nephrectomy for accessible tumors, standard transperitoneal or retroperitoneal techniques are effective in the hands of many. During procedures where intact specimen removal is required, such as nephroureterectomy for urothelial carcinoma or live donor nephrectomy, HALS takes advantage of the required incision throughout the entire procedure rather than just at the conclusion.

For some procedures HALS is less useful, or may even be a hindrance. Laparoscopic simple nephrectomy can be

**Box 85.1 Advantages and disadvantages of hand-assisted laparoscopic surgery compared to standard laparoscopy.**

### Typical advantages

- Faster
- Easier
- More control in operating room by surgeon
- Better control of vascular injury
- Reduced need for conversion to open surgery
- Enhanced teaching

### Typical disadvantages

- Larger incision
- Sometimes necessitates suboptimal port placement
- Hand can get in the way
- Increased wound complication rate
- Slightly greater intensity and duration of convalescence
- More upper extremity pain for surgeon

**Box 85.2 General situations in which hand assistance is most useful.**

- Intact specimen removal is required
- Limited experience:
  - With laparoscopy in general
  - With specific procedure
- Difficult procedure
  - Large specimen
  - Reoperation
  - Perihilar mass that limits access to vasculature
  - Other processes (inflammation, fibrosis, etc.) that render dissection difficult
- Medical comorbidities necessitate rapid procedure

performed in a straightforward manner with standard transperitoneal or retroperitoneal techniques unless the specimen is inflamed (e.g. pyonephrosis or xanthogranulomatous pyelonephritis) or very large (e.g. autosomal dominant polycystic kidney disease). Standard laparoscopic techniques are also adequate for renal cyst resection and adrenalectomy in most cases. For reconstructive procedures such as laparoscopic pyeloplasty or nephropexy, there is little advantage to HALS. Although there has been some interest in HALS for pelvic procedures, most urologists use a standard or robot-assisted laparoscopic approach to minimally invasive pelvic surgery.

## Conclusions

HALS is technically easier than standard laparoscopy, with a "shorter learning curve" for most procedures. The current devices are easily applied and effective. Although there is considerable variation in port placement, especially with regard to right nephrectomy for right-handed surgeons, the general techniques are standardized. Unless there is extensive laparoscopic experience, HALS offers more rapid operating times and a tendency toward lower need for conversion to open surgery than standard laparoscopy for most extirpative renal procedures. These advantages come at the price to the patient of slightly greater intensity and duration of convalescence, and an increased wound complication rate, compared to standard laparoscopy. The surgeon is at greater risk of suffering upper extremity pain. Given prior experience, HALS offers minimal if any improvement over standard laparoscopy for straightforward renal procedures, reconstructive procedures, and most pelvic procedures. HALS is most useful for difficult extirpative laparoscopic procedures, and when intact extraction is desired.

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# 86

# Laparoscopic Exit: Specimen Removal, Closure, and Drainage

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## Introduction

Laparoscopic techniques (standard and robot-assisted) have revolutionized the field of urologic surgery over the past quarter century and have established their role in the management of the entire spectrum of benign and malignant urologic diseases [1–3]. A growing body of evidence has demonstrated that these minimally invasive techniques allow quicker postoperative recovery for patients, ultimately improving their quality of life. On the other hand, the spread of laparoscopic techniques has resulted in unique complications specifically associated with their implementation [4–6]. Most urologic laparoscopic procedures are performed via the transperitoneal approach. However, the laparoscopic retroperitoneal access follows the same principles to exit the surgical field safely.

This chapter focuses on the technique and instrumentation needed to safely and effectively accomplish the final step of any laparoscopic or robotic urologic procedure, which has been referred to as "laparoscopic exit" [7]. This step can be divided into three key segments, each one important and each with specific challenges related to the unique conditions under which laparoscopy is conducted: specimen retrieval, incision closure, and drainage. Any shortcuts have a strong potential to convert a straightforward case into a formidable venture with unintended postoperative complications such as delayed bleeding, dehiscence, or a postoperative hernia, increasing patient morbidity.

The "laparoscopic exit" should follow a systematic, step-by-step approach (Figure 86.1) as described in the following sections.

## Specimen retrieval

Entrapment and extraction of surgical specimens are important steps that require specific laparoscopic skills and knowledge. Previous familiarity with materials and devices used during this step and knowledge of the specimen dimensions will ensure the safe removal of the surgical specimen, especially during oncological surgery to prevent tumor seeding in the extraction site [8, 9]. The retrieval site must be planned to optimize the cosmetic and pain-related outcomes.

### Retrieval devices

#### Commercially available devices

A wide variety of single-use retrieval devices are commercially available. All these devices feature sac permeability, resistance, stability, and easy handling. However, each one has specific characteristics, and the use of one over the others is mainly dictated by surgeon's preference as well as availability. These devices come in different sizes (5–15 mm), and the use of one size depends on the size of the specimen to be retrieved. In urology, a 10 mm bag is usually suitable for the laparoscopic partial nephrectomy, radical prostatectomy, adrenalectomy, or lymphadenectomy, whereas a larger 15 mm bag is needed for larger specimens retrieved during radical cystectomy or radical nephrectomy.

Retrieval devices can be divided into two categories:

- *Pure sacs* (Table 86.1) are primarily made of polyurethane and their closure involves a purse-string mechanism. Examples of this category include LapSac™, SimplyStrong™, Endobag™, and Trapbag™.

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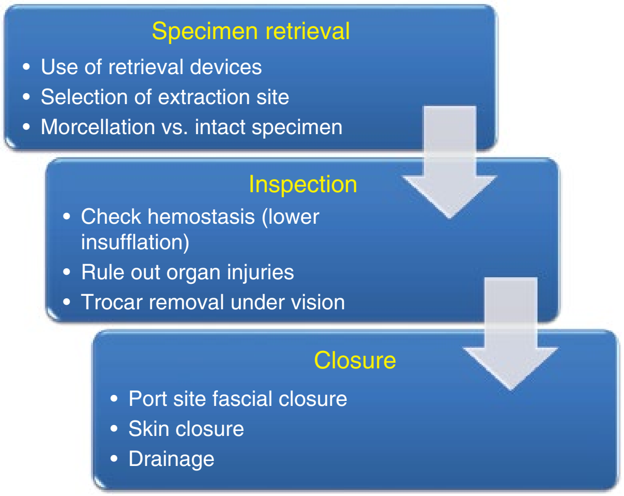
Specimen retrieval
• Use of retrieval devices
• Selection of extraction site
• Morcellation vs. intact specimen
Inspection
• Check hemostasis (lower insufflation)
• Rule out organ injuries
• Trocar removal under vision
Closure
• Port site fascial closure
• Skin closure
• Drainage

**Figure 86.1** Exit strategy in laparoscopic and robotic procedures: a step-by-step systematic approach.

**Table 86.1** Laparoscopic entrapment devices: simple bags.

| Name | Description |
|---|---|
| SimplyStrong™ (Genicon, Winter Park, FL, USA) | Nylon with polymer coating; monofilament cinch string without introducer; grab points to extract bag; radiopaque thread |
| Endobag™ (Covidien/ Medtronic) | 5 in × 8 in; supplied in a dispensing tube; 10–12 mm trocar |
| TrapBag™ (Karl Storz, Tuttlingen, Germany) | Transparent; insertion through a pusher; memory wire; self-opening; “fish trap” patented system |
| LapSac™ (Cook Medical, Bloomington, IN, USA) | Reinforced nylon with integral polyurethane inner coating and polypropylene drawstring; 10–12 mm trocar; not self-opening |

- *Sacs with plunger and opening/closing system* consist of a bag collapsed into a cylindrical tube (plunger) that is introduced through the trocar, allowing the deployment of the bag via an opening system. A purse-string mechanism allows the bag to close (Table 86.2). Examples of this category include GeniStrong™, Endopouch™, TRS™, Inzii™, and Endo Catch™.

Pure sacs were commonly used before the advent of devices with a plunger and pouches with mouth opening deployment capability. Placement of retrieval bags with plungers must be done under direct visualization to avoid injuries to the abdominal organs, ensure adequate opening of the bag, and verify complete entrapment of the surgical specimen with closure of the bag to prevent spillage or partial removal of the specimen.

**Table 86.2** Laparoscopic entrapment devices: bags with closing/opening system.

| Name | Description |
|---|---|
| GeniStrong™ (Genicon) | Nylon with polymer coating; transparent introducer; preloaded spring automatically opens bag upon deployment; flexible metal ring holding bag mouth open for specimen loading; in different sizes: small and medium for 10 mm trocar; large for 12 mm trocar; XL for 15 mm trocar; rigid plastic shaft for stability; indicator for bag orientation; radiopaque thread |
| Endopouch™ retriever (Ethicon) | One-handed deployment, bag opening maintained by a metallic ring, string with a slip knot enables closing the bag; 10 mm diameter; 4 in × 6 in size |
| Anchor Tissue Retrieval System™ (ConMed Corp., Utica, NY, USA) | Nylon material; automatic opening; different sizes for 10–15 mm trocars; multiple use in single patient |
| Inzii™ Retrieval System (Applied Medical, Rancho Santa Margarita, CA, USA) | Also in 5 mm size; allows multiple uses in a single patients |
| Endo Catch™ (Covidien/Medtronic) | 10 mm or 15 mm; polyurethane pouch |

### Homemade (low-cost) devices

Alternative “low-cost” solutions have been described to minimize costs, such as the use of sterile gloves and other materials, but the safety and efficiency of these devices have not been tested to ascertain industry guidelines and quality assurance [10].

## Morcellation

Morcellation is the mechanical fragmentation of an (entrapped) specimen into smaller pieces using a manual or morcellator technique. It is used to minimize the extraction site incision, optimizing cosmetic and pain-related outcomes.

Morcellation has been closely scrutinized in gynecology due to the risk of bag perforation and bowel injuries [11]. The other concern relates to the challenges faced by the pathologist in accurately staging and defining the surgical margins. The use of morcellation in urology has been limited and is mainly restricted to laparoscopic benign cases; it is performed under laparoscopic visualization. Furthermore, no advantage of morcellation (over intact specimen extraction) could be found in studies looking at postoperative recovery, wound-related complications, and surgery-related quality of life [12, 13].

### Extraction site: where and how?

Extraction of the intact specimen can be accomplished through different sites depending on the size of the specimen. Small specimens (prostate, lymph nodes, or adrenal gland) can be easily removed by extending a trocar site.

A larger specimen can present a more challenging scenario to the laparoscopic surgeon during procedures such as a radical nephrectomy. In this case, different access options can be considered (Figure 86.2):

- Port site extension or connecting two port site incisions (paramedian or lower quadrant)
- Umbilical
- Pfannenstiel incision
- Incising a previous abdominal scar
- Natural orifice (vaginal or rectum) extraction.

Factors to consider when choosing between these options are the patient's preference, the surgeon's experience, cosmetic result, and risk of related complications.

Many surgeons prefer an umbilical or periumbilical incision due to familiarity with the midline abdominal wall anatomy. In this case, the incision is made through the umbilical scar to optimize the cosmetic outcome. This method has been popularized with the recent adoption of laparoendoscopic single-site (LESS) surgery, where the entire procedure can be performed through a periumbilical incision [14].

Several investigators have reported the risk of complications associated with the extraction sites. Elashry et al. found a higher risk of hernia when using lower flank port connecting incision for specimen removal and suggested a midline or subcostal incision instead, especially when other risk factors (such as obesity) are present [15]. Bird et al. compared three different sites (umbilical, paramedian, and lower quadrant) and found that incisional hernias were more likely to occur in patients with high body mass index and/or paramedian extraction site [16].

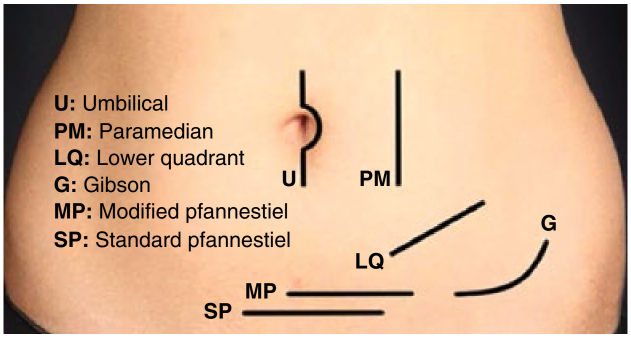

**Figure 86.2** Extraction sites for laparoscopic nephrectomy/nephrouretcerectomy.

The use of a Pfannenstiel incision after laparoscopic nephrectomy has been associated with potential advantages of better cosmesis and reduced pain [17]. During a transperitoneal laparoscopic nephrectomy, a Pfannenstiel incision can be used [18]. A skin incision is made about two fingerbreadths above the pubic symphysis. Instead of incising all the planes transversally along the same plane as originally described [18], just the skin can be incised transversally while the fascia is incised vertically, and the rectus muscles can be spread to enter the peritoneal cavity; this incision has been adopted for laparoscopic donor nephrectomy [19]. In the case of retroperitoneal nephrectomy, a "modified" Pfannenstiel incision can be used where the skin incision is biased toward the side of the nephrectomy, and after the anterior rectus fascia is exposed, a paramedian incision is made medial to the lateral border of the rectus muscle [20]. Then, after perforating the transversalis fascia, the Retzius (retroperitoneal) space is entered, and blunt finger dissection is used to gain access to the upper retroperitoneum [20]. In cases where this cannot be used (such as the presence of prior suprapubic incisions or in morbidly obese patients), a muscle-splitting extraperitoneal Gibson incision can be used [21]. The Pfannenstiel incision has also been described for LESS surgery [22]. Surgeons should be aware of the risk of ilioinguinal and iliohypogastric neuropathy with lower abdominal incisions [23].

In some female patients the transvaginal route can be performed by a laparoscopic transverse colpotomy made at the posterior fornix. After the specimen is extracted via the vagina, the posterior colpotomy is repaired transvaginally. The authors pointed out that vaginal extraction is indicated in patients with an intact uterus and a surgically unoperated pelvis where vaginal adhesions are not present [24, 25]. Vaginal extraction is not indicated (because of size concerns) for younger nulliparous females, those with atrophic vaginitis, vaginal infection, or when the specimen is too large. More recently, the transvaginal route has gained momentum with the introduction of natural orifice transluminal endoscopic surgery (NOTES) [26].

## Inspection

After completion of the laparoscopic procedure, careful examination of the surgical field is mandatory to rule out inadvertent injury to adjacent organs and to check the hemostasis. Intuitively, this is a fundamental step to minimize the risk of unrecognized intraoperative complications that can lead to significantly increased surgical morbidity, requiring more challenging management in the postoperative period.

Inadvertent organ injury can happen not only during the procedure itself but also very early when laparoscopic access is gained [27]. This more commonly occurs in special situations, such as when extensive adhesiolysis is needed [28]. Depending on the anatomical region where the surgery is performed, key structures need to be inspected. For right-sided renal procedures, the liver and duodenum should be examined and for left-sided procedures, the spleen and distal pancreas are frequently mobilized and retracted to access the kidney via transperitoneal laparoscopic approach [29, 30]. Diaphragmatic injuries can happen during dissection of the upper pole of the kidney but often changes in ventilation and oxygenation are observed requiring immediate action [31]. For pelvic procedures, attention should be paid to the small bowel, sigmoid colon, nerves, and vascular structures [32].

Careful inspection is also required to identify unrecognized bleeding, which can be tricky in the conditions under which laparoscopy is performed (i.e. with pneumoperitoneum). Although arterial bleeding is usually evident and easier to recognize, venous bleeding may be masked by abdominal pressure (~15 mmHg) during the laparoscopic procedure. Therefore, a key step of the “laparoscopic exit” is to lower the insufflation pressure to a minimum (<5 mmHg) and ensure proper hemostasis. In case of extraction of larger specimens requiring an extended incision, we recommend that the trocar site fascia defects should have a preplaced port site defect suture using a fascia closure device.

### Trocar removal

Trocars should always be removed under direct vision because inadvertent bleeding from the trocar sites can go unrecognized and create postoperative complications [33]. A bleeding trocar site should be managed by temporary tamponade with the trocar until the surgeon is ready to place a fascia suture to control the bleeding as described later in this chapter [34]. Bleeding at a trocar site can be challenging, especially in cases of morbidly obese patients where there is a thick subcutaneous layer. If the bleeding cannot be controlled endoscopically, the skin incision can be extended to have better exposure, identify the source of bleeding, and obtain proper control. A Foley catheter can also be introduced into the trocar site and used as a temporary pressure device by inflating the balloon to compress the vessel [35].

The last trocar to be removed should be the 10–12 mm trocar, leaving the optics inside the trocar without the valve cap so that insufflation gas and pressure can be removed from the intraperitoneal cavity with the assistance of the anesthesiologist (positive pressure with the ventilator). Then the trocar can be withdrawn while the fascia suture is pulled and the scope is removed, avoiding bowel herniation and entrapment.

## Port site fascial closure

Trocar site closure is performed to prevent possible port site hernias [36]. Shalhav et al. compared fascial nonclosure after using radially dilating trocars versus fascial closure after using cutting trocars and found no hernias after a mean follow-up of about five months [37]. Other investigators reported that ports <10 mm (8 mm robotic ports, 5 mm ports, and 3 mm mini-laparoscopic ports) do not require routine closure since the risk of hernia is minimal [38]. Nevertheless, case reports of herniation occurring even in 5 mm ports have been reported [39].

A variety of techniques and devices, either disposable (Figure 86.3) or reusable (Figure 86.4), have been used to obtain port site fascial closure. Maintenance of the pneumoperitoneum is of utmost importance to facilitate this step as it allows a safe distance to be kept between the abdominal wall and intra-abdominal viscera while endoscopic view can assist the closure [40].

In general, three different techniques can be used (Figure 86.5): intracorporeal manipulation under direct endoscopic vision, extracorporeal manipulation under direct endoscopic vision, and closure without direct endoscopic control. The use of one method over the other depends on surgeon’s preference and experience.

### Intracorporeal closure

Intracorporeal closure techniques have the advantage of maximizing safety by avoiding the risk of visceral injuries because they are performed under direct endoscopic

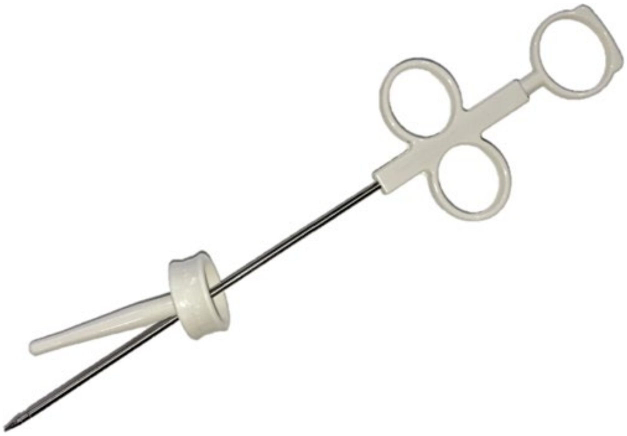

**Figure 86.3** Carter–Thomason laparoscopic port closure device: disposable.

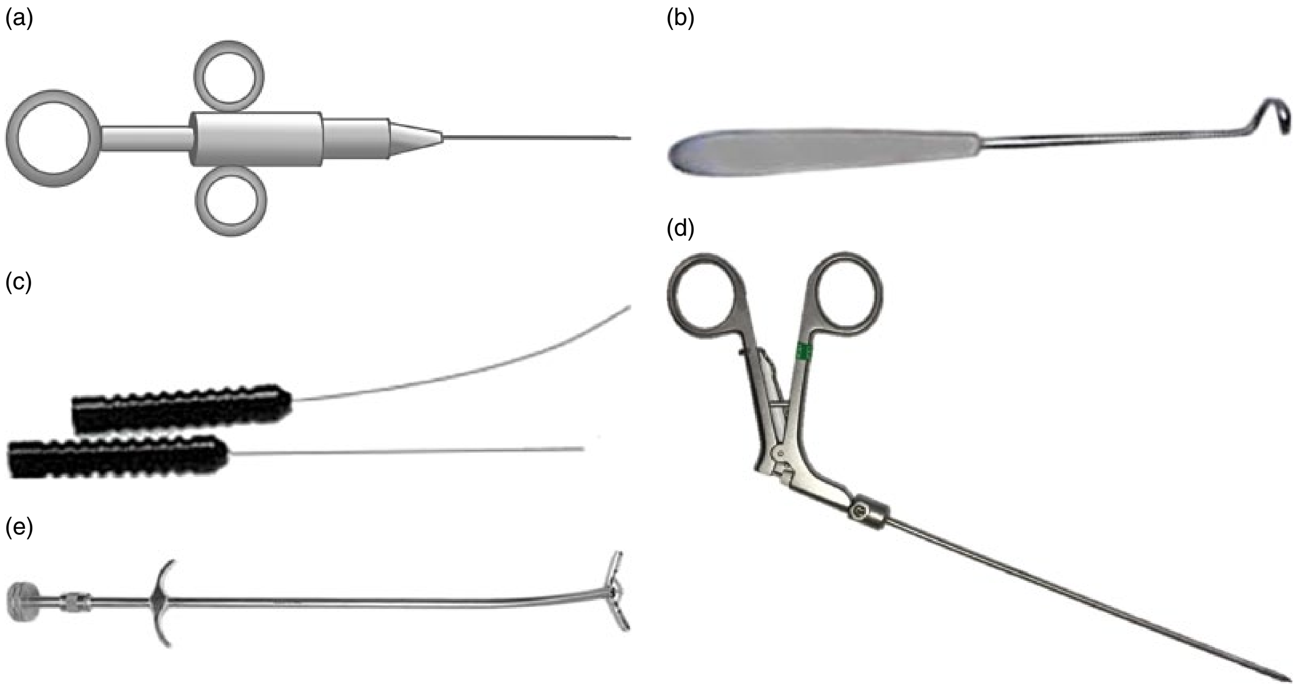

**Figure 86.4** Reusable laparoscopic port closure devices: (a) suture passer; (b) Deschamps needle; (c) Maciol suture needles; (d) reusable Carter–Thomason trocar incision closure; (e) Lowsley retractor.

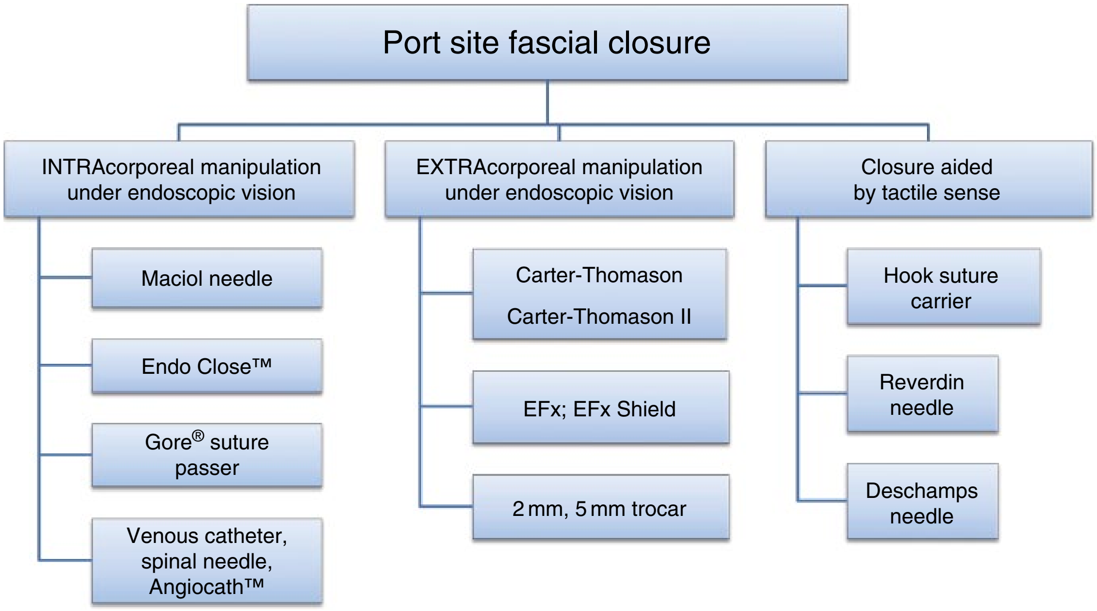
Port site fascial closure
INTRAcorporeal manipulation under endoscopic vision
Maciol needle
Endo Close™
Gore® suture passer
Venous catheter, spinal needle, Angiocath™
EXTRAcorporeal manipulation under endoscopic vision
Carter-Thomason
Carter-Thomason II
EFx; EFx Shield
2 mm, 5 mm trocar
Closure aided by tactile sense
Hook suture carrier
Reverdin needle
Deschamps needle

**Figure 86.5** Overview of techniques for port site fascial closure.

vision (Figure 86.6). For this type of closure, various devices can be used [41]. The Maciol reusable suture needle set consists of a set of three needles: two suture introducers (one with a straight tip and one with a curved tip) and one suture retriever. An absorbable suture is placed percutaneously by using the introducer needle while the trocar remains in place. The retrieval needle is placed 180° from the initial suture passage and is used to grasp the end of the suture. A laparoscopic grasper is used to place the end of the suture into the retriever. Then, the trocar is removed and the fascia is pulled and closed by tying the suture. The Endo Close™ (Covidien/

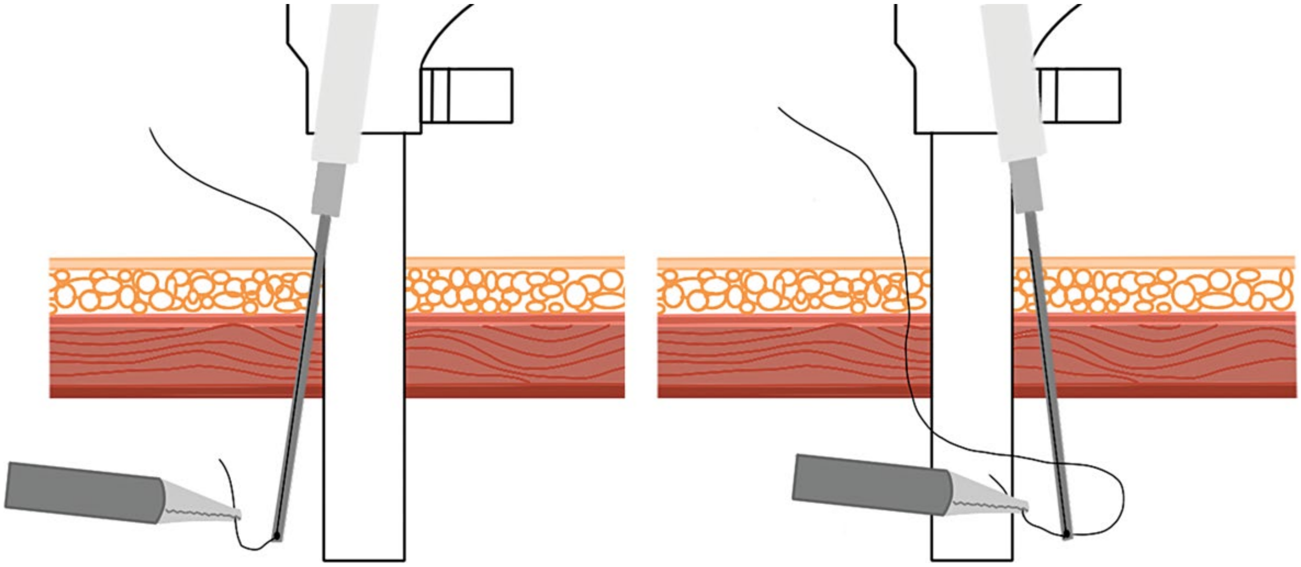

**Figure 86.6** Intracorporeal fascial closure techniques.

Medtronic, Minneapolis, MN, USA) is a spring-loaded disposable device which is loaded with a suture before being introduced into the abdomen between the trocar and the skin edge. The suture is released, and the device is placed 180° from the first passage. A laparoscopic grasper is needed to place the suture in the open notch of the device and the device is pulled together with the trocar so that the suture can be tied to close the fascia. The Gore™ Suture Passer (W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) is a reusable device that works with a similar principle. While the trocar is maintained in place, the suture is loaded into the instrument, then passed on one side of the trocar, then released from the passer, and then grasped with a laparoscopic grasper. At this point, the passer device is removed and then inserted again on the opposite side of the trocar so that the suture is placed again back in the jaw of the passer, locked and pulled out so that the trocar can be removed and the suture tied down.

Low-cost methods without using any particular device have also been described to achieve intracorporeal closure. A venous catheter, a 15G spinal needle, or a 14G Angiocath needle have all been used to aid in fascial closure [40].

### Extracorporeal instruments

The most common technique used to close a trocar site is extracorporeal manipulation with endoscopic vision. A variety of disposable devices can be used for this purpose [40]. The Carter–Thomason CloseSure™ system (Cooper Surgical, Trumbull, CT, USA) consists of two parts: the pilot guide and the suture passer. Fascial closure can be obtained by four easy steps: the suture passer is used to punch the suture through the pilot guide, fascia, muscle, and peritoneum. On the opposite side, the suture passer is inserted through the wound so the suture can be pulled, encompassing the peritoneum, muscle, and fascia. The pilot guide is removed and the suture is tied. Other devices such as the Carter–Thomason II (Cooper Surgical, Trumbull, CT, USA), the Weck EFx™ (Teleflex Medical, Research Triangle Park, NC, USA), and the Weck® EFx Shield™ (Teleflex) are used with similar processes. In an in vitro cadaver trial, del Junco et al. found EFx to be superior in terms of time needed to complete defect closure, safety, and facility, and the Carter–Thomason to be better regarding maintenance of the pneumoperitoneum [42]. Others have described the use of a 2 mm trocar and sleeve (Miniport™, Covidien/Medtronic, Minneapolis, MN, USA) or a 5 mm trocar to obtain a safe and efficient port site closure [40].

### Standard technique

In this group of techniques, hand-sutured closures are performed, and several reusable devices can be used to help, such as the hook suture carrier [43], the Lowsley retractor [34], Reverdin needle [44], and Deschamps needle [45] (Figure 86.7). Most of the time there is no endoscopic view, and therefore a tactile sense should be used to aid in the closure. A "dual hemostat" technique, in which one hemostat is placed into the wound to lift the fascia and one to retract the overlying subcutaneous tissue, was suggested by Spalding et al. [46]. A standard technique of hand-sutured closure can be adopted where the skin is retracted; a Kocher clamp is used to grasp the

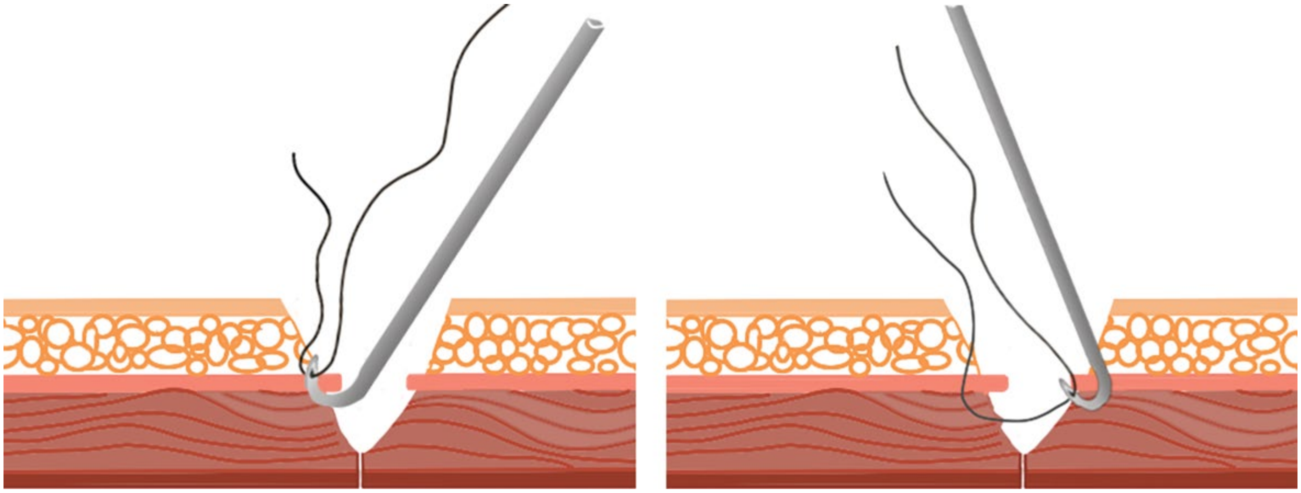

**Figure 86.7** Closure performed without endoscopic view: suture carrier.

fascia on either side and to lift it upward. A figure-of-eight suture is placed with endoscopic view preventing visceral injury [47]. This technique is easy in cases involving thin patients, but it becomes more challenging in cases involving large amounts of subcutaneous tissue.

## Skin closure

Before skin closure, the port site should be irrigated. Appropriate skin closure is a crucial step for any surgical procedure because obtaining cosmetically acceptable results translates into high patient satisfaction. Skin closure consists of a suture placed in the dermis to provide tensile strength and a suture in the epidermal layer to align the skin edges [48]. Port site skin closures are most commonly performed by running a subcuticular closure, with or without skin tape (steri-strip), as it enhances the cosmetic result and is useful for closing wounds with equal tissue thickness and in which virtually no tension exists. Usually, an absorbable suture (poliglecaprone 4-0 Monocryl®) can be used for this purpose.

### Skin adhesives

Fast-acting adhesives represent an alternative to formal skin closure. These adhesives dry quickly and can be used for laparoscopic port site wounds [49]. Two examples of commercially available adhesives are Dermabond® (2-octylcyanoacrylate; Ethicon, Inc., Somerville, NJ, USA) and Indermil® (*n*-butyl 2-cyanoacrylate; Covidien/Medtronic, Minneapolis, MN, USA). It is essential to obtain a dry surface with good edge-to-edge approximation before applying these glues. Cost remains a drawback on these materials when compared to traditional sutures. Several studies comparing adhesives to sutures for the closing of skin wounds have been reported, but there is insufficient evidence that port site wound closure technique by tissue adhesives is superior to traditional suture closure technique with regard to wound infection, wound dehiscence, and patient satisfaction [50].

## Drainage

Drainage after urologic laparoscopic and robotic procedures is used to allow prompt postoperative diagnosis of potential complications, which can vary depending on the procedure performed (Table 86.3). One should be aware that various drain-related complications are possible, such as hematoma, pain, and loss of a drain in the abdominal cavity. Therefore, the risks and benefits of using a drain should be considered after each procedure. In general, each surgeon has his or her preferences regarding drainage. Radical nephrectomy does not require drainage in most cases because potential postoperative bleeding can be identified by looking at clinical parameters such as vitals and urine output. Similarly, nephroureterectomy does not require drainage because the risk of urine leakage from the bladder opening is prevented by the use of a Foley catheter. A different scenario is presented by laparoscopic/robotic partial nephrectomy where there is a potential risk of both hemorrhage [51] (from the renorrhaphy site) and urine leakage [52, 53], which are both directly correlated to tumor complexity. On the other hand, recent evidence has suggested that a drain can be safely omitted in a majority of robotic partial nephrectomies because it seems to have minimal benefit [54–56].

**Table 86.3** When and why a drain is left in major urologic laparoscopic procedures.

| Procedure | Drainage | Rationale |
|---|---|---|
| Nephrectomy | Usually no | Only if high concern for bleeding |
| Partial nephrectomy | Yes | Identification of urine leak and hemorrhage from resection bed |
| Nephroureterectomy | Usually no | Urine leak from bladder prevented by Foley |
| Pyeloplasty | Yes | Early identification of urine leak |
| Adrenalectomy | Usually no | Only if high concern for bleeding |
| Lymphadenectomy | Yes | Risk of lymphocele, if extended dissection |
| Radical prostatectomy | Yes | Identification of urine leak |
| Radical cystectomy | Yes | Identification of urine leak; identification of dehiscence of bowel suture |

The use of a drain after minimally invasive radical prostatectomy helps to identify and manage urine leakage from the urethrovesical anastomosis. Risk factors for urine leakage have been identified (obesity, prostate size, previous prostatic surgery, difficult anastomosis, or anastomosis under tension) and drain output is a primary method of diagnosis [57]. On the other hand, watertight anastomosis verified intraoperatively does not require drainage [58].

Over the past five years, minimally invasive radical cystectomy has become popular. The adoption of robotic surgery has also facilitated the standardization of intracorporeal urinary diversions [59]. Radical cystectomy is a procedure that carries a high risk of complications even for experienced surgeons [60]. Complications include urine leakage (from the ureterovesical anastomosis as well as the urethra-neobladder anastomosis for orthotopic diversion), and bowel anastomosis leakage.

## Types of drains

Different types of drainage systems may be classified as closed systems, with or without suction, and open systems (Figure 86.8). The Jackson–Pratt® wound drain (Cardinal Health, Dublin, OH, USA) is a closed-suction silicone drain with a bulb (100 ml). The Hemovac® (Zimmer Surgical, Inc., Dover, OH, USA) and the Davol® (C.R. Bard, Inc., Covington, GA, USA) are larger, closed-suction drains (400 ml) that feature a collapsible disk shape. The Penrose drain is a passive drain made of soft latex that is open at both ends; it is rarely used for laparoscopic procedures. Closed-suction drains can

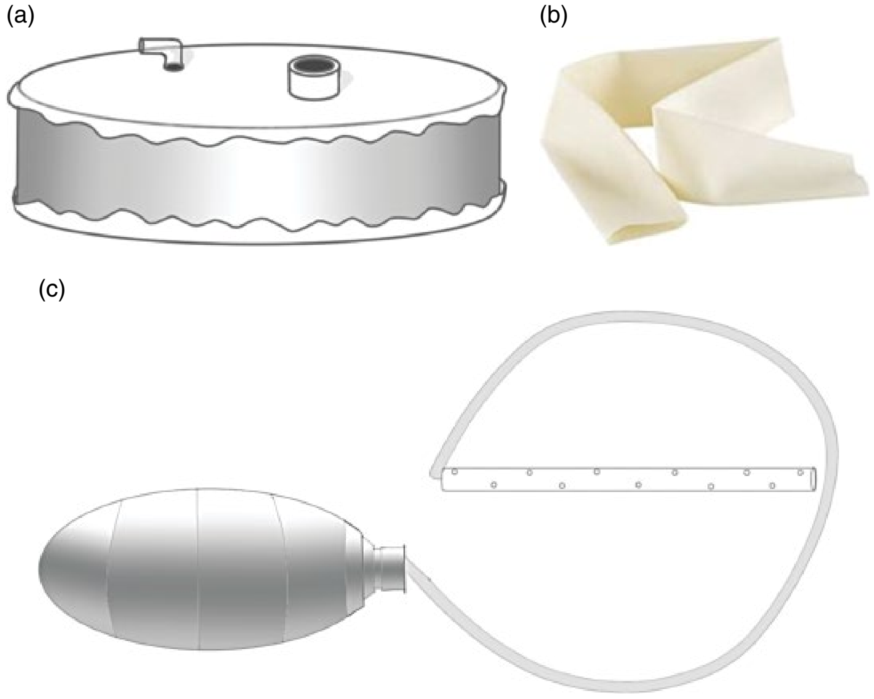

**Figure 86.8** Types of drains. (a) Hemovac; (b) Penrose drain; (c) Jackson–Pratt drain.

increase the risk of urinary fistula by creating continuous negative pressure.

### Technique of drain placement (see Videos 86.1 and 86.2)

Placement of a drain during a laparoscopic procedure is straightforward and can be done in various ways. The drain tube can be threaded into the intra-abdominal cavity through the desired port, and the distal end of the tube can be positioned at the desired location under endoscopic vision when the abdomen is still insufflated. In another method, the proximal end of the tube is threaded through a first port and out through a second access port to draw the distal end of the tube into the intra-abdominal cavity. Some tricks can be used to aid in drain placement. For example, one 5 or 10 mm port and the tip of a grasper (inserted through another port) can be aligned together so that the grasper is threaded inside the lumen of this port. By railroading, the port is gradually withdrawn while still holding the grasper tip inside so that the closed grasper jaws are brought out through the port site and the port is removed. At this point, the distal end of the drain is fed over one of the open jaws of the grasper. While holding the drain in the closed grasper, the drain is gently pulled into the intra-abdominal cavity and then positioned in the desired location under vision.

Once the drain is placed in the desired position, it is critical to secure it in place by placing a drain stitch, which is usually a nonabsorbable (silk or nylon) suture. During this step, the drain should be clamped to avoid leakage of $CO_2$ and maintain the pneumoperitoneum.

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# Part 3 Complications

## 87

## Complications in Urologic Laparoscopy

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### Introduction

Although laparoscopy has decreased the morbidity related to many urologic procedures, the solutions to complications arising in the minimally invasive environment frequently have no direct open surgical counterpart. For example, laparoscopic access is often obtained through a variety of initially blind punctures where viscera and blood vessels are susceptible to unique injuries. The insufflated abdomen presents specific potential physiologic complications, complex instrumentation can malfunction catastrophically, and inadvertent injury can occur outside the laparoscope's field of view due to unobserved instrument gestures. Laparoscopy therefore requires a specialized knowledge base, and demands a unique set of troubleshooting skills. Whereas textbooks have been devoted to laparoscopic complications, this chapter will cover the main areas pertinent to the urologist in training, as well as for the practicing urologist wishing to broaden their knowledge.

Since urologic laparoscopy is no longer in its infancy and surgical complexity has increased, warnings and advice about complications from the dawn of laparoscopy may no longer be appropriate. For example, open conversion is less often required for the contemporary surgeon than it was in the past (in early series prior to 2000 conversion was as high as 2.1% [1]). Although the threshold to convert must remain low, and the window to address an evolving complication is short, the options and expertise to intervene without making an incision have expanded. The surgeon must exercise particular care during the learning period; multiple studies in the urologic [2, 3] and general surgical literature [4] have demonstrated an inverse relationship between surgeon experience and complication rates.

Complications in this chapter are organized by major category: (i) access, (ii) physiologic, (iii) patient positioning, (iv) end-organ (vascular, bowel, solid organ), (v) postoperative, and (vi) miscellaneous. Where appropriate, complications pertaining to specific urologic procedures will be highlighted. Since robotic techniques have essentially duplicated laparoscopic counterparts for all procedures, all complications discussed herein and their management are generalizable to robotic surgery. The classification schema proposed by Clavien–Dindo will not be specifically reviewed, but the reader is urged to review this separately [5].

### Access complications

Regardless of the method used to gain initial deliberate entry into the peritoneal (or retroperitoneal) cavity, access remains a significant source of morbidity and potential mortality. The incidence of any type of access injury ranges from 5 in 10 000 to 3 in 1000 [6]. In a recent literature review of 41 articles, including almost 700 000 procedures for which Veress needle access was used, 1575 (0.23%) injuries occurred [7]. The majority (92%) of these injuries were minor. Although the risk of access injury is low, it is not negligible, and a surgeon is statistically likely to encounter several over the course of a career.

The following access techniques are available:

- *Veress needle (closed entry)*, whereby a hollow needle with a retractable blunt tip is passed across the abdominal wall. Upon transperitoneal entry, the blunt cannula springs back into place, theoretically blunting the needle tip. Insufflation is then carried out through the needle.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

- *Hasson (open entry)*, whereby access is gained via a mini-laparotomy approach and all layers are entered sharply [8].
- *Optical trocar*, a camera-guided approach where the camera sits within the trocar's transparent conical-tipped obturator, and all layers of the abdominal wall can be seen as the trocar is advanced [9]. This technique can be employed alone in a desufflated abdomen or following initial insufflation via a closed (Veress) needle.
- Other techniques, less commonly used in urology, include radially expanding trocars and direct trocar insertion.

A 2008 Cochrane literature review comparing open and closed entry techniques found that there was insufficient evidence to recommend one technique over another [10]. No technique is foolproof. Experts acknowledge, however, that a prospective study powered to detect a meaningful difference would require thousands of patients and is unlikely to be organized. Generalized underreporting of complications further hampers attempts to define the true incidence of entry complications. However, a careful review of smaller studies reveals some take-home points. The incidence of vascular injury is probably higher with closed techniques [11]. Bowel injury is equally likely with open and closed entry techniques [12], but there may be a higher chance of immediate diagnosis with an open technique, since the injured bowel is directly visualized. Even so, delayed diagnosis of bowel injury has occurred following open access as well [13].

The nuances of safe access are highly subject to individual surgeon preference. As such, evidence-based literature only goes so far, and there is no substitute for hands-on bedside training. In our opinion, for instance, Veress needle safety checks, such as aspiration and saline drop, can provide valuable clues when performed correctly and in conjunction with verifying a low opening pressure (ideally $< 9$ mmHg). A published report on this matter, however, concluded that the ancillary needle checks provided little useful information apart from opening pressure [14]. The literature must be interpreted with caution in this arena, since the most important factor in gaining safe access is surgeon familiarity and mastery of a given approach.

Flexibility to use a different technique when called for is crucial. When the surgeon encounters difficulty gaining access by any approach, the advice to *change something* is prudent. A quote widely attributed to Einstein captures this concept: "The height of insanity is repeating the same thing over and over and expecting a different result." Stubborn repetition of the same maneuver invites complications. In a difficult access situation, careful reassessment of landmarks, checking for faulty equipment, and evaluating approach angles, can make all the difference. The trocar design must not create false reassurance, as even shielded trocars have not been shown to decrease access injuries. Also, be aware that in obese patients, reliable surface landmarks, such as the association between the umbilicus and aortic bifurcation, are lost.

The preventative guidelines in Box 87.1 are not data driven, but rather based on our experience. They are applicable for all types of laparoscopic access.

## Physiologic complications

Pneumoperitoneum is associated with potential complications and physiologic alterations both from its mechanical compressive effects on blood vessels and viscera, and

**Box 87.1 Preventative guidelines for laparoscopic access.**

1) Prior to skin incision, ensure that you have a working camera, insufflation, cautery, and laparoscopic suction.
2) Choose an entry site at a safe distance from prior scar, as underlying adhesions may be present.
3) With multiple prior abdominal surgeries, strongly consider open (Hasson) access.
4) If a Veress needle is chosen, decide a priori on the number of "attempts" you will allow before switching to an open access technique (we recommend three at most). Complications increase as attempts increase [11].
5) If you believe that elevating the abdominal wall is important, elevate the fascia (with a traction suture, Kocher clamp, or hand grasping and lifting the abdominal wall); do not elevate the skin only, as this will *increase* the distance to the peritoneal cavity.
6) Make sure Foley bladder decompression and orogastric tube stomach decompression have been instituted (especially in the pediatric population).
7) Ensure anesthesia has achieved complete muscle relaxation. A possible cause of high opening pressure (Veress access) other than preperitoneal needle placement is incomplete patient relaxation.
8) After the trocar has been placed, look in with the camera immediately. If vascular injury has occurred, the window for diagnosis and intervention is short. Do not waste precious time cleaning the camera lens prior to your first look inside.

by its potential entry into the bloodstream and subcutaneous tissues. Carbon dioxide is utilized because it is widely available, noncombustible, colorless, and readily absorbed. An unfortunate by-product of its favorable diffusion properties is the potential to decrease blood pH with prolonged absorption. Patients with severe pulmonary disease in whom the ability to counteract acidosis with hyperventilation is impaired may have a relative contraindication to laparoscopy [15], but this is rarely encountered clinically.

Although other pulmonary changes are best considered expected alterations rather than complications, they warrant mention nevertheless. Metabolic acidosis from hypercapnia can typically be measured in the form of expired $CO_2$. With mechanical ventilation, the clinical consequences are typically insignificant [16]. The mechanical compressive effects of pneumoperitoneum on the diaphragm causes increased intrathoracic pressure, increased peak airway pressure, and decreased vital capacity.

Hemodynamic effects of pneumoperitoneum are variable and difficult to generalize [16], but a prospective study by Meininger et al. thoroughly assessed this question by studying 10 patients undergoing robotic prostatectomy using a central venous catheter in place [17]. They were able to accurately measure cardiac output using thermodilution, cardiac index (CI), heart rate, mean arterial pressure (MAP), systemic vascular resistance (SVR), and central venous pressure (CVP), and correlate these with Trendelenburg position as well as pneumoperitoneum. The only hemodynamic parameter associated with Trendelenburg was an increase in CVP. Pneumoperitoneum only resulted in an increased MAP. Importantly, cardiac output was not affected either by Trendelenburg position or by pneumoperitoneum. The reader should note that other studies have demonstrated conflicting results in this arena.

Two important clinical scenarios are frequently encountered. First, the patient is found to have profound bradycardia as an initial response to peritoneal insufflation. The abdomen must be swiftly desufflated and anticholinergics administered. If the physiologic response occurs during a closed (Veress) entry technique, rapid desufflation is not immediately possible, as this can only be carried out after primary trocar placement. In this difficult scenario, the surgeon must proceed rapidly without placing the patient at risk from overly aggressive trocar insertion. Attention to safe trocar placement is well worth a few extra seconds of bradycardia.

Second, if an air embolus is suspected, the often cited Durant maneuver [18] is suggested to prevent the “air lock” from sitting in the right ventricular outflow tract. In the original study, animals that were positioned left side down had improved hemodynamics. In this position with the right side up, and furthermore in Trendelenburg, theoretically the air is prevented from entering the pulmonary outflow tract. A central venous catheter may be inserted to aspirate the air. Some authors have since pointed out that these effects have not been reliably reproduced in humans, and the position may be cumbersome and impractical in an emergency situation [19]. Nevertheless, the presentation of air embolus is dramatic, especially if Veress needle high-pressure insufflation directly into a major vessel is the cause. The patient develops sudden hypoxia, hypercarbia, and cardiovascular collapse.

The overall incidence of subcutaneous emphysema is 0.4–2.3% [20]. Subcutaneous emphysema is typically clinically insignificant and resolves without specific intervention. It may occur with initial preperitoneal Veress needle insufflation. Alternatively, a combination of a snug skin incision and loose fasciotomy around a trocar allows gradual development of ongoing subcutaneous emphysema during surgery. During lower tract laparoscopy, subcutaneous emphysema in the scrotum and penis is not a subtle finding, and should be manually decompressed at the conclusion of the case.

The presence of subcutaneous emphysema underscores the ability of pressurized gas to diffuse between body compartments [20]. Gas may similarly enter the pleural cavity, mediastinum, and pericardial space. Small collections of air in these spaces, without clinical instability, can typically be managed conservatively since $CO_2$ is readily absorbed.

## Complications of patient positioning

The surgeon often relies on gravity and patient positioning for adequate exposure during minimally invasive genitourinary procedures. Patient positioning, and at times prolonged operative times, predisposes the patient to four potentially painful and debilitating problems if precautions are not taken: neuropraxia/neuropathy, rhabdomyolysis, compartment syndrome, and pressure ulcers [15]. Complications in this arena are position- and therefore procedure-specific. In a large series of urologic laparoscopic procedures compiled from 15 centers and over 1600 cases, the overall incidence of neuropraxia was 2.7%, including rhabdomyolysis in 0.4% [21]. Risk factors included obesity, longer operative times (>5 hours), and advanced patient age. In a postoperative patient with oliguria and myalgias, clinical suspicion of rhabdomyolysis is paramount, creatinine kinase should be checked, and the patient should be alkalinized expeditiously.

For upper tract laparoscopy, with the patient flexed in flank position, the following maneuvers are important:

use of axillary roll, avoiding excessive flexion, and padding all pressure points. For lower tract surgery, with the patient supine with arms tucked and legs variably positioned per surgeon preference, hands should be in an anatomic position (thumbs up) and sheets to "tuck" arms must not be overly snug around the arm.

## End-organ complications

### Vascular injury

Bleeding complications account for a substantial portion of laparoscopic complications. For example, intraoperative and postoperative hemorrhage accounted for 40% of all perioperative complications in a single institution analysis of urologic laparoscopic procedures from 1997 to 2006 [22]. The overall incidence of vascular injury during urologic laparoscopy is in the range 0.4–1.7% [1, 2].

The most feared vascular injuries carrying the highest chance of mortality when injured are the great vessels and their immediate branches: aorta, vena cava, and iliac vessels. Mesenteric vascular injury can also be a source of major bleeding. The most common scenario is injury by initial blind Veress needle puncture. This may initially manifest as blood aspirated from the needle. Alternatively, vascular puncture from primary trocar insertion can occur. In either case, possible causes include incorrect angle of insertion and/or uncontrolled axial insertion force. In case of injury, if secondary trocars can be swiftly inserted, holding pressure at the bleeding site with a gauze sponge and laparoscopic grasper (unrolled gauze will fit through a 12 mm trocar) usually gives the surgeon time to assess the situation and, if required, proceed with laparotomy in a controlled fashion [23].

Depending on the bleeding severity and origin, the surgeon must decide whether to use thermal energy, clips, or suture ligatures. With massive hemorrhage, immediate laparotomy is often required. One has precious seconds to determine whether initial laparoscopic attempts at control are feasible or futile. A hand-assist port may be placed as an intermediary to open conversion. If open conversion is required, the laparoscope should be lifted up to the abdominal wall and rapid incision made directly over it. In such an emergency, the incision should be generous for maximal exposure. Compression of the bleeding site allows time for anesthesia to catch up with resuscitation, and allows surgeons with appropriate expertise, such as vascular surgery, to join the team.

The epigastric vessels are the most commonly injured minor blood vessels during trocar or Veress needle insertion [24], when these are placed laterally off midline (Figure 87.1). Using a Carter–Thomason wound closure device [25], sutures placed above and below the bleeding site are usually sufficient to control the bleeding.

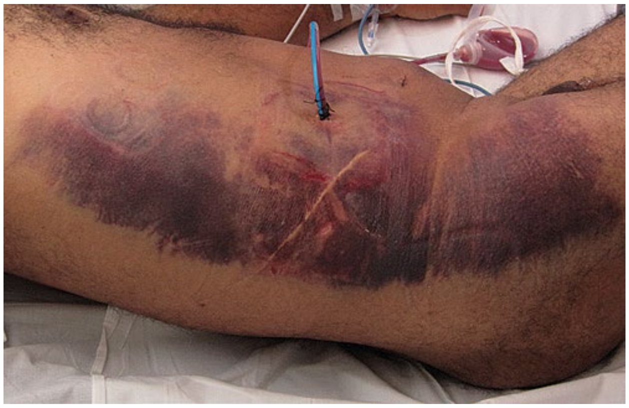

**Figure 87.1** Abdominal wall hematoma.

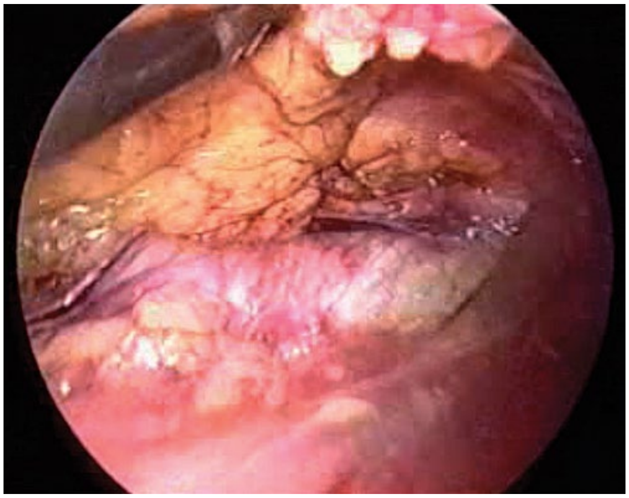

**Figure 87.2** Cava transected with vascular stapler, incorrectly identified as a renal vein.

A vascular complication specific to retroperitoneal laparoscopic right-sided nephrectomy is inadvertent ligation of the inferior vena cava (IVC) mistaken for the renal vein [26]. The cause is a lack of orientation to anatomic landmarks. During retroperitoneoscopic surgery, the psoas muscle must be maintained as the "surgical horizon" to maintain orientation. The renal vein must be verified to be heading towards the kidney (90° up, if the psoas horizon is maintained), with expected caliber. Most importantly, the renal vein–IVC junction above and below must be confirmed, as a prerequisite to renal vein ligation. If IVC transection is recognized (Figure 87.2), open vascular repair is suggested.

Bleeding is the main complication following partial nephrectomy (1.3–4.3%) [27]. One of the more common causes of intraoperative bleeding is an unclamped, unrecognized accessory renal artery. Great care must be

**Box 87.2 Bleeding set.**

- Two laparoscopic needle drivers
- Lapra-Ty and/or Weck clips, with appliers
- Laparoscopic Satinsky clamp
- Bulldog clamps, various sizes
- Surgicel absorbable hemostat
- Gauze sponge
- 2-0 Vicryl, SH needle, 10 cm long with Lapra-Ty at the end
- 2-0 Vicryl, CT-1 needle, 10 cm long with Lapra-Ty at the end
- Titanium clip applier, 5 and 10 mm (available in room, unopened)

taken both in evaluating preoperative axial imaging and during intraoperative hilar dissection to detect such variations. Delayed bleeding in the setting of hemodynamic stability can be addressed with selective embolization. In cases of hemodynamic instability, re-exploration is warranted. An attempt to ligate bleeding vessels is reasonable, but nephrectomy may be indicated if a single bleeding site is elusive or patient instability does not allow for renorrhaphy. In a large series of laparoscopic partial nephrectomy, reoperation was required in 2% and elective laparoscopic radical nephrectomy was performed in 0.5% [28]. When delayed bleeding manifests as hematuria, vascular fistula should be considered, and can be managed effectively with endovascular embolization.

As with any type of injury, prevention of vascular injury is best. A vascular injury "kit" should be prepared with each case (Box 87.2). Dissection should be performed in layers, widely completing more superficial layers before progressing deeper. Vascular injury of varying severity will occur, but poor exposure and "working in a hole" at the outset will severely limit the ability to control an injury. If staplers are used for vascular control, the stapler should be applied a few millimeters distally to provide a stump to grasp in case of catastrophic stapler malfunction [29].

## Bowel injury

The overall incidence of bowel injury in urologic laparoscopy (Figure 87.3) is approximately 0.2–0.7% [2, 3]. Since initial laparoscopic entry is one of the most common times for complications of any sort, a discussion of bowel complications is intimately related to access (see earlier). Rather than examining procedure-based datasets, a 2001 review examined international claims arising from access injuries from 1980 to 1999 and revealed that small bowel was the most commonly injured individual organ [13]. In this study, which included 594 injuries in 506 patients, claims were compiled both from legal suits made against a physician, and through mandatory device-related incidents reported to the US Food and Drug Administration (FDA). When multiple structures were injured, the most frequent combinations involved both a vascular structure and bowel. Of great practical concern was the observation that diagnosis was delayed greater than 24 hours for approximately half of all large and small bowel injuries.

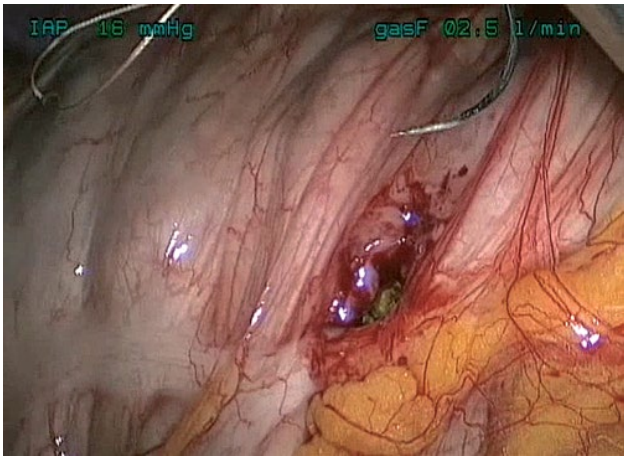

**Figure 87.3** Colon injury with primary trocar.

By far the most important take-home message regarding bowel injuries is that the injury may be subtle and early recognition is essential. In the study by Chandler et al., whereas small bowel injury conferred an odds ratio of 1.7 for patient mortality, greater than 24-hour delay in diagnosis increased the odds ratio to 3.7 [13]. Even more humbling is that because vascular injuries present so dramatically, delayed bowel injuries are more likely to cause death than major retroperitoneal vessel injury. In another injury-based database based on Medical Device Reports, the mortality rate in cases of delayed bowel injury was 21% [30].

When caused by a Veress needle puncture or trocar tip, laparoscopic repair of large or small bowel with intracorporeal suturing is readily accomplished. For large tears, or when significant adhesions preclude adequate assessment of the full extent of injury, open conversion and repair is recommended.

Trocar site herniation is another potential source of morbidity, occurring in approximately 1% of cases where bladed trocars are used [31] (Figures 87.4 and 87.5). Standard recommendations for port-site fascial closure include all trocar sites in children and trocar sites greater than 10 mm in adults [32]. The latter has been challenged, since newer dilating (nonbladed) trocars leave a much smaller fascial defect than the diameter of the trocar itself [33]. In our opinion, with modern trocar design there is seldom an indication for bladed disposable trocars as their use invites both vascular injury and postoperative herniation.

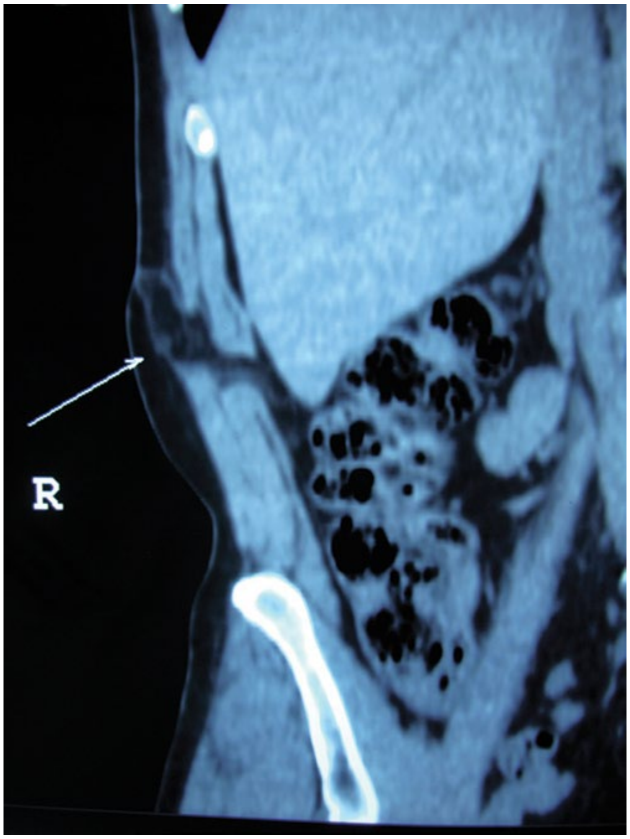

**Figure 87.4** Trocar site hernia.

Rectal injury, one of the most significant injuries during laparoscopic prostatectomy, occurs in approximately 0.5% of cases [34]. During the dissection, all areas of the rectum in relation to the posterior prostate surface are potentially at risk. Rectal injury can happen at the prostate base (incision too posterior through Denonvilliers' fascia), mid gland (wide neurovascular bundle resection), or apex. Preoperative bowel preparation allows for primary closure alone, since lack of gross fecal contamination may obviate the need for concomitant fecal diversion [35, 36]. Intraoperative diagnosis of even small injuries is best performed by instilling air per rectum with the pelvis filled with irrigant, whereby bubbling confirms rectal injury. Digital rectal examination or transrectal balloon placement may reveal larger injuries. Rectal injury may be further complicated by pelvic abscess (0.1%) or rectourinary fistula (0.1–1%) [37].

Predisposing factors for rectal injury include those that impair tissue integrity and/or obscure tissue planes. These include periprostatic fibrosis from multiple biopsies, prior prostate or rectal surgery, previous radiotherapy, locally advanced tumors, prior hormonal therapy, and prostatic infection. A non-nerve-sparing dissection with a wider dissection plane is also a risk factor, and the surgeon must therefore not be complacent in the belief that non-nerve sparing is an easier operative plane.

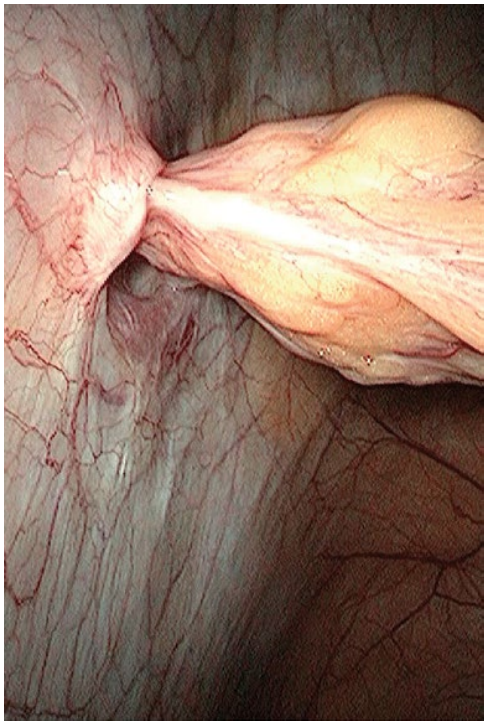

**Figure 87.5** Trocar site hernia at time of repair.

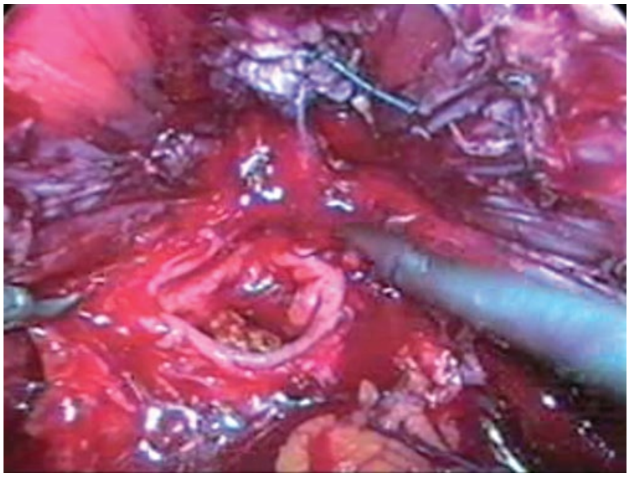

**Figure 87.6** Rectal injury during laparoscopic prostatectomy.

Rectal injury (Figure 87.6) can be managed laparoscopically or robotically without open conversion [38]. The defect should be closed primarily in at least two layers of nonabsorbable suture. The integrity of closure can be tested by instilling air in the rectum and watching for bubbles in a fluid-filled pelvis. By tacking the rectum laterally to the levator muscles, the rectal closure is drawn away from the urethrovesical anastomosis, minimizing the chance of fistula. A pedicle of omentum can be brought in over the rectal closure. Diverting colostomy or loop ileostomy should be considered in cases of tension at the rectal closure, massive fecal spillage, prior radiotherapy, and delay in diagnosis. A closed suction drain should be placed, and the patient covered with broad-spectrum antibiotics. A cystourethrogram must be performed prior to catheter removal to exclude urine leak, which may progress to rectourethral fistula if not recognized.

### Visceral injury

Of solid viscera, the liver and spleen are most at risk during right and left upper tract urologic laparoscopy, respectively. In one of the largest reviews of 2775 urologic laparoscopic procedures, the spleen was injured in 3.2% and the liver in 1.1% of cases [3]. In a meta-analysis broken down by procedure, the spleen was injured in 0.5% of radical nephrectomies and 1.3% of donor nephrectomies [39].

Most liver lacerations respond favorably to argon beam coagulation. For both liver and splenic lacerations, hemostatic adjuncts such as Floseal® (Baxter, Deerfield, IL, USA) and Surgicel® (Ethicon Biosurgery, Somerville, NJ, USA) are also useful. As a last resort, splenectomy should always be considered for severe bleeding or deep lacerations unlikely to resolve with standard maneuvers. The liver and spleen are injured similarly when retracted with an instrument tip rather than a broad surface (Figure 87.7). On the left side, complete mobilization of the spleen from the upper aspect of Gerota's fascia must be accomplished in order to avoid retraction injury.

One commonly encountered scenario is right-sided upper tract (renal or adrenal) surgery in a patient who has previously undergone cholecystectomy and in whom the liver is adherent to the posterior parietal peritoneum over Gerota's fascia. Rather than dissecting the liver directly, the liver should be mobilized with its adherent fascial layers by making an early incision into Gerota's fascia. By entering the retroperitoneum early and reflecting adherent tissue with the liver, injury may be avoided altogether.

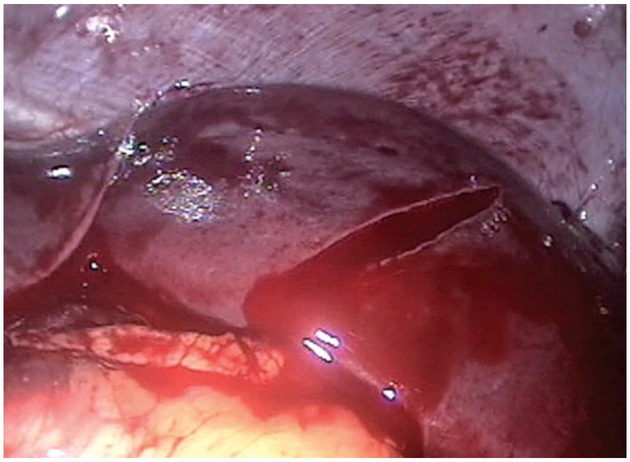

**Figure 87.7** Splenic laceration during specimen entrapment.

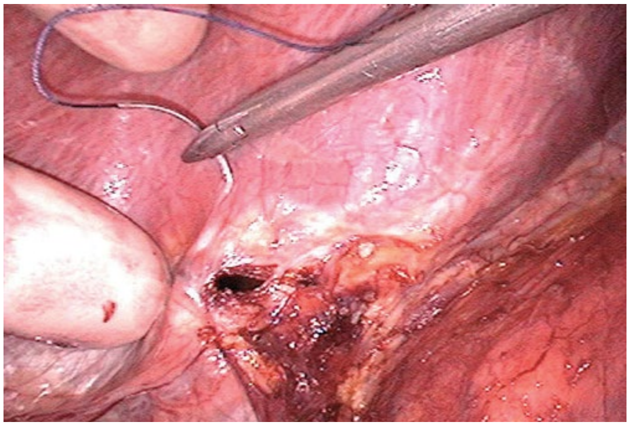

**Figure 87.8** Diaphragm injury.

The risk of diaphragm injury during urologic laparoscopy was 0.7% in one series [40]. This may occur deliberately as part of planned wide resection of a tumor invading the diaphragm, or inadvertently while dissecting in close proximity to it (Figure 87.8). The first indication that the pleura has been transgressed is a sudden billowing of the diaphragm into the abdominal cavity as the pneumoperitoneum rushes into the chest cavity [41]. Small injuries do not require open conversion to repair. A purse-string suture can be placed laparoscopically around a red rubber catheter exiting through a trocar and immersed in water. As anesthesia expands the lung, the air is evacuated and the suture is rapidly tied down as the catheter is withdrawn [40].

## Postoperative complications

Perioperative complications can be classified as either intraoperative or postoperative. In large series, postoperative complications account for approximately half of all complications [1]. The main complications of concern are bleeding (hemorrhage requiring reoperation or transfusion, operative site hematomas), urinoma, and wound complications (infection, hernia). Depending on the procedure, ileus and lymphocele formation are also of concern. The surgeon must be aware that "getting out" safely is as important as gaining access. In this regard, specific maneuvers should be part of standard practice.

Safe laparoscopic exit must include watching all trocar sites for active bleeding after trocar removal. For extirpative procedures requiring an extraction incision, reinsufflating and looking back after fascial closure provides useful information. Lack of bowel entrapment should be confirmed beneath the incision. If significant blood has accumulated during the period of desufflation, an exhaustive search for the bleeding site can obviate the need for re-exploration in the postoperative period. Significant postoperative bleeding presenting with hypotension, anemia, and abdominal distention is a clear sign of hemorrhage, but signs may be more subtle. If a surgical drain has been placed, the rate of filling and quality of fluid are important indicators of bleeding, but absence of blood in the drain does not exclude bleeding. Initial hemoglobin levels may be unchanged before serial measurements uncover anemia.

If surgical exploration is required for postoperative complications, relaparoscopy may be attempted in select cases [42, 43]. If a drain has been placed, it can be used to insufflate the abdomen. Open exploration is frequently required, but generalizations in this regard are difficult. For instance, re-exploration for bleeding following partial nephrectomy in a stable patient may be ideally suited to the laparoscopic approach as exposure of the renorrhaphy bed will be feasible. In contrast, bleeding following cystectomy and neobladder will be difficult laparoscopically as the urinary diversion and mesentery are now space-occupying structures obscuring view, and open exploration is warranted.

Urine leak in the postoperative period is pertinent after laparoscopy, pyeloplasty, and prostatectomy. Management of urine leak after pyeloplasty is initially conservative, as the majority will resolve following a period of encouraging maximal drainage (ureteral stent, Foley catheter, perirenal drain). A persistent vesicourethral anastomotic leak after laparoscopic radical prostatectomy is an uncommon complication with an unclear incidence (Figure 87.9). In one series, the incidence of leak requiring reoperation was 0.9–2.5% [42]. Most urinary leaks occur in the immediate postoperative period and are usually self-limiting with prolonged bladder drainage. Rarely, the surgeon encounters an anastomotic leak that does not resolve in the first two weeks.

Several conservative interventions are available for prolonged vesicourethral anastomotic leaks (Figure 87.10). These include prolonged retropubic and bladder drainage, passive rather than active drainage, advancing the drain away from the leak, bladder catheter traction, and bladder catheter needle-vented suction [44]. Particularly when the ureteral orifices are near the anastomosis, invasive techniques should be performed, including placing internalized or externalized ureteral stents. In case of ileus, abdominal pain, and/or urinoma, cystoscopy can provide information as to the degree of anastomotic separation. Laparoscopic re-exploration can be performed, the intra-abdominal urine evacuated, and the anastomosis either redone entirely or additional sutures placed.

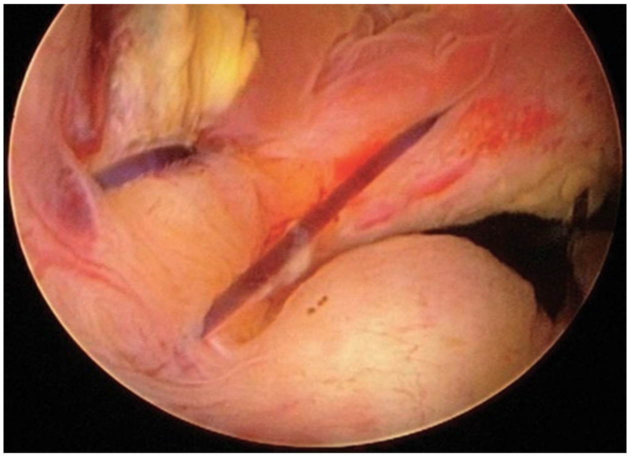

**Figure 87.9** Urine leak at urethrovesical anastomosis; anastomotic separation on cystoscopic view.

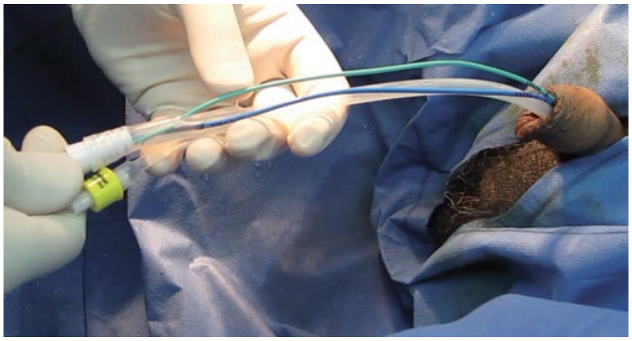

**Figure 87.10** Bilateral externalized ureteral catheters alongside Foley catheter for urethrovesical anastomotic leak.

## Miscellaneous complications

### Obturator nerve

The incidence of obturator nerve injury reported for open prostatectomy is 0.1–1%, and for minimally invasive prostatectomy 0.3% [45]. Given that the obturator nerve is fixed at either end, nerve mobilization to gain additional length is not feasible. As such, in the case of nerve loss, an interposition nerve graft may be necessary. If possible, an end-to-end reanastomosis with fine suture is ideal.

To avoid obturator nerve injury, a thorough understanding of normal anatomy is crucial, as this structure is one of the most reproducible, and its position scarcely varies in relation to bony landmarks. During lymphadenectomy, the lymph node packet should first be mobilized distally and reflected completely from the anterior surface of the nerve. When ligating the packet, it should be retracted medially, such that the full nerve is in view. Placing a clip parallel and medial to the course of the nerve will prevent inadvertent nerve injury.

## Ureteral injury

Ureteral injury is uncommon during laparoscopic upper tract surgery as its course is familiar to urologists. However, it is occasionally subject to injury during the learning curve of laparoscopic and robotic prostatectomy where its proximity to the seminal vesicle and bladder neck (ureteral orifices) are unexpected and unfamiliar. Ureteral injury was initially reported during the Montsouris posterior approach to the seminal vesical dissection, where the ureter was mistaken for the vas deferens [46]. In general, this is from errant dissection too far laterally. Double checking before ligating or dividing a tubular structure will prevent ureteral injury in this context. The other area of potential ureteral injury is the trigone. Care must be taken both during the posterior bladder neck dissection and during the anastomosis to identify the ureteral orifice. The incidence of ureteral injury during laparoscopic prostatectomy is approximately 0.8% [36, 47].

When ureteral injury is diagnosed intraoperatively, management depends on the injury type. Focal contusion without thermal energy may be managed conservatively with a ureteral stent alone. Suture repair and stenting of partial lacerations are appropriate. For complete transection, end-to-end anastomosis may be possible, but reimplantation is often a safer solution. When detection is delayed, repair is dictated by the location and extent of the injury, with the majority of injuries below the iliac vessels being managed with reimplantation. Percutaneous antegrade balloon dilatation may be suitable for delayed ureteric anastomotic stricture (Figure 87.11).

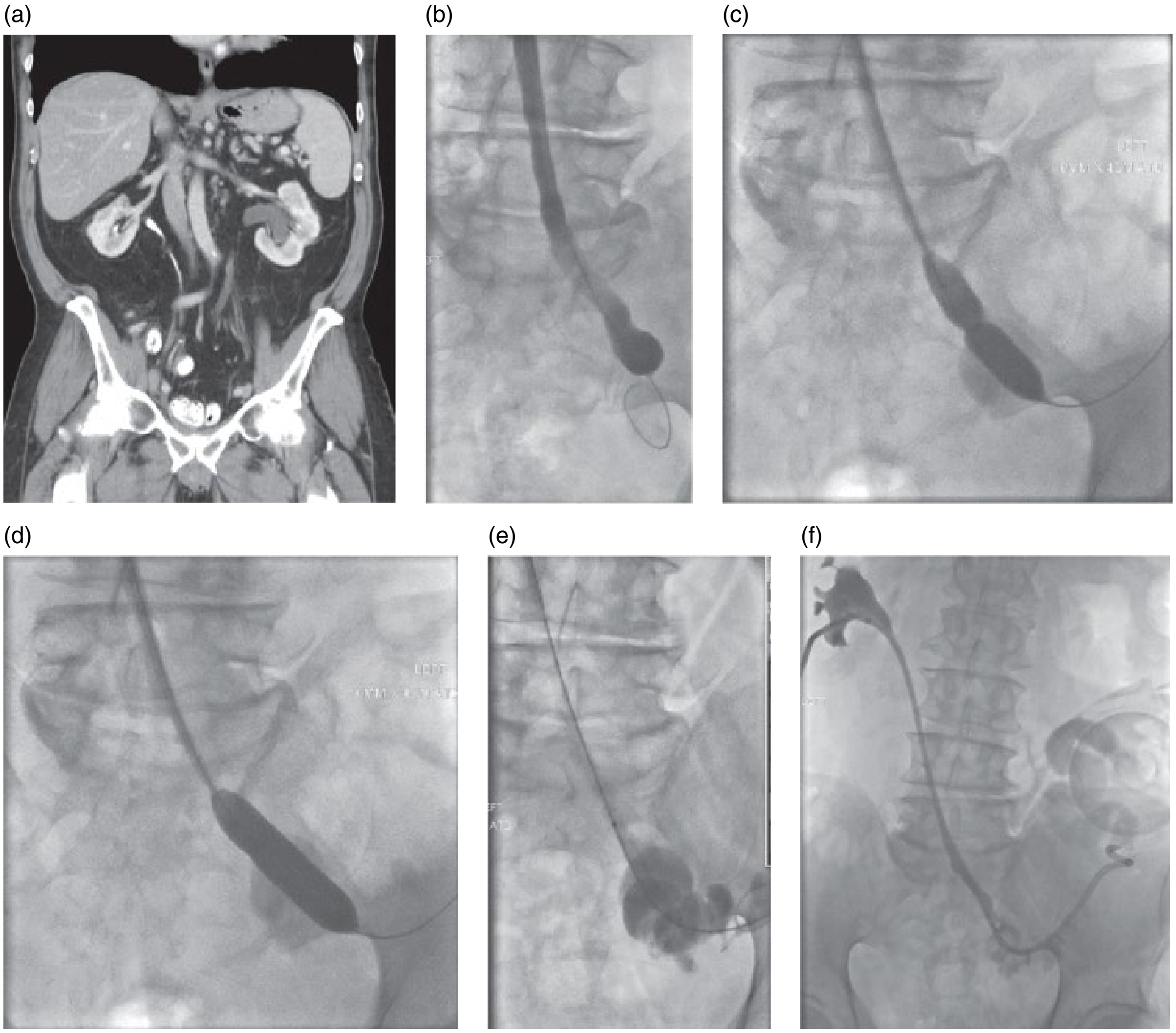

**Figure 87.11** Left ureteroenteric anastomotic stricture after robotic cystectomy. (a) Left hydroureteronephrosis on CT scan. (b) Cut-off point on antegrade nephrostogram. (c, d) Balloon dilation. (e) Contrast flow into ileal loop. (f) Nephroureteral stent in place.

## Conclusions

Comprehensive preoperative planning and surgeon preparation can minimize or prevent complications from minimally invasive surgery. Particular care must be exercised during the learning curve, as multiple series have demonstrated that complications decrease with experience. The impact and sequelae of complications when they do occur can be minimized by rapid recognition and appropriate treatment. Humility is important; the first step in recognizing complications is being open to their occurrence. With this broad overview, the reader should be better placed to avoid complications, equipped to swiftly diagnose them, and more able to intervene should they occur.

See accompanying Video 87.1.

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# Complications of Laparoscopy Including Robotics

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## Introduction

With the increasing utilization of laparoscopy and robotics in urologic surgery over the past two decades, we have observed a shift in the type and frequency of surgical complications that can occur. Although minimally invasive surgery (MIS) provides great morbidity advantages when performed skillfully, the surgical approach differs greatly from the open alternatives. A surgeon transitioning to MIS must learn to recognize and treat a specific set of typical problems associated with this surgical method.

The management of surgical complications truly begins with the anticipation of a potential event. Without anticipation of these critical micro-events, complication prevention cannot occur. Preparing for surgery is the most important step in this process and will lay the groundwork for a safe, high-quality operation. Reviewing the medical history and relevant imaging immediately prior to surgery and identifying steps of the operation that may be particularly challenging for an individual patient are common sense but critical. Taking this disciplined approach, even to routine procedures highly familiar to the surgeon, will help avoid preventable complications.

Many of the techniques fundamental to complication avoidance in surgery have been developed and applied successfully by the aviation industry. The implementation of a presurgical checklist and timeout is familiar to most surgeons. These steps ritualize the presurgical review and improve communication among members of the operating room team. Their value has been well demonstrated in various studies [1–6], with the World Health Organization promoting its use in a global healthcare initiative [7, 8]. Beyond the checklist, a very impressive tool in modern aviation safety is called Crew Resource Management (CRM) [9]. The captain and crew of American Airways Flight 1549, who saved all passengers by landing in the Hudson River, referred to CRM as the key to successfully managing a potentially catastrophic complication. CRM aims to optimize the effort of the team in utilizing all resources and information available to a flight crew. A core component of CRM is communication, with the goal of facilitating cooperation. Pilots are encouraged to learn from errors, be willing to accept help from the crew, and use all available resources to make decisions. Many of these skills can be adapted for professional interactions in the operating room (OR) [10, 11]. The surgeon should be open-minded and pay attention to concerns brought forward by surgical assistants, anesthesiologists, or OR nurses. Likewise, the surgeon's instruction should be followed efficiently. Although implementation of such safety methodology has been shown to improve surgical outcomes, the current lack of standardized measurement tools limits possible conclusions [8].

Laparoscopy and robotic-assisted surgery have critically altered the interaction in the OR between the surgeon and other team members. On the positive side, the situation awareness of all team members is improved as everyone can see the surgical field on the video monitor and follow the progress of the operation. Conversely, a robotic procedure poses a unique challenge as the surgeon is not physically present at the bedside and has to rely on continuous feedback from the assistant. Without effective communication by vigilant bedside personnel, the surgeon may be completely unaware of a potentially dangerous evolving situation while his or her head is buried in the robotic console. Alas, even a highly experienced operating robotic surgeon can no longer single-handedly

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monitor and control all activity at the operative field. This distributes some of the responsibility for identifying and preventing intraoperative complications onto the shoulders of potentially less experienced or knowledgeable OR staff, possibly increasing risk.

If a complication does occur in the OR, there is great value in providing a debriefing afterwards with all the team members involved. Direct feedback will help prevent avoidable mistakes in the future. Likewise, regular reporting of complications in a morbidity and mortality conference provides an opportunity for valuable peer review and education, which may decrease future complication rates.

## Pneumoperitoneum – considerations and complications

The insufflation of $CO_2$ for the maintenance of a pneumoperitoneum or inflated retroperitoneal space is generally performed at a pressure of 15 mmHg. At the initiation of pneumoperitoneum, severe bradycardia can occasionally be observed and should be anticipated by the anesthesia staff. Bradycardia may occur regardless of the patient's age and health status and is most likely an effect of a vagal stimulation caused by peritoneal stretch and irritation [12]. This can be seen more commonly during rapid abdominal insufflation through a large-bore trocar. Prompt desufflation of the abdomen combined with anticholinergic agents will resolve this in most cases, although in rare circumstances this phenomenon can lead to arrhythmias and cardiac arrest [12, 13]. The safest approach is to insufflate slowly at a low flow rate to a pressure of 12–15 mmHg. We also routinely notify the anesthesiologist verbally at the onset of insufflation, communicate actively during this phase concerning the patient's heart rate, and respond rapidly with desufflation if significant bradycardia develops. If the patient stabilizes swiftly and the anesthesiologist can rule out other potential causes of bradyarrhythmia, the case can generally be resumed without further restrictions.

$CO_2$ embolus is a rare but potentially lethal complication of peritoneal or retroperitoneal insufflation. Both the laparoscopic surgeon and anesthesia staff must maintain a low threshold to suspect $CO_2$ embolus if problems develop with intraoperative hemodynamics and/or oxygenation. Although $CO_2$ embolus can occur at any point in a laparoscopic procedure, the period of initial abdominal insufflation is a high-risk step. Malposition of either a Veress needle or primary trocar into a vessel or parenchymal organ can result in $CO_2$ embolus. The risk can be mitigated by using an optical trocar for initial access and by utilizing good Veress needle technique. In particular, aspiration from the Veress needle prior to insufflation is critical to assure that the needle tip does not lie within a vessel with attendant blood return. The incidence of $CO_2$ embolism during laparoscopy is exceedingly low but can have a fatal outcome with a reported mortality of 28% [14]. Clinical symptoms include systemic hypotension, dyspnea, cyanosis, tachycardia or bradycardia, arrhythmia or asystole [15]. Treatment entails desufflation, ventilation with 100% oxygen, head-down and left lateral decubitus (Durant's) position. In severe cases, an attempt to aspirate gas bubbles from the right atrium through a central line may be indicated.

Laparoscopic and robotic surgery are regularly performed with $CO_2$ insufflation pressures of 12–15 mmHg. However, elevation of the insufflation pressure to 20 mmHg is a common response to venous bleeding during a procedure. This increase in pressure can be remarkably effective in controlling bleeding and facilitating visualization. An increased insufflation pressure does have the potential to worsen venous return, renal blood flow, cardiac output and myocardial function, restrict diaphragmatic excursion, and increase $CO_2$ absorption, leading to hypercapnia and metabolic acidosis [16, 17]. Metabolic acidosis is compensated through hyperventilation and elimination of $CO_2$ through the lungs as well as by recruitment of endogenous buffer systems. Patients with limited pulmonary reserve will have less capacity to compensate for prolonged or high-pressure insufflation and need to be closely monitored for their reduced ability to eliminate excessive $CO_2$. Some authors have documented the safety of performing laparoscopic surgery under prolonged insufflation pressures of 20 mmHg in patients with normal pulmonary function [18]. It is important to recognize that traditional insufflators allow substantial fluctuation in abdominal pressure throughout surgery in response to leaks, suctioning, and instrument exchanges. More sophisticated modern insufflation systems, such as the AirSeal® device (Conmed, Utica, NY, USA), hold a very steady insufflation pressure at whatever value is selected and can withstand continuous suctioning without dropping pressure. Therefore, prolonged pressure at 20 mmHg using an AirSeal may be significantly more disruptive to normal hemodynamics, oxygenation, and acid–base balance than standard insufflation. We recommend elevating insufflation pressure to 20 mmHg as needed for bleeding but making a conscious effort to return to pressures of 12–15 mmHg as soon as it is feasible to do so during the case.

Abdominal insufflation can result in impaired renal function and low urine output during a laparoscopic procedure. These effects are believed to result from increased intra-abdominal pressure as well as hormonal changes from activation of the renin–angiotensin–aldosterone system [19]. Hemodynamic changes have a direct effect on parenchymal microperfusion and can lead to acute tubular necrosis and reduced glomerular filtration rate [20, 21]. Although these effects usually do not impair long-term renal function, patients with underlying chronic kidney disease may experience more significant transiently reduced urine output. Individual cases of irreversible kidney damage have been reported but these are relatively rare events [22]. Decreased urine output during insufflation should be anticipated and anesthesia staff should avoid overaggressive fluid resuscitation, which can lead to fluid overload and pulmonary complications [23].

The specific parameters of abdominal insufflation may also influence the degree of postoperative pain following laparoscopic surgery. Lower insufflation pressures have been clearly associated with decreased postoperative shoulder pain after laparoscopic cholecystectomy [24, 25]. Likewise, a prospective randomized trial demonstrated improved postoperative pain after laparoscopic gynecologic surgery when insufflation pressures were kept to 8 mmHg as compared to 12 or 15 mmHg [26]. In summary, we recommend keeping the duration of abdominal insufflation as brief and the pressure as low as possible for adequate surgical visualization to minimize the risk of intraoperative and postoperative sequelae.

## Patient positioning – considerations to prevent complications

Patient positioning must meet several requirements. The first, and most critical, consideration is assuring patient safety. The patient should be secured adequately to the table and all bony prominences and potential pressure points should be well padded. These considerations are especially critical in obese patients. Initial abdominal laparoscopic access often occurs in the supine position and the bed will often need to be moved prior to robot docking (i.e. tipped to the side). Testing the stability of the patient during bed movement is an important step before surgical draping. The anesthesia team must also have access to invasive lines and noninvasive monitoring sites (such as a blood pressure cuff) to allow troubleshooting during intraoperative care.

The second consideration in positioning is to provide acceptable access to the operative field for the surgeon so that the procedure can progress appropriately. The limited operating envelope of the da Vinci™ S and Si systems (Intuitive Surgical, Inc., Sunnyvale, CA, USA) constrains some of these choices for individual procedures unless redocking is planned. Patient positioning should take into account the docking path and position of the robot. The da Vinci Xi system provides substantially more flexibility in defining the operating envelope, allowing all four quadrants of the abdomen to be accessed from a single docking position. Likewise, potential conflicts of the robotic arms outside the patient should be factored into both patient and port positioning. These options may be limited in very thin patients or those of small stature. Even for laparoscopic procedures without robotic assistance, positioning the patient such that gravity can act to retract bowel is generally advantageous. This often means modified flank position for kidney cases and lithotomy with Trendelenburg position for pelvic cases. In all cases, the possibility of conversion to open surgery should be considered in positioning, particularly early in a minimally invasive surgeon's learning curve.

We position our laparoscopic and robotic kidney cases in a modified flank position (lateral decubitus) (Figure 88.1a). The side of the surgical site is elevated (left kidney–left side up) and the patient rests on a gel

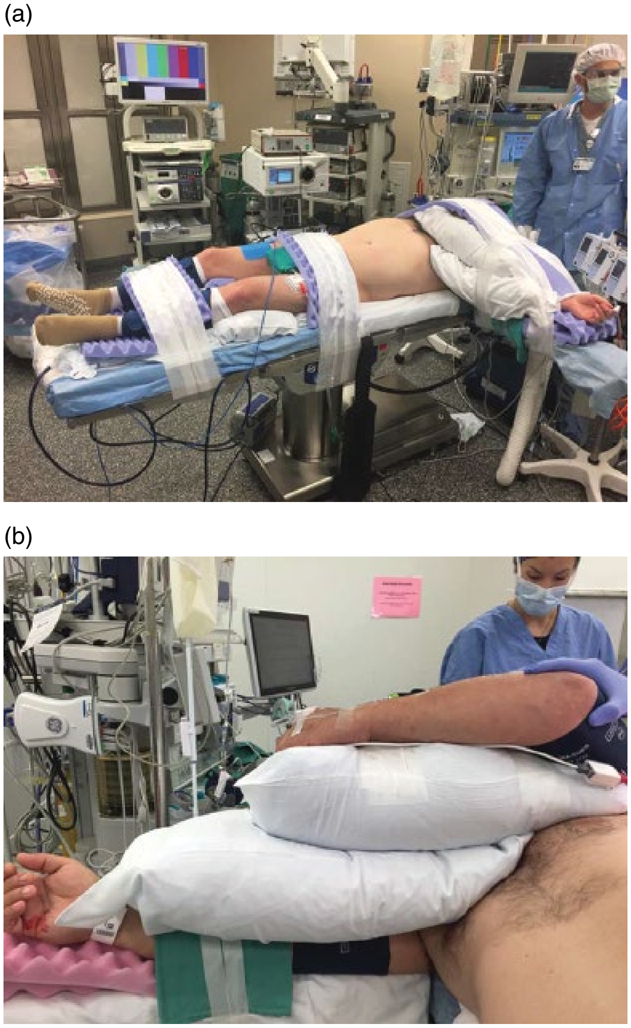

**Figure 88.1** (a, b) Example of patient positioning for laparoscopic and robotic renal surgery.

roll supporting the shoulders and the hip. The ipsilateral arm is brought over the contralateral side and is supported by pillows (Figure 88.1b) to pad all possible pressure points while avoiding overextension at the shoulder or elbow joints. Some surgeons prefer to place the ipsilateral arm along the patient's side to minimize potential contact with the cephelad robotic arm when working low in the retroperitoneum. The skin is covered with surgical foam and the patient is secured to the table with 3-inch (7.5 cm) silk surgical tape at the level of shoulders, hips and feet. We always test the position of the patient by turning the table sideways before the surgical skin preparation. For obese patients, we prefer to use extra tape and padding at the level of the hips and shoulders. Testing of the secure position prior to applying the drapes can help to reveal any weak points.

Patient positioning for pelvic surgery with the da Vinci S or Si systems requires Trendelenburg with the head down (30–40°) and the legs in lithotomy position. Since the da Vinci Xi system allows the arms to pivot on an overhanging boom, lithotomy position can be omitted for pelvic procedures with this system. To prevent the patient from shifting, the arms are usually secured on the sides with or without metal or plastic sleds. We use surgical foam and tape across the chest to prevent shifting toward the head. Custom-made support systems are available, providing additional support of the shoulders and holding the body in place (TrenGuard™, Pink Pad™) without tape across the chest. For obese patients undergoing pelvic surgery, assuring that the patient can be adequately ventilated when in steep Trendelenburg position should be confirmed with the anesthesia team prior to skin incision.

## Nerve injuries

The most common complications in laparoscopy are vascular, bowel, or adjacent organ injuries but peripheral nerve injuries related to positioning can have a substantial impact on postoperative quality of life. Nerve injuries result in up to 16% of anesthesia-related malpractice claims [27]. A recent analysis of >380,000 anesthesia cases across all surgical specialties revealed only 112 cases of true perioperative nerve injury (0.03%) but 13% of the detected injuries occurred during urologic surgery [28, 29]. Moreover, a review of 2775 urologic laparoscopic cases reported postoperative neuromuscular pain in 5.4% of patients [30]. Knowledge of the most sensitive pressure points can help to reduce the incidence of these type of injuries. The most common injuries arise from overstretching the brachial plexus, or compression of the peroneal or ulnar nerves.

## Rhabdomyolysis

Careful padding is also warranted to prevent postoperative rhabdomyolysis, a pressure-induced tissue injury leading to necrosis of muscle cells. Multiple factors associated with rhabdomyolysis, including hypovolemia, myoglobinuria, and metabolic acidosis, may cause acute kidney injury or renal failure [31]. Rhabdomyolysis is a relatively rare complication of urologic surgery. A recent outcome analysis reported only 870 events out of more than one million urologic cases [32]. However, a known risk factor for rhabdomyolysis is prolonged operative time [33]. This can be a significant risk in laparoscopic and robotic cases early in a surgeon's learning curve. The incidence of rhabdomyolysis in urologic laparoscopic cases has been reported to be as high as 1% [33, 34]. Immediate postoperative muscular pain, particularly in the buttock, hip, or flank should raise concern for potential rhabdomyolysis. Treatment consists of aggressive hydration and diuresis. Hemodynamic support and temporary dialysis may be required in more severe cases.

## Extremity compartment syndrome

Compartment syndrome of an extremity is increased pressure within a closed fascial compartment resulting in perfusion compromise and tissue injury [35]. This most frequently occurs in the trauma setting but can be diagnosed after surgery. In the setting of urologic procedures, compartment syndrome much more commonly involves the lower extremities. The terminology for cases in the lower limb is "well leg compartment syndrome" (WLCS) and will typically occur after prolonged surgery in the lithotomy position. Modifiable factors including heel support, modified lithotomy, avoidance of Trendelenburg and ankle dorsiflexion, as well as the use of intermittent compression devices may reduce the incidence. Extremity compartment syndrome is a clinical diagnosis and should be considered in cases of severe leg pain, lower limb swelling, plantar hypoesthesia, absence of pulse, and pallor. Confirmation of compartment pressures can be performed using a needle inserted into the compartment and connected to a pressure transducer [36, 37]. The treatment is immediate surgical decompression with fasciotomy.

## Infectious complications

The risk of urinary tract infection following laparoscopic surgery should not exceed that following open surgery. Clearly documenting a negative urine culture prior to any procedure in which the urinary tract will be violated is appropriate surgical practice. For laparoscopic nephrectomy, the rate of postoperative urinary tract infection has been reported to be 1.4% [38]. Even though some laparoscopic procedures may have significantly longer operative times than their open equivalents, this does not appear to result in an increased risk of sepsis, pneumonia, or surgical site infection [38].

## Thromboembolic complications

Thromboembolic complications, including deep venous thrombosis and pulmonary embolus, are some of the most common complications occurring after major surgery. A full description of risk mitigation and management of these complications is outside the scope of this chapter and the reader is referred to detailed recent reviews on this topic [39–42]. Several lines of evidence suggest that thromboembolic complications are less common in minimally invasive urologic, colorectal, and gynecologic procedures as compared to their open counterparts [43–45]. This is despite longer operative times and the negative influence of pneumoperitoneum on venous return for laparoscopic procedures.

## Intraoperative surgical complications

### Vascular injuries and intraoperative bleeding (see Video 88.1)

The most common type of intraoperative complication in urologic laparoscopic surgery is vascular injury, which has been reported to occur in 1.7–1.9% of cases [30, 46]. Urologic procedures in the retroperitoneum and the pelvis require identification, dissection, and preservation of major vessels including the aorta, vena cava, renal arteries and veins, superior mesenteric artery, inferior mesenteric artery, and iliac arteries and veins. The frequency of vascular injuries during urologic surgery differs from gynecologic surgery, when the most common vascular injuries occur during trocar insertion [47, 48]. Placement of trocars into a desufflated abdomen is strongly discouraged and has been associated with serious vascular injuries [49, 50]. During closed insufflation, placement of a Veress needle should not be limited only to the umbilicus. However, the surgeon should be aware of which structures are at risk for injury when placing the needle elsewhere in the abdomen (Figure 88.2).

The most effective way to avoid injury to major vessels is to anticipate the micro-events that lead to these complications in advance. One critical step is a thorough review of the relevant imaging preoperatively to identify any vascular anomalies and establish the relationship of the pathology in question to vascular structures. Early in a surgeon's experience, the use of multi-plane reconstructions and CT-angiograms may aid in defining this anatomy.

For nephrectomy procedures, prior knowledge of the number of arteries and veins serving the kidney facilitates a safe procedure. For retroperitoneal surgery on the left side, critical anatomic factors to anticipate include the presence of a large lumbar vein behind the renal artery, the location of the adrenal vein and the presence or absence of a retroaortic renal vein component. (Figure 88.3) The surgeon also needs to recognize the often intimate relationship of the superior mesenteric artery to the renal hilum to prevent a catastrophic complication [51]. On the right side, the junctions of the gonadal and adrenal veins to the vena cava are weak points that should be treated with caution. In pelvic surgery, the iliac vessels and branches are the primary source of major bleeding. Laparoscopic and robotic surgery provide less tactile feedback to aid in dissection, so these approaches demand the surgeon to maintain proper orientation and use visual cues to identify and preserve major vessels [52]. This is particularly critical in robotic cases where shifting orientation by 90° requires only a twist of the surgeon's wrists and may go unrecognized by both the console surgeon and bedside assistant. The robotic arms are also very strong and can inadvertently avulse major vessels if not monitored visually by the console surgeon [53]. In the case of a large renal mass, parasitic vessels due to neoplastic angiogenesis should be taken into consideration as well as the presence of regional lymphadenopathy that may limit safe access to the hilar vessels. In rare cases with bulky retroperitoneal lymphadenopathy, presurgical embolization of the renal artery may be advantageous [54–56]. Finally, for complex cases requiring vena caval thrombectomy, anatomy and the urologic surgeon's experience level should determine whether preoperative vascular or cardiothoracic surgery consultation is indicated. It is important to recognize that vascular surgeons facile with laparoscopic or robotic surgery are uncommon so their involvement may require open conversion at many institutions.

It makes sense to differentiate between two types of vascular injuries: (i) those intraoperative injuries that are immediately recognized and definitively dealt with during surgery; and (ii) unrecognized injuries that result in bleeding requiring blood transfusion, surgical exploration, or endovascular intervention in the postoperative period. A single institutional analysis from the Cleveland Clinic in 2007 reported intraoperative hemorrhage in 2.3% and postoperative bleeding events in 2.7% of 1867 laparoscopic oncologic cases [57]. Access-related vascular

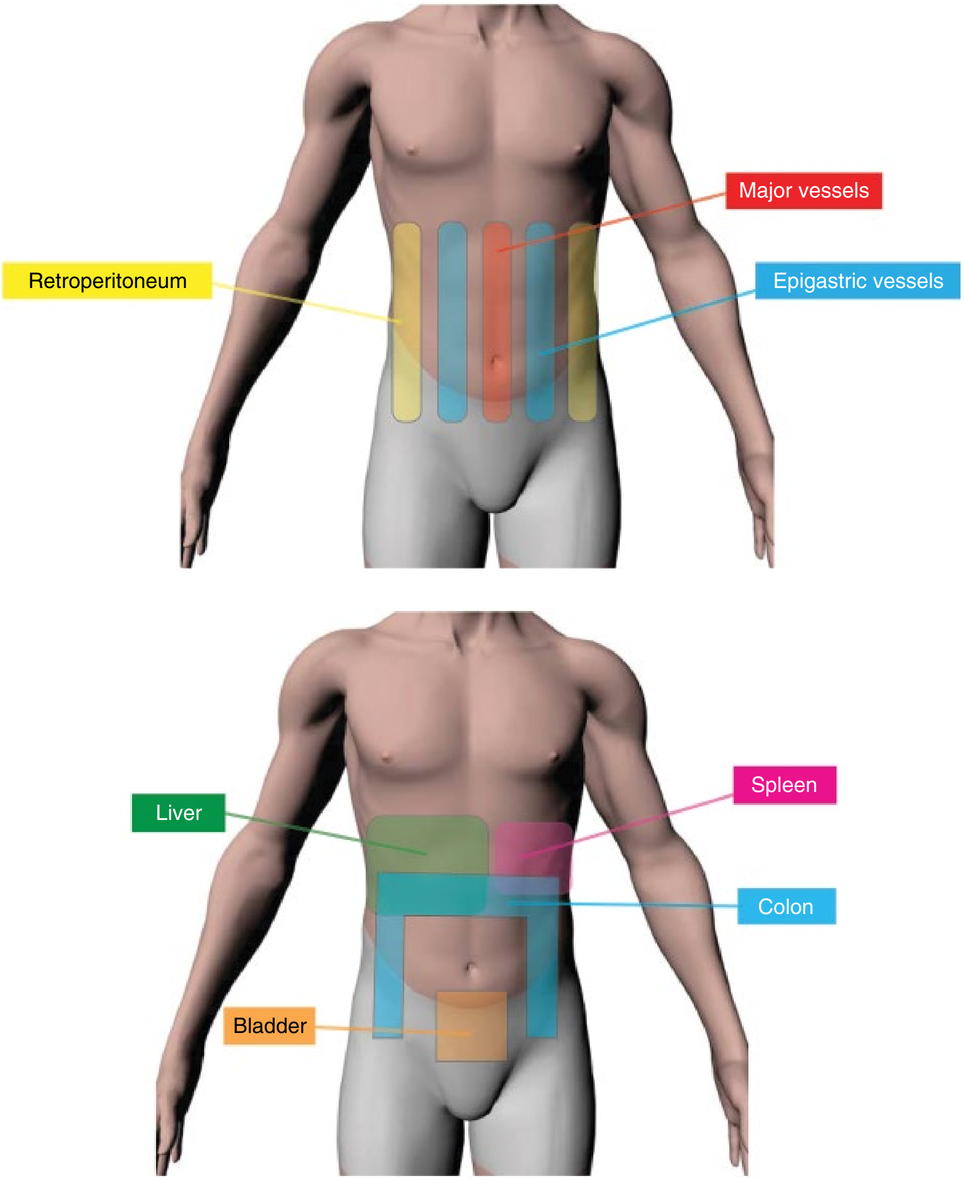

**Figure 88.2** Structures at risk during placement of a Veress needle for insufflation throughout the abdomen.

injuries most often involve the epigastric arteries or superficial vessels of the abdominal wall [58].

The minimally invasive surgeon should have a regimented plan in place to address bleeding during laparoscopic and robotic surgery. This process can be broken down into two phases: an initial "damage control" phase and a subsequent "definitive control" phase (Figure 88.4). During the damage control phase, the surgeon must rapidly assess (i) the scale of the bleeding; (ii) whether it is of arterial or venous origin; (iii) whether it can be temporarily controlled with local pressure; and (iv) whether definitive control will likely outmatch the surgeon's minimally invasive skill set and require open conversion. The first move in a moment of brisk bleeding should always be to apply pressure. This can be achieved by either grasping the vessel or stump involved or by applying pressure with a quickly inserted gauze (either an opened 4 × 4 sponge or a thin-profiled laparotomy pad designed to pass through a 12 mm trocar). The laparoscopic suction device is also very useful in safely exerting pressure. The vast majority of venous vascular injuries can be temporarily controlled with pressure and do not require rapid open conversion. This is a much wiser course of action than firing multiple clips in a semi-blind fashion as these clips may significantly compromise later attempts at definitive control if they are not immediately effective. Next the insufflation pressure should be raised to 20 mmHg. This will help to reduce most venous bleeding

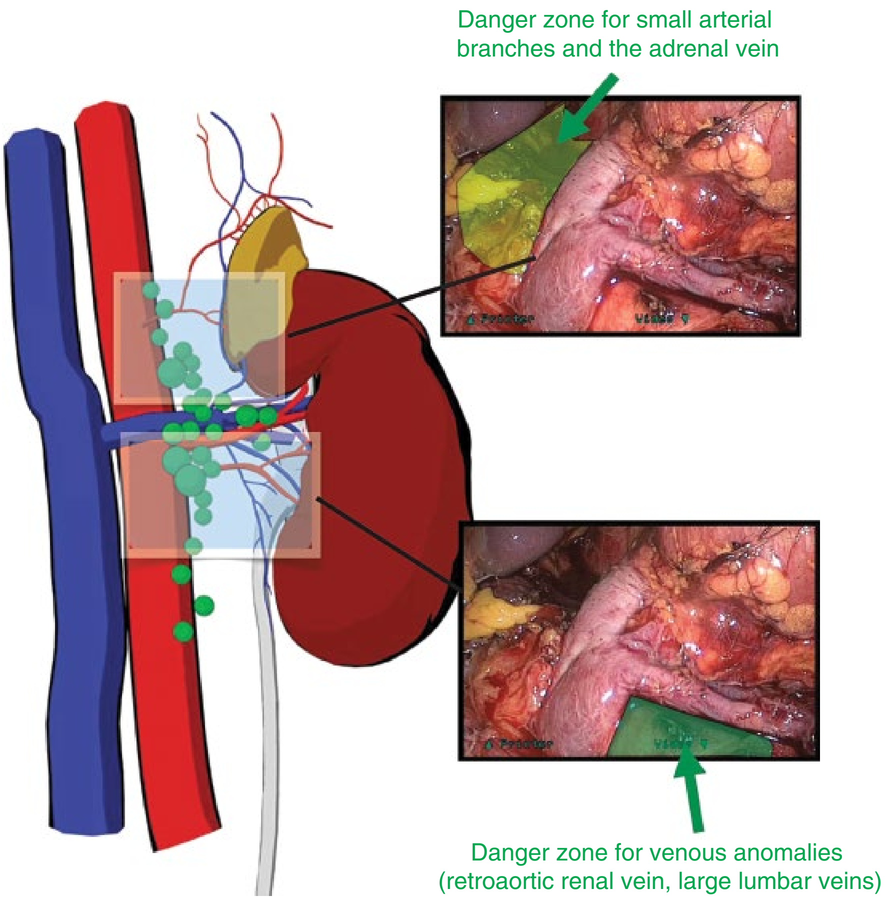
Danger zone for small arterial branches and the adrenal vein
Danger zone for venous anomalies (retroaortic renal vein, large lumbar veins)

**Figure 88.3** Example of anticipating micro-events during left renal dissection that can result in preventable vascular injury.

Phase I (Damage Control)

1. How bad is the blood loss potential?
2. Is this likely arterial or venous in origin?
3. Can I realistically handle this laparoscopically with my skill set?

**Short term damage control maneuvers**

Notify anesthesia that there is a problem
Attempt to grasp the vessel or stump
Elevate pneumoperitoneum pressure
Introduce gauze and hold pressure

Phase II (Definitive Control)

1. Reassess response to damage control maneuvers
2. Decide on goal:
   a. Solve laparoscopically/robotically
   or
   b. Facilitate safe open conversion

**Permanent control**

GO GO

Get the necessary help in the room
Place additional ports, get more exposure
Clip, staple, bipolar, suture to solve problem
Try to avoid creating additional problems during fix

**Figure 88.4** Managing intraoperative bleeding during minimally invasive surgery.

and improve visualization. Communication is key in this situation. Stay calm and explain to the OR staff and anesthesiologist the situation and give specific instructions as to what is needed next. Anesthesia may need to catch up on fluid management or have blood transported into the room.

If temporary local control can be achieved with pressure and increased pneumoperitoneum, the next step is to set the stage for the definitive control phase. This may require placement of additional ports to facilitate laparoscopic suturing or improve exposure, getting additional or more experienced surgical assistants in the room, or accumulating specialty equipment needed for definitive control (e.g. Lapra-Ty® or Hem-o-lock® Clip appliers, proline sutures, etc.). In cases where local pressure is effective but exposure precludes definitive control, an assistant can be assigned to hold pressure while the primary surgeon performs additional dissection to improve access to the injury. If the surgeon feels that open conversion may ultimately be needed, this would be the time to prepare those instruments.

Smaller scale bleeding can usually be controlled by using either bipolar cautery or a radio frequency vessel sealant device (e.g. Ligasure™ or Enseal®). Larger vessels requiring repair can be closed by laparoscopic suturing. We prefer to use a 4-0 prolene suture on an SH needle with a Lapra-Ty and a knot on the end. A first pass through the both sides of the defect will approximate the edges and allows the surgeon to apply tension, facilitating exposure and the next throw. This approach is particularly applicable to vena caval injuries and does not require the placement of intracorporeal knots in a bloody field. Hilar bleeding during nephrectomy may often create a situation where the laparoscopic stapler has to be used earlier than anticipated for vascular control. Early mobilization of the kidney with lifting of the lower pole and dissection of the upper pole before marching toward the hilum is a good policy that improves exposure of the hilum and provides more options should a vascular injury subsequently occur. An important consideration prior to using a vascular stapler is the location of any metal or plastic vascular clips around the hilum which could cause a stapler misfire. We prefer to exclusively use a vessel sealer for perihilar dissection and only place clips after the vascular stapling has been completed. The adrenal and lumbar veins can be taken with a vessel sealer in most cases. A harmonic scalpel is a valid alternative but this device does not provide an auditory tone confirming vascular sealing and has an unguarded vibratory blade that can achieve high temperatures and injure surrounding structures if not carefully controlled. Always confirm the correct position of the stapler prior to firing. In a nondonor nephrectomy, it is usually advisable to move the stapler away from the caval or aortic insertion toward the kidney so as to leave a controllable stump behind in case of a misfire event (Figure 88.5). It is also critical to visualize the tip of the stapler prior to firing. This prevents loading too much tissue for effective staple occlusion and avoids pass-pointing and potential injury to structures behind the vessel.

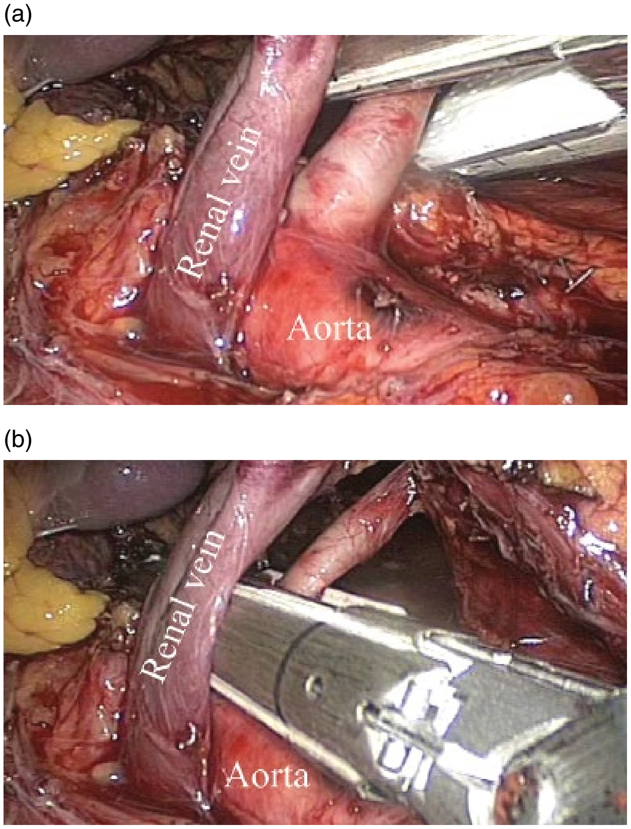

**Figure 88.5** Alternatives for endovascular stapler placement on the left renal artery. (a) Safer position: placing vascular stapler more distal on the renal artery to leave a stump. This makes it far easier to control should the stapler misfire. If a stapler misfire occurs, this position also allows proximal control of the renal artery prior to opening the stapler and may prevent major bleeding. Adequate exposure of the proximal artery minimizes the chance that an early branch will not be controlled by the stapler in this position. (b) More risky position: placing the vascular stapler flush to the surface of the aorta to transect the renal artery. In the event of a stapler misfire, this leaves a hole in the aorta which is far more difficult to control than a long renal artery stump. Note that the position flush with the abdominal aorta (b) may be necessary when it is essential to preserve vascular length (i.e. donor nephrectomy), but provides far fewer options for vascular control should the stapler misfire.

The specific circumstances of brisk bleeding during robotic surgery require some elaboration. Robotic-assisted laparoscopic procedures separate the console surgeon from the bedside assistant and necessarily create challenges during active bleeding. The robot provides some advantages, particularly during the definitive control phase, due to faster and more precise suturing. However, during the damage control phase, the robotic system may be disadvantageous. The bedside assistant is generally responsible for suctioning and providing exposure, rapidly changing instruments, and inserting gauze. Depending on the skill and experience level of the bedside assistant, this may not be ideal in a high-pressure situation. The console surgeon is also not scrubbed and is physically separated from the operative field, which can limit options to take over during critical steps of damage control.

In some cases, the scale of the vascular injury is simply too substantial to control with a minimally invasive approach. The goal in these situations should be a controlled, methodical open conversion that minimizes unnecessary blood loss and allows efficient control of the injury and completion of the surgery. The choice of incision should be dictated by what needs to be accomplished, not by the position of preexisting laparoscopic ports. For retroperitoneal cases, a subcostal or midline incision will likely be the most advantageous. In robotic cases, rapid removal of the robot from the field may be necessary and should be planned in advance. Maintaining pneumoperitoneum as long as possible may be beneficial in minimizing blood loss from large venous injuries. Prepacking the area with laparoscopic trocar-compatible laparotomy pads may also be advantageous prior to opening. Although rapid "crash" open conversions are occasionally required in cases of large arterial injuries, a controlled and organized open conversion will minimize blood loss when feasible.

## Postoperative bleeding

Postoperative bleeding, outside of the setting of uncontrolled coagulopathy, is usually due to an unrecognized vascular injury. During laparoscopic surgery, the pneumoperitoneum may tamponade venous bleeding that may manifest after the case is concluded and the abdomen is desufflated. Careful assessment of the entire operative field at low insufflation pressures (<10 mmHg) is prudent prior to desufflation and trocar removal. Trocars should also be removed under direct laparoscopic vision to exclude injuries to abdominal wall vessels (i.e. epigastric arteries) that may bleed postoperatively. Patients who are hemodynamically stable and present in a delayed fashion with declining hemoglobin can often be managed conservatively with blood transfusion. When re-explored, these patients frequently do not have a correctable source of blood loss [59]. In contrast, when patients present with early hemodynamic instability after laparoscopic surgery, surgical re-exploration is indicated and may identify an arterial injury that can be controlled.

A complication specific to nephron-sparing kidney surgery is the formation of renal arteriovenous fistulas or pseudoaneurysms [60–63]. A result of a vascular injuries within the kidney parenchyma during partial nephrectomy, pseudoaneurysms typically declare themselves 1–3 weeks after surgery with gross hematuria or other clinical signs of a bleeding [64]. These injuries are also seen after percutaneous nephrostolithotomy and renal biopsies. Selective angiographic embolization is usually the modality of choice to control bleeding and preserve renal function in these cases [64, 65].

## Injury to bowel and adjacent organs

Bowel injuries occur most frequently during abdominal access for laparoscopic surgery. A Cochrane meta-analysis reported equivalent complications rates for open versus closed (Veress) techniques with regards to their complication rate with an overall rate of visceral injury upon entry of 0.13% [66]. For closed access, common sense dictates avoiding the site of previous surgical scars. Once the Veress needle is placed, we prefer to aspirate with a syringe to ensure that neither blood nor bowel contents are encountered. Some surgeons prefer a saline drop test to be assured of proper placement within the peritoneal cavity. The goal is to avoid insufflation of a hollow or solid viscus or a vessel, which might lead to $CO_2$ embolus.

Today, there are a wide range of innovative technologies available to aid safe abdominal access in complex laparoscopic cases. These include the widespread use of optical trocars, which allow the surgeon to monitor passage of the trocar through the sequential layers of the abdominal wall. Other useful tools include 1.9 Fr laparoscopes that can be passed through a 2 mm trocar, working laparoscopes that facilitate lysis of adhesions, and single-site trocar options that allow open access and the use of multiple instruments through the same site (i.e. GelPOINT™; Applied Medical, Rancho Santa Margarita, CA, USA). The full spectrum of available options is beyond the scope of this chapter but the reader is directed toward several comprehensive reviews of this topic in the literature [66–68].

If a bowel injury with the Veress needle is suspected, a separate attempt to achieve access elsewhere in the abdomen may be indicated. Leaving the original needle in place aids in identifying the site of injury once laparoscopic access has been achieved elsewhere. Most injuries from a Veress needle do not require bowel resection although they may warrant reinforcement with an interrupted suture.

Sharp injuries to small and large bowel during operative dissection, when identified expeditiously, can generally be repaired primarily. Unfortunately, the most common laparoscopic bowel injuries are caused by electrocautery and should be managed more aggressively [69]. Fulgurated tissue needs to be excised before the enterotomy can be closed. For small bowel or colon injuries, interrupted suture with 3-0 polyglactin or silk on an SH needle. In cases of more significant injuries, a bowel resection and re-anastamosis may be required. Intraoperative general surgery consultation should be considered in these cases.

Many iatrogenic laparoscopic bowel injuries, particularly those caused by electrocautery or thermal injury, will not be recognized intraoperatively and will present in a delayed fashion [70]. In a recent large meta-analysis of >450 000 gynecologic laparoscopic procedures, 41% of the 604 bowel injuries presented in a delayed fashion [71]. In the urologic literature, as high as 69% of laparoscopic bowel injuries presented in a delayed fashion [69]. Some of these injuries are missed because they occur outside the surgeon's visual field due to instrument insulation defects or capacitive coupling [72, 73]. The risk of these injuries may be lessened by using shielded instruments with active electrode management [74]. The clinical presentation of delayed bowel injury after laparoscopic surgery can be subtle. These patients often present without the fever, leukocytosis, and diffuse abdominal exam findings (involuntary guarding, rebound tenderness) indicative of generalized peritonitis after open surgery. In contrast, patients who sustain bowel injuries during laparoscopic surgery often present with more subtle findings: localized trocar pain, abdominal distension, diarrhea, and leukopenia followed by cardiopulmonary collapse due to sepsis [69]. Surgeons should maintain a high index of suspicion for bowel injury in laparoscopic patients who do not progress appropriately after surgery and should have a low threshold to image these patients with CT scans.

Pancreatic injuries during urologic laparoscopy are rare (<0.5%) [75] but the organ is at risk due to the proximity of the pancreatic tail to the hilum of the left kidney and the left adrenal gland. Unrecognized pancreatic injuries can result in very significant morbidity. Management of pancreatic injuries identified during laparoscopic surgery often requires complex decision-making and we encourage intraoperative consultation with general surgery in these cases. In the absence of a clear injury but with some index of suspicion, draining the area with a close suction drain may be warranted.

Injuries to the spleen may occur during the release of the splenic flexure and the mobilization of the kidney from its splenic attachments during left nephrectomy or renal mobilization. Splenic injuries occur in 0.55–5.1% of these patients [76, 77]. Most splenic injuries result from indirect traction rather than direct perforation of the spleen with laparoscopic instruments. Small superficial capsular splenic tears can often be managed with a combination of bipolar cautery, argon beam coagulation and hemostatic products such as Surgicel® (Ethicon, Cincinnati, OH, USA) and fibrin glues [78]. More substantial and deeper lacerations to the spleen may require concurrent splenectomy [79]. Again, maintaining a low threshold to consult general surgery to assess a laparoscopic splenic injury and guide decision-making is appropriate.

## Injuries and complications associated with the urinary tract

Injuries to the urinary tract can occur during retroperitoneal and pelvic laparoscopic and robotic procedures. Identification and preservation of the ureters is an important step of procedures involving the kidney or pelvic vasculature. Likewise, injuries to the bladder can occur during pelvic surgery and should be identified and closed. Although ureteral injuries are uncommon during urologic, colorectal, and gynecologic procedures (<1% incidence), the relative risk of ureteral injury with laparoscopic surgery may be 4- to 6-fold higher than during open surgery [80, 81]. When ureteral injuries are identified intraoperatively, they can usually be repaired using minimally invasive techniques in experienced hands.

Variants of laparoscopic partial nephrectomy, including the robotic-assisted form, are now commonly applied procedures to treat most T1 and a subset of T2 renal masses. Over the past decade, the range of tumor characteristics considered appropriate for partial nephrectomy has expanded to include larger, more central and more complex tumors. These procedures often entail entry intro and resection of the kidney collecting system. However, the risk of postoperative urine leak remains <5% [82–85]. Management includes percutaneous drainage of the urinoma and occasionally collecting system decompression with either an internal ureteral stent or a nephrostomy tube if there is distal obstruction and poor drainage. In the absence of a large devascularized renal segment, almost all urine leaks with eventually close with conservative management.

## Injuries to the diaphram and pleura

The rate of inadvertent diaphragmatic and pleural injury during renal and adrenal laparoscopic surgery has been reported to be between 0.7 and 3.6% in large series of laparoscopic urologic cases [30, 86]. Despite the relative rarity of this complication, an unrecognized injury can result in tension capnothorax and cause significant intraoperative respiratory and hemodynamic distress. Diaphragmatic injuries occur most commonly when removing large upper pole renal or adrenal tumors or in the setting of substantial retroperitoneal inflammation obscuring normal tissue planes (i.e. xanthogranulomatous pyelonephritis). "Billowing" of the diaphragm during laparoscopic surgery should raise concerns about a diaphragmatic injury. Good communication between

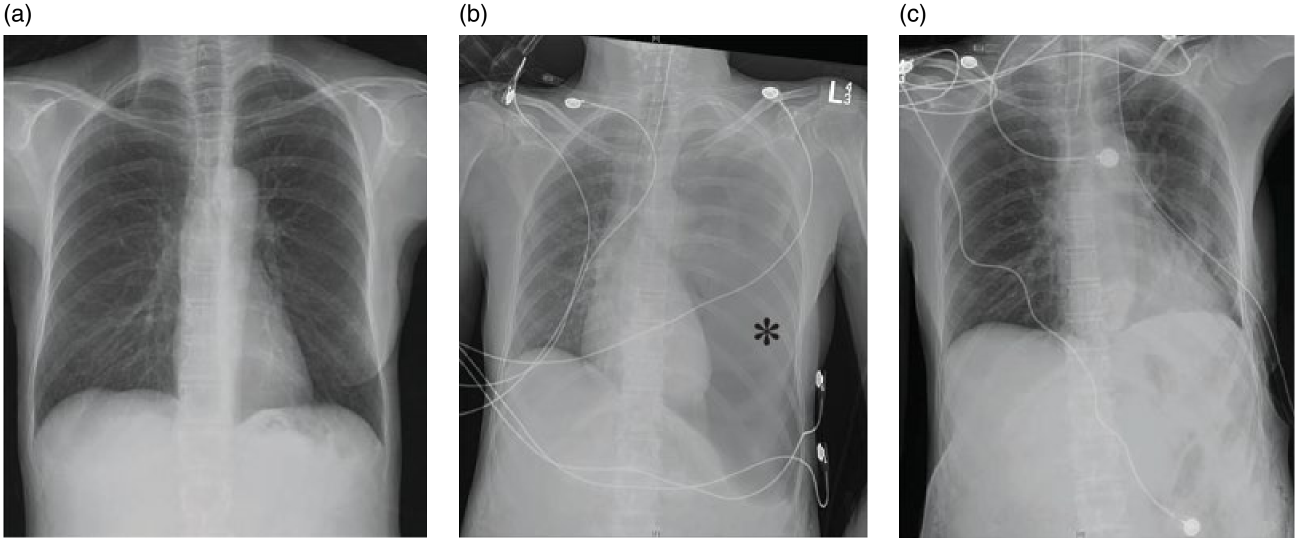

**Figure 88.6** (a) Preoperative. (b) Large left tension capnothorax (*) resulting in intraoperative respiratory and hemodynamic compromise during laparoscopic renal surgery. (c) Resolution with laparoscopic diaphragm repair and thoracostomy tube placement.

the surgical and anesthetic teams is important to recognize and address this problem uneventfully. Most small diaphragmatic/pleural injuries can be easily repaired laparoscopically with evacuation of $CO_2$ from the pleural space [86, 87]. Mesh and gelatin matrix have been used to successfully repair larger defects in the diaphragm [86, 88, 89]. Since $CO_2$ is much more rapidly absorbed than room air, a small to moderate capnothorax can often be managed conservatively without placement of a thoracostomy tube in a stable patient [90]. After diaphragmatic repair, we recommend an on-table chest radiograph prior to extubation to confirm lung reinflation. Patients with a large residual capnothorax or a tension capnothorax with hemodynamic/respiratory distress should be managed with immediate thoracostomy tube placement prior to extubation (Figure 88.6).

## Lymphatic leaks and chylous ascites

Injuries to small lymphatic vessels are common during laparoscopic retroperitoneal and pelvic dissection and generally heal without major sequelae. High-risk procedures for more significant leaks include those requiring extensive dissection along major vessels: retroperitoneal lymphadenectomy, donor nephrectomy and pelvic lymphadenectomy. Lymphatic leaks from damaged low pressure lymph channels can be challenging to identify under standard pneumoperitoneum pressures. Meticulous surgical technique to achieve lymphostasis using mechanical clips and vessel sealing devices can decrease the risk of postoperative lymphatic leaks and lymphocele formation. This is particularly important in the pelvis where lymphoceles can compromise venous return from the lower extremities and may increase the risk of deep venous thrombosis [43, 91, 92].

Chylous ascites (CA) is the accumulation of chyle (lymphatic fluid) within the peritoneal cavity (Figure 88.7) and can be a devastating complication of retroperitoneal laparoscopic surgery [93, 94]. CA can also result from congenital defects, inflammatory processes, or trauma. Following laparoscopic nephrectomy, the incidence of CA has been reported to be between 0.6 and 5.9% [95]. Abdominal aortic surgery is responsible for >80% of patients presenting with postoperative CA [96], likely due to injury to retroperitoneal lymphatics and the cisterna chyli [93]. The anatomic location of the cisterna chyli posterior to the left diaphragmatic crus puts it at risk during extensive vascular dissection above the left renal hilum, such as that required for laparoscopic donor nephrectomy [97, 98].

Clinically, CA may present early after surgery with milky fluid draining from surgical drains or directly from trocar sites. If assayed, the triglyceride content of this fluid will be high. Patients may be asymptomatic or manifest signs of ileus and abdominal distension. Untreated CA can result in severe malnutrition and protein loss. Once diagnosed, dietary management can be effective in controlling CA. Since dietary fat content determines the volume of lymphatic fluid derived from the bowel, fat restriction and a diet limited to medium-chain fatty acids can slow lymphatic leak. In many cases, total parenteral nutrition may be necessary to control the leak over a period of weeks. For persistent CA, management options include somatostatin analogs, paracentesis for symptom control, lymphoscintography, lymphangiography and occasionally surgical exploration [93–95].

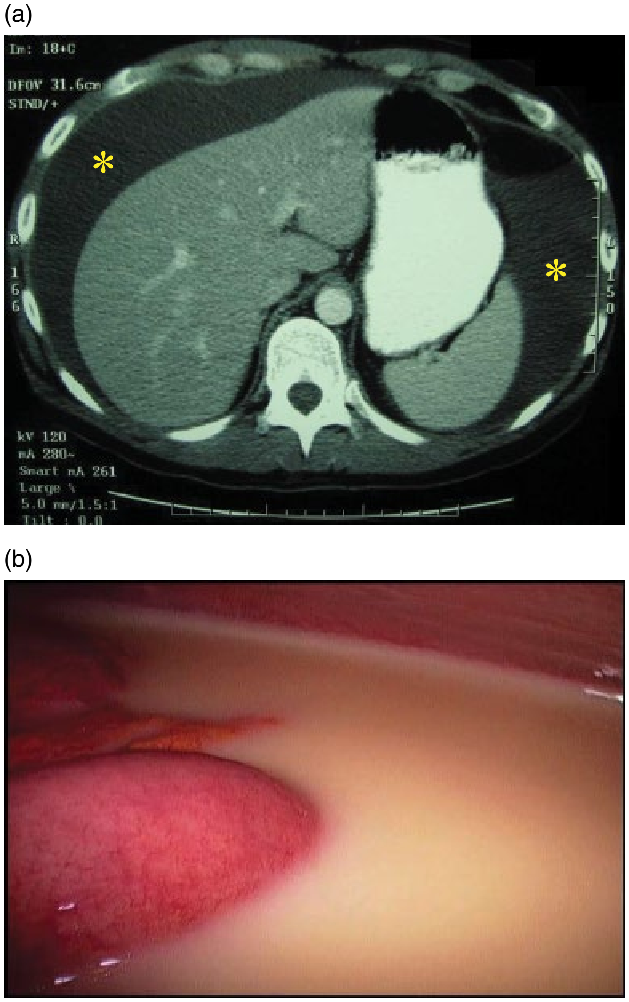

**Figure 88.7** Chylous ascites following retroperitoneal lymphadenectomy for testes cancer. (a) CT scan demonstrating a large volume of low-density fluid in the peritoneal cavity (*). (b) Intraoperative view of milky intraperitoneal fluid during exploratory laparoscopy eight weeks after the original lymphadenectomy [93]. *Source*: Link RE, Amin N, and Kavoussi LR. Chylousascites following retroperitoneal lymphadenectomy for testes cancer. *Nat Clin Pract Urol* 2006;3(4):226–232. Reproduced with permission of Nature Publishing Group.

## Complications of robotic surgery

Robotic surgical systems have been used for urologic procedures since 2000 [99,100]. In addition to the complications seen in laparoscopic surgery, there are adverse events specific to the use of a robotic system. Software, electrical, or mechanical malfunctions may result in interruption or prolongation of a surgical procedure, conversion to laparoscopic or open surgery, reoperation, and, in rare instances, patient injury.

Device and instrument malfunctions include system errors, loss of video or imaging problems, falling of broken or burnt pieces into the patient's body, electrical arcing or sparking of instruments and broken tip covers, instruments not recognized by the system, instruments not working, and unintended or unstoppable instruments started without the surgeon's command [101, 102]. The electrical current leaking from monopolar scissors may result in thermal injury, and uncontrollable instruments may lead to direct tissue or organ injury.

Although device malfunction accounts for most of the reported adverse events, surgeon error during robotic surgery could also be a factor. There is a loss of tactile sensation during robotic surgery, and this lack of haptic feedback is usually adequately compensated for by the use of visual cues. However, in the hands of an inexperienced surgeon, robotic instruments may apply large forces on tissue, resulting in tissue injury.

Patient positioning is also critical during robotic procedures. For lengthy procedures, improper positioning of the patient may result in nerve injury and pressure ulcers. While a time-limited steep Trendelenburg position such as the one used during robotic prostatectomy is safe, a prolonged steep Trendelenburg has been shown to increase intraocular pressure in a time-dependent fashion [103, 104], and there have been reports of ischemic optic neuropathy after lengthy procedures in patients with preexisting ocular disease [105, 106]. It may also cause reduced venous outflow from the head, resulting in laryngeal edema and difficult extubation [107]. Shifts in patient position may sometimes go unnoticed as the surgeon is in a console away from the patient, and the robotic arms and extensive draping may partially block the view of the patient [108]. If this displacement is substantial, it may result in the robotic arms or the camera head delivering pressure damage to body parts such as the iliac crest, chest, or head.

Robotic instrument malfunctions are infrequent and most do not result in complications [102]. With adequate preventive measures, proper training and experience, robotic urologic surgery is at least non-inferior to laparoscopic or open surgery in terms of complication rates [109–111].

## Conclusion

In this chapter, we outline the common complications associated with laparoscopic and robotic urologic surgery. These complications are a function of (i) the specific physiologic stresses associated with pneumoperitoneum; (ii) the technical challenges inherent in the use of laparoscopic and robotic surgical instruments; and (iii) the organs and structures at risk in the retroperitoneum and pelvis where these procedures take place. Complications are unavoidable during surgery but anticipating and controlling the micro-events that cause them can help to minimize risk.

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# Pelvic Lymphadenectomy

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## Introduction

Pelvic lymphadenectomy is the most accurate method of diagnosing lymph node involvement in patients with genitourinary malignancies. In practice, this is most commonly seen in patients with prostate and bladder cancer, but may also be performed in patients with penile or urethral cancers. Histologic confirmation of metastatic disease within the pelvic lymph nodes provides significant prognostic data and potentially therapeutic benefit. Additionally, this information may help guide the decision for future, adjuvant therapy [1, 2]. Minimally invasive pelvic lymphadenectomy (laparoscopic or robotic) offers a nodal yield similar to that from open surgery, but with improved convalescence [3]. Herein we describe the anatomy, procedure, and complications of minimally invasive pelvic lymph node dissection. Our procedure section specifically describes the robotic approach, but an identical dissection can be performed laparoscopically with similar benefits in visualization during the procedure and recovery afterwards.

### Accepted templates for pelvic lymph node dissection

There are varying definitions describing the extent of a pelvic lymph node dissection. Herein we describe the technique for each. The "limited template" (LT), also known as the standard template, lymph node dissection involves the nodes of the obturator fossa between the obturator nerve and external iliac vein. The lateral border of the dissection is the pelvic sidewall and medial border is the bladder. The tissue removed includes from the node of Cloquet to the bifurcation of the iliac vein proximally. The LT is commonly performed for low- and intermediate-risk prostate cancer. The "extended template" (ET) includes all the nodes in the LT, in addition to the nodes surrounding the external iliac artery back to the level of the common iliac artery at the level of the ureter crossing into the deep pelvis. The dissection also includes the tissue laterally from the external iliac artery to the genitofemoral nerve. Also included is tissue surrounding and deep to obturator nerve. The ET often includes the nodes in the presacral area. A "super extended template" (SET) includes the nodes of the LT and ET in addition to the nodes around the proximal common iliac artery and veins bilaterally up to the bifurcation of the aorta and the periaortic nodes up to the inferior mesenteric artery.

## Prostate cancer

Lymph node metastases in prostate cancer are reported to range from 4% to 6% in patients undergoing lymphadenectomy [4]. Nodal spread is associated with higher Gleason score, higher pT stage, older age, and higher incidence of positive surgical margin [5]. In addition, the number of positive lymph nodes found at surgery impacts overall survival. Patients with 1 or 2 positive nodes were found to have a clinical recurrence-free survival (no physical, radiographic, or symptomatic evidence of recurrence) of 70% and 73% at 10 years, whereas those with greater than 5 positive nodes were found to have a clinical recurrence-free survival of 49% at 10 years. This study did not compare prostate specific antigen (PSA), only recurrence between these groups. Overall survival between these two groups at 10 years was 74% versus 49% [6]. Touijer et al. reported a 78% overall 5-year progression-free probability for all prostate cancer risk groups, but noted a 49% 3-year progression-free probability in lymph node-positive patients. All of these patients experienced a clinical recurrence within 5 years [7].

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## Lymph node imaging

Imaging has been consistently unreliable in diagnosing nodal metastases, particularly in patients with low-risk disease. The size criteria to identify possible lymph node involvement vary from 0.5 cm to 2 cm, although a lymph node with a short axis of 1 cm or greater is generally considered clinically abnormal. Computed tomography (CT) and conventional magnetic resonance imaging (MRI) have both demonstrated poor sensitivity for detecting nodal disease; one meta-analysis reported a pooled sensitivity of 0.42 and 0.39, respectively [8]. Evaluation of fluoromethylcholine positron emission tomography (PET)/CT for detection of lymph node metastases demonstrated a sensitivity and specificity of 73.2% and 87.6%, respectively. Neither the sensitivity nor the specificity is adequate enough to recommend PET/CT for routine use [9]. High-resolution MRI with magnetic nanoparticles has been shown to improve the sensitivity of detection of lymph node metastases, but has not yet been adopted as a recommended imaging option as availability of this technology is limited [10, 11]. Although current imaging modalities may not be ideal, significantly elevated preoperative PSA or high-risk biopsy pathology should prompt preoperative imaging. The American Urological Association (AUA) recommends preoperative imaging to evaluate for nodal disease in patients with clinically localized prostate cancer and a PSA greater than 20 ng/ml, locally advanced disease, or a Gleason score greater than or equal to 8 [12] (Table 89.1). The National Comprehensive Cancer Network (NCCN) recommends preoperative imaging with bone scan and pelvic CT or MRI if patients are cT1 and PSA greater than 20 ng/ml, cT2 and PSA greater than 10 ng/ml, locally advanced disease, symptomatic disease, or cT1–2 with a nomogram probability of lymph node involvement greater than 10% [13].

**Table 89.1** American Urological Association (AUA) and National Comprehensive Cancer Network (NCCN) criteria for preoperative imaging to evaluate for metastatic disease.

| American Urological Association | National Comprehensive Cancer Network |
|---|---|
| Clinically localized disease and PSA >20 ng/ml | T1 and PSA >20 ng/ml |
| Locally advanced disease | T2 and PSA >10 ng/ml |
| Gleason Score 8, 9, or 10 | Locally advanced or symptomatic disease |
| | Probability of lymph node positivity >10% |

## Who should undergo pelvic lymphadenectomy?

In an attempt to determine the need for pelvic lymphadenectomy, several nomograms exist to risk stratify patients prior to surgery. The Partin tables incorporate preoperative PSA, clinical stage, and biopsy Gleason score to predict the possibility of lymph node involvement, in addition to other adverse pathologic features (such as organ-confined disease, extraprostatic extension, and seminal vesical involvement). These tables were recently updated and confirmed the increased possibility of pT3 and N1 disease in patients with a PSA level >10 ng/ml. The Partin tables recommend that a pelvic lymphadenectomy be performed if the predicted probability of positive nodal disease is greater than or equal to 4%. This value gave the optimal ratio of appropriate to inappropriate lymphadenectomy [14].

Researchers from Memorial Sloan Kettering Cancer Center and several other institutions published a nomogram using similar variables of pretreatment PSA, clinical stage, and biopsy Gleason score. The negative predictive value of this nomogram was 0.99 when the predicted chance of lymph node involvement was less than 3%, thus obviating the need for lymphadenectomy in this subset of patients [15].

Briganti et al. recommended that patients with low-risk prostate cancer (Gleason 6, PSA <10 ng/ml, cT1c or cT2a) not routinely undergo pelvic lymphadenectomy as the chance of positive lymph nodes in these patients is less than 5% (Table 89.2). Intermediate-risk prostate cancer (Gleason 7, PSA between 10 and 20 ng/ml, or cT2b) carries a risk of positive lymph nodes between 3.7 and 20.1%, therefore, Briganti suggests lymphadenectomy should be performed if the nomogram risk is 5% or greater. All high-risk prostate cancer patients (Gleason 8–10, PSA >20 ng/ml, or cT2c) should undergo a pelvic lymph node dissection, as estimated risk is 15–40% for discovering positive lymph nodes [16].

**Table 89.2** European Association of Urology (EAU) and Briganti et al. recommendations for performing pelvic lymphadenectomy.

| EAU/Briganti – risk | Probability of positive lymph node | PLND? |
|---|---|---|
| Low (Gleason 6, PSA < 10, cT1c, cT2a) | Less than 5% | No |
| Intermediate (Gleason 7, 10 < PSA < 20, cT2b) | Greater than 5% | Yes |
| High (Gleason 8–10, PSA >20, cT2c) | 15–40% | All high-risk patients should undergo PLND |

PLND, pelvic lymph node dissection.

The European Association of Urology (EAU) guidelines for pelvic lymphadenectomy are based on a nomogram using a cohort of patients who underwent open prostatectomy and extended pelvic lymph node dissection template (ET). The EAU recommendation is to perform lymphadenectomy in patients who have a predicted positive nodal risk greater than 5% (based on findings by Briganti et al.). Using this cutoff for low-risk individuals, unnecessary pelvic lymph node dissection would be avoided in 65% of patients. This has been externally validated in a cohort of patients undergoing a robot-assisted radical prostatectomy, assuming that an adequate extended lymph node dissection is performed (i.e. at least 15 lymph nodes removed). Of note, in this study, there was no anatomic standardization of the pelvic lymph node dissection. Tissue within the obturator fossa and along the external iliac vein was removed in all patients. However, tissue along the internal and common iliac vessels was removed based on the individual surgeon's clinical judgment [16, 17].

Finally, the NCCN recommends performing a pelvic lymphadenectomy in patients with low- and intermediate-risk prostate cancer whose nomogram predicts a greater than 2% chance of positive lymph nodes (Table 89.3). All high-risk patients should undergo an extended template lymphadenectomy if surgery is performed [13].

**Table 89.3** National Comprehensive Cancer Network (NCCN) recommendations for performing pelvic lymphadenectomy.

| NCCN – risk | Probability of positive lymph node | PLND? |
|---|---|---|
| Low | If >2% | Yes |
| Intermediate | If >2% | Yes |
| High | | All patients |

## Rationale for extended pelvic lymphadenectomy template in prostate cancer

Lymphatic drainage from the prostate follows a fairly predictable pattern, with low chance of skip lesions. Drainage occurs first to the pelvic nodes in the external iliac, obturator, internal iliac, and presacral lymph node packets. Lymph drainage may then ascend to the common iliac and retroperitoneal lymph nodes; however, this is generally seen only in patients with high-risk prostate cancer [18]. Pelvic lymph node mapping in prostate cancer has demonstrated that the most common location for a positive lymph node was the internal iliac region (35%), followed by the external iliac region (26%), the obturator fossa (25%), presacral region (9%), common iliac region (3%), and the aortic bifurcation (1%) [19]. There has been some controversy over the extent of lymph node dissection given the technical difficulties and the potential for further and possibly unnecessary complications. Early reports of extended lymphadenectomy published complication rates of 12–24% and included lymphocele, lymphedema, and thromboembolic events. This led to development of the limited dissection template or the obturator fossa packet [20]. Clark et al. prospectively randomized 123 patients undergoing radical retropubic prostatectomy to an extended lymph node dissection on one side and a limited lymph node dissection on the opposite side. The majority of these patients were T1c (72%) and Gleason 6 (68%). Positive lymph node metastases were similarly found between the extended (3.3%) and the limited (2.4%) groups ($P = 0.15$). In patients with complications attributed to the lymph node dissection (i.e. lymphocele, lower extremity edema, deep venous thrombosis, pelvic abscess, ureteral injury) the complication occurred 75% of the time on the side of the extended node dissection. Although this finding was not clinically significant ($P = 0.08$), the authors concluded that an extended lymph node dissection does not yield a higher rate of positive lymph nodes and that there may be a trend toward higher complications with an extended pelvic lymph node dissection [21]. On the other hand, Eden et al. describe a series of 374 men who had a pelvic lymph node dissection during laparoscopic radical prostatectomy. Of these, 253 men had a standard lymph node dissection, while 121 men underwent an extended template. The operative time for an extended template was significantly longer by a median of 26.5 minutes (180 vs. 206.5 minutes, $P < 0.001$). Although there were more complications (i.e. bowel injury, neurovascular injury, lymphocele) with an extended template as compared to a standard template (8.3% vs. 3.6%), this was not found to be statistically significant ($P = 0.10$). Importantly, in patients undergoing an extended pelvic lymph node template versus a standard template, there was a significantly higher total lymph node yield (17.5 vs. 6.1, $P = 0.002$) as well as a higher rate of detection of lymph nodes harboring metastatic disease (9.6% vs. 0.8%, $P = 0.01$) [22].

The important distinction comes in patients with intermediate- and high-risk disease. A significant amount of nodal disease may occur outside of the ST, thus the importance of extending the template to include the common iliac, internal iliac, and presacral regions. Several studies demonstrate that almost 60% of patients harbored positive lymph nodes along the internal iliac vessels; in fact, this was the only site of lymphatic spread in 12–25% of patients undergoing prostatectomy [19, 23]. By extending the template of dissection, more lymph nodes are removed and the accuracy of staging improves. Briganti et al. demonstrated that the number of nodes removed is directly proportional to the probability and ability of detecting lymph node involvement. For each lymph node removed, the probability of accurately predicting lymph node involvement in a patient with prostate cancer increases by 6%. If fewer than 10 nodes are removed, there is less than 10% probability of finding lymph node involvement if it actually exists. In contrast, as the number of nodes removed increases from 10 to 30, the probability of detecting positive lymph nodes increases substantially. This plateaus when 28 lymph nodes are removed, resulting in a 90% ability to accurately predict whether or not lymph node involvement is present [24]. Maccio et al. have recommended submitting the entire pelvic lymph node specimen, including fatty tissue, for pathological evaluation, not just examining visually enlarged or palpable nodes. Incidence of nodal metastasis was significantly higher when all fatty tissue removed at the time of dissection was histologically evaluated. This minimized pathologic diagnostic bias and helped to determine the presence of micrometastatic disease [5].

In addition to improving the accuracy of disease staging, an extended lymph node dissection may improve survival. Abdollah et al. found that in pN1 patients with prostate cancer, cancer-free survival rates increased as the number of lymph nodes removed increased. For example, at 10 years after surgery, the cancer-free survival for a patient with 8 lymph nodes removed was 74.7%; this improved to 96.0% when 36 lymph nodes were removed. In general, survival rates were significantly higher in pN1 patients with more than 14 lymph nodes removed compared to patients with less than 14 lymph nodes removed [25]. Extended lymph node dissection may also improve the survival in pN0 patients as well. Joslyn et al. reported that when greater than 10 lymph nodes were removed, node-negative patients were found to have a 15% decreased risk of prostate cancer death [26].

## Bladder cancer

The standard of care for muscle invasive urothelial cell carcinoma of the bladder is radical cystectomy with bilateral pelvic lymph node dissection. Positive lymph node status and pathologic stage are associated with a worse overall prognosis and survival. Approximately 25% of patients undergoing radical cystectomy are found to have lymph node metastases [27]. These patients have a reported 5-year recurrence-free survival of 33% and overall survival of 26% [28]. An aggressive surgical approach has consistently demonstrated both a diagnostic and therapeutic advantage [29, 30].

### Preoperative imaging

Initial metastatic workup for patients with muscle invasive urothelial carcinoma includes cross-sectional, contrast-enhanced imaging with either CT or MRI. Sensitivity and specificity of these imaging studies are suboptimal, similar to lymph node detection in prostate cancer [31, 32]. Roughly 25% of individuals whose preoperative imaging studies were negative for lymph node involvement were found to have lymph node involvement on final pathology [27]. PET/CT has been evaluated as a potential modality; however, the false-negative rate was 33% and it has not been found to be helpful in evaluating patients with primary bladder cancer. Thus it is currently not a recommended imaging option [33].

### Template for pelvic lymphadenectomy during radical cystectomy

The template for pelvic lymphadenectomy in urothelial cell carcinoma is controversial insofar as it has been shown repeatedly that increasing the node yield results in improved survival, yet it is common for surgeons both in academia and community practices to omit part or all of the dissection. At a minimum, the dissection should include an ET lymph node dissection: removing tissue overlying the external iliac, internal iliac, presacral, obturator fossa, and distal common iliac up to the crossing of the ureter [27] (Figure 89.1). A SET has been advocated

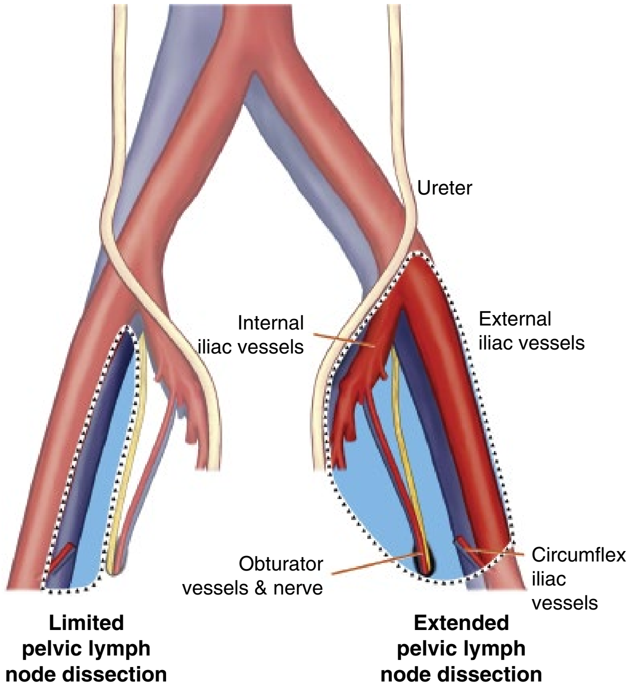
Ureter
Internal iliac vessels
External iliac vessels
Obturator vessels & nerve
Circumflex iliac vessels
Limited pelvic lymph node dissection
Extended pelvic lymph node dissection

**Figure 89.1** Template of dissection for extended pelvic lymphadenectomy. *Source:* Yuh B, Walter A, Heidenreich A et al. The role of robot-assisted radical prostatectomy and pelvic lymph node dissection in the management of high-risk prostate cancer: a systematic review. *Eur Urol* 2014 May;65(5):918–927. Reproduced with permission of Elsevier.

by some groups for improved staging and therapeutic benefit and includes removal of tissue along proximal common iliac artery and vein, the distal vena cava and aorta up to the level of the inferior mesenteric artery [34]. Although an ET or SET lymph node dissection has been shown to increase operative times by at least 60 minutes, there does not appear to be an increase in perioperative morbidity, complications, or blood transfusions [35].

### Therapeutic benefit of pelvic lymphadenectomy and rationale for extended template dissection

Extended pelvic lymph node templates (ET) result in improved staging accuracy as well as improved overall survival when compared to LT dissection [27, 33, 36]. It is unclear if the SET is superior to the ET in terms of recurrence-free survival [34]. Regardless of the template, it appears there is a tangible benefit to removing a greater number of lymph nodes during a radical cystectomy for high-risk bladder cancer. Herr et al. reported on a group of 322 patients with muscle invasive transitional cell carcinoma who underwent radical cystectomy and bilateral pelvic lymphadenectomy, 258 (80%) of whom had node-negative disease and 64 (20%) with node-positive disease. In both node-negative and node-positive patients, there was a statistically significant survival advantage when a greater number of nodes were removed. For example, in node-negative patients, when 9 or more lymph nodes were removed a statistically significant survival advantage was demonstrated as compared to removal of 4–7 nodes or 0–3 nodes. Furthermore, in node-positive patients, a significant survival advantage was found when more than 14 nodes were removed, as compared to removal of 9–14 or 1–8 nodes. In addition to complete surgical removal, the authors also note the importance of a thorough pathological assessment when examining the specimen [37]. Leissner et al. demonstrated that when <16 lymph nodes compared with >16 lymph nodes were removed during surgery, 5-year recurrence-free survival rates improved from 63% to 85% in organ-confined tumors and 40–55% in locally advanced tumors [29]. Both node-negative and node-positive patients appear to benefit from an ET lymph node dissection. Patients with organ-confined, lymph node-negative disease were found to have a 90% 5-year recurrence-free survival after extended pelvic lymph node dissection as compared to a 71% 5-year recurrence-free survival with a more limited ST pelvic lymph node dissection [38]. In addition, 5-year recurrence-free survival in patients with lymph node-positive disease was improved in patients undergoing an extended lymph node dissection versus a limited dissection (24% and 7%, respectively) [33].

In an effort to understand further the importance of lymph node positivity in bladder cancer, the concept of lymph node density has been described. Lymph node density is defined as the number of lymph nodes containing metastatic disease divided by the total number of lymph nodes removed. This concept helps to risk stratify patients with node-positive disease. Variations in surgical templates and technique of gross pathology analysis must be considered when using lymph node density. It is also difficult to compare these data across institutions as there are large variations in technique of gross analysis of the node packets. For example, some centers send node packets separated by anatomic location. Other centers send the pelvic node packet en bloc. These differences may affect total node count. However, in general, multiple groups have demonstrated that higher lymph node density translates into poorer overall survival [39].

## Surgical anatomy

In general, the pelvic lymph node dissection is performed during the same operative time as primary tumor removal (i.e. during radical prostatectomy or radical cystectomy) (Figure 89.2). When performed robotically or laparoscopically, we recommend performing any extended (ET or SET) node dissection prior to primary tumor removal. We prefer this approach because the node dissection arguably requires the highest level of concentration of the entire procedure. Performing the node dissection first allows the surgeon maximum concentration for the meticulous dissection in and around the large vessels of the pelvis. Moreover, the surgical anatomy prior to the cystectomy can become slightly altered after ligation of the vascular pedicles (i.e. excessive staple lines or clips near the internal iliac vessels can create challenges dissecting in this area). A transperitoneal approach is recommended for ET or SET dissections, as the visualization is improved of the proximal aspects of the dissection near the common iliacs when compared to an extraperitoneal approach. Prior to the procedure, the pelvic anatomy is inspected. In the midline, along the anterior abdominal wall, is the urachus or median umbilical ligament. This spans from the dome of the bladder cephalad to the umbilicus. On either side, lateral to the urachus are the medial umbilical ligaments (obliterated umbilical arteries), originating from the internal iliac arteries as the first anterior branch. The ureter will be identified medial to the medial umbilical ligaments, an important anatomic landmark for ureteral mobilization during cystectomy. Lateral to the medial umbilical ligaments are the lateral umbilical folds, under which are the inferior epigastric arteries. It is important to be aware of these folds in order to avoid injury, especially

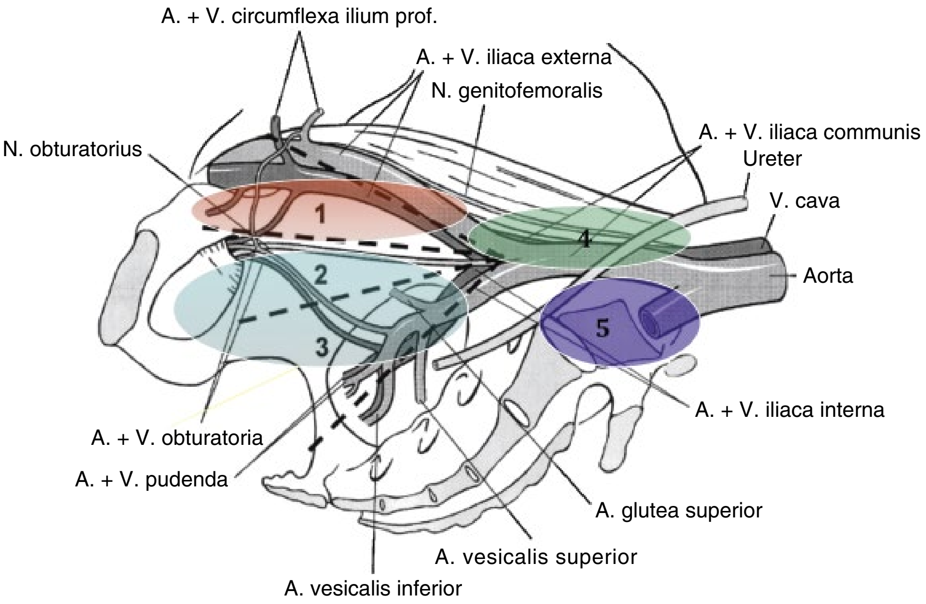

**Figure 89.2** Anatomic limits of pelvic lymph node dissection (PLND). Area 1 (red): limited PLND. Areas 1–3 (blue): standard PLND. Areas 1–4 (green): extended PLND. Areas 1–5 (purple): superextended PLND. A, arteria; V, vena; prof, profunda; N, nervus. *Source:* Ploussard G, Brigante A, de la Taille A et al. Pelvic lymph node dissection during robot-assisted radical prostatectomy: efficacy, limitations, and complications – a systematic review of the literature. *Eur Urol* 2014 Jan;65(1):7–16. Reproduced with permission of Elsevier.

during trocar placement and bladder mobilization from the anterior abdominal wall.

The abdominal aorta bifurcates near the level of L4 into the right and left common iliac arteries. The common iliac arteries are in danger of injury during initial, periumbilical trocar placement. The ureter crosses over the common iliac artery and into the pelvis just proximal to the bifurcation of the common iliac into the external and internal iliac arteries. The external iliac artery is found lateral and anterior to the external iliac vein, exiting the pelvis through the femoral canal. The pelvic organs are supplied by branches of the internal iliac artery, including the superior and inferior vesical arteries, obturator artery, vaginal and uterine arteries (in females), middle rectal artery, internal pudendal artery, and the inferior gluteal artery. Importantly, the left common iliac vein runs underneath the right common iliac artery. This structure may easily be injured during an extended lymph node dissection as tissue is cleared around the common iliac vessels and bifurcation of the aorta. In particular, during a presacral node dissection the left common iliac vein is often found under a layer of nodal tissue just proximal to the sacral promontory. This needs to be identified during the dissection to avoid inadvertent injury.

The ureter runs anteromedial to the internal iliac artery and its branches (i.e. the medial umbilical artery and the superior and inferior vesical arteries). In females, the ureter runs underneath the uterine artery, contained in the cardinal ligament. This is a common area of ureteral injury during gynecologic procedures. The ureter then courses posterior to the vas deferens, inserting into the trigone of the bladder. The vas deferens, or the round ligament in the female, exits the internal inguinal ring, running medially, over the external iliac vessels and anterior to the ureter.

The genitofemoral nerve is the lateral border of the pelvic lymph node dissection. This nerve runs along the anterior surface of the psoas muscle, medial to the gonadal vessels and lateral to the external iliac vessels. The genitofemoral nerve splits with the genital branch running through the internal ring with the spermatic cord and the femoral branch running to supply the anterior thigh. The obturator nerve has components of the second, third, and fourth lumbar nerves and supplies the motor function of the adductor compartment of the thigh as well as the sensory function of the medial thigh. The nerve exits the medial border of the psoas muscle behind the bifurcation of the internal and external iliac veins, and runs laterally along the pelvic sidewall. The internal iliac artery is found medial and below the nerve, while the external iliac vessels are found lateral and above the nerve. Posterolateral to the common iliac vessels is the fossa of Marseilles. This area includes the tissue lateral to the common iliac vein over the obturator nerve as it exits the psoas muscle. In this region is presciatic lymph tissue, commonly incorporated in the extended pelvic lymph node dissection. The obturator nerve exits the pelvis distally through the obturator foramen.

## Robotic port placement and robot positioning

The patient is placed in the supine position with legs split and pressure points carefully padded, including the heels, calves, elbows, wrists. Pneumo-boots and subcutaneous heparin are used for thrombosis prophylaxis. The patient's right arm is placed in an arm protective device (ArmGuard$^{TM}$, D.A. Surgical, Chagrin Falls, OH, USA) securing it at his or her side. The patient's left arm is secured at his or her side. A Trendelenburg patient restraint device (e.g. TrenGuard 405$^{TM}$, D.A. Surgical) is placed above the neck and shoulder supports are secured by Velcro to the operative bed. The patient is then placed in full Trendelenburg position to ensure that they are secured. The patient is returned to flat supine position and prepared and draped in sterile fashion. A Foley catheter is placed on the sterile field. Abdominal access is achieved via either a Veress or Hassan technique, depending on surgeon preference. Once proper placement of the needle is confirmed, the abdomen is insufflated to 15 mmHg through the umbilicus. The abdomen is not marked for potential trocar sites until fully insufflated, as landmark positioning will change (Figure 89.3).

For those surgeons using the da Vinci Si system (Intuitive Surgical Inc., Sunnyvale, CA, USA), a 12 mm camera port marking is placed in the midline, superior to the umbilicus. The da Vinci Xi system uses an 8 mm camera placed at the same location. The first and second 8 mm robotic ports are placed roughly 8 cm lateral to the umbilicus and 18–20 cm cephalad from the base of the penis (Figures 89.4 and 89.5). We routinely move these ports in a cephalad direction, especially if an ET node dissection or an intracorporeal urinary diversion is planned. Thus, in these cases, the ports are often at the level of the umbilicus or slightly above. The right anterior superior iliac spine (ASIS) is palpated and the 12 mm assistant port is placed in a triangulated location between the ASIS and the right 8 mm robotic port. The left ASIS is palpated and the robotic third working arm port is placed at a location which is triangulated between the ASIS and the robotic second port. Finally, a 5 mm port is placed in the right upper quadrant in a

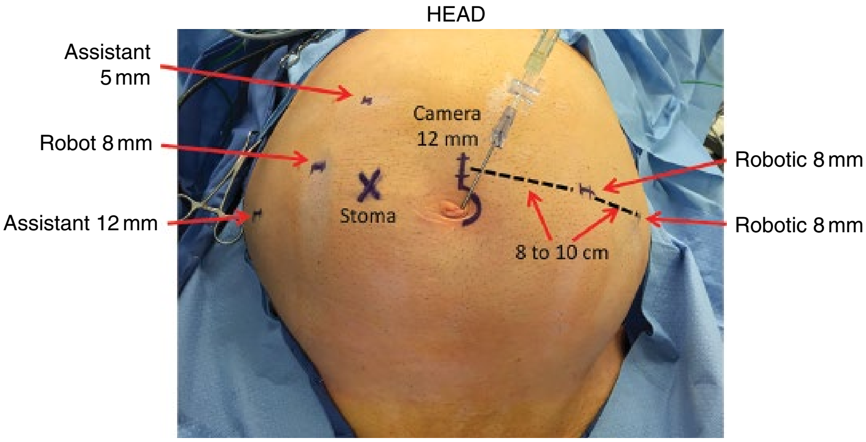
HEAD
Assistant 5 mm
Robot 8 mm
Assistant 12 mm
Camera 12 mm
Stoma
8 to 10 cm
Robotic 8 mm
Robotic 8 mm

**Figure 89.3** Port site marking for robot-assisted laparoscopic radical cystoprostatectomy. All ports are moved cephalad for urinary diversion and extended lymph node dissection. A port site should not be compromised to accommodate the proposed stoma site.

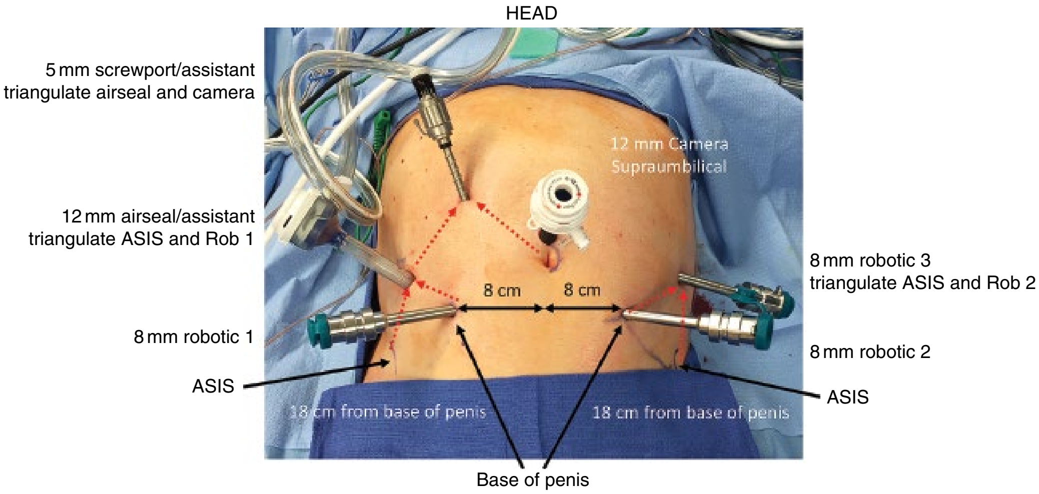
HEAD
5 mm screwport/assistant triangulate airseal and camera
12 mm airseal/assistant triangulate ASIS and Rob 1
8 mm robotic 1
ASIS
12 mm Camera Supraumbilical
8 cm
8 cm
8 mm robotic 3 triangulate ASIS and Rob 2
8 mm robotic 2
ASIS
18 cm from base of penis
18 cm from base of penis
Base of penis

**Figure 89.4** Trocar placement for robot-assisted laparoscopic prostatectomy. ASIS, anterior superior iliac spine.

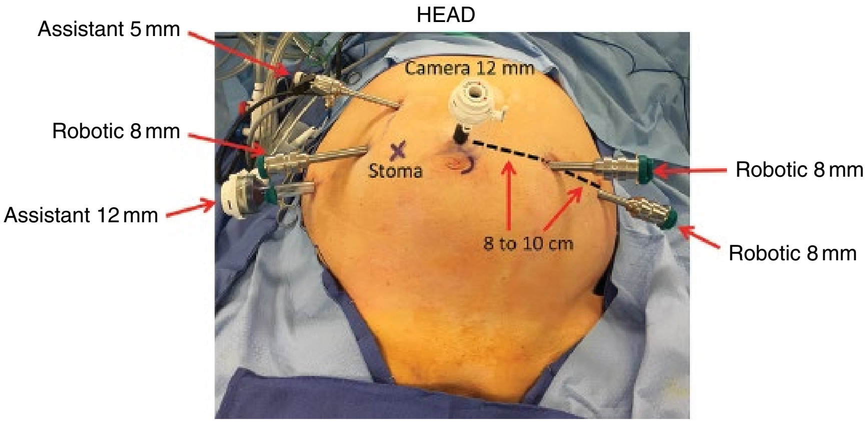

**Figure 89.5** Trocar placement for robot-assisted laparoscopic radical cystoprostatectomy. All ports are moved cephalad for urinary diversion and extended lymph node dissection. A port site should not be compromised to accommodate the proposed stoma site.

triangulated location between the camera port and the robotic first arm, although this may be moved slightly in a lateral direction, so that it is cephalad to the robotic first arm.

All port sites are infiltrated with 0.5% bupivacaine prior to incision. The abdomen is entered visually using a 0° laparoscope through a 12 mm optical bladed visualization trocar (Visiport$^{TM}$, Medtronic, Minneapolis, MN, USA) above the umbilicus. The abdomen is inspected for injury, evidence of metastatic disease, and feasibility of proposed port site placement (ensure no significant potential for bowel injury due to adhesive disease). Each port site is incised and the trocar placed under direct vision. The patient is then placed in a moderate Trendelenburg position (about 15–20°), with just enough tilt to allow the small bowel to fall out of the pelvis with some gentle retraction by the assistant. If present, adhesions are taken down to allow for optimal exposure and bowel mobilization. We routinely avoid steep Trendelenburg position to avoid associated airway difficulties as well as elevated intracranial and intraocular pressures.

The robotic patient cart is then prepared for docking. It is brought between the split legs of the patient, such that the robot is directly facing the perineum. It is important to place the robotic arms at an adequate height so as not to impinge on the lower extremities of the patient either while docking or during the procedure itself. In particular, the robotic third working arm can impact the toes of the patient in Trendelenburg position. A 0° or a 30° telescoping camera lens may be used. It is our practice to use monopolar scissors in the robotic right hand, fenestrated bipolar forceps and Maryland bipolar forceps in the robotic left hand, and Prograsp forceps in the robotic third arm. The assistant has access to a small bowel atraumatic grasper, suction, laparoscopic clips, laparoscopic needle driver and scissors, and a spoon.

## Procedure

Robotic pelvic lymph node dissection is generally performed during the same procedure as the prostatectomy or cystectomy. If an extended pelvic lymph node dissection (ET) is planned, it is most easily performed prior to beginning the prostatectomy or cystectomy so as to maintain the normal anatomic planes without disruption from staple lines or clips. If a standard template is planned (lower risk prostate cancer) then this can easily be performed either before or after the prostatectomy.

During robotic prostatectomy, the first step is the identification of landmarks. These include the medial umbilical ligament, the ureter, the vas deferens, and the external iliac artery (Figure 89.6).

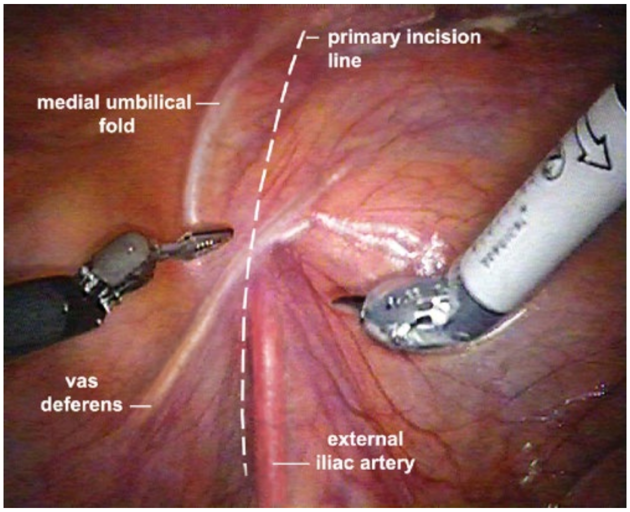

**Figure 89.6** Primary incision line and identification of landmarks (right side). *Source:* Feicke A, Baumgartner M, Talimi S et al. Robotic-assisted laparoscopic extended pelvic lymph node dissection for prostate cancer: surgical technique and experience with the first 99 cases. *Eur Urol* 2009 Apr;55(4):876–884. Reproduced with permission of Elsevier.

Once the pelvis has been cleared of significant adhesive disease, the ureter is most easily identified at the pelvic brim as it crosses over the common iliac artery. We routinely perform right-sided lymphadenectomy first by identifying and, if necessary, dissecting the right ureter away from the pelvic sidewall. The sigmoid colon is often adhered to the left pelvic sidewall, allowing this to be easily retracted out of the pelvis and away from the right sidewall. This facilitates visualization of the right iliac vessels and right ureter. To begin, a peritoneal incision is created over the right ureter and extended medially to the sigmoid mesentery. The ureter is then identified and peritoneum incised anterior to the ureter as it courses down into the deep pelvis. The fatty tissue around the ureter is dissected with the ureter and care is taken not to skeletonize the ureter and strip it of its blood supply. The ureter is dissected down to the bladder hiatus, clipped and divided distally. It is dissected proximally to the level of the mid ureter as it overlies the psoas muscle. During the dissection the bedside assistant should have a grasper or probe which can be placed under the ureter to create mild countertraction, aiding in the dissection. Once the ureter is clipped distally and dissected proximally, the extended pelvic lymph node dissection for radical cystectomy can begin. If an ET dissection is being performed prior to a prostatectomy, the peritoneal window is created over the ureter as described above, however the ureter is identified and gently retracted cephalad to begin the node dissection over the bifurcation of the iliac artery.

To begin the lymph node dissection, the adventitia overlying the right common iliac artery is incised to reveal the direct surface of the vessel. We use a fenestrated bipolar grasper in the left hand and a curved monopolar scissors in the surgeon's right hand. The bipolar grasper is used to help with hemostasis of the tissue over the artery and the tissue is "split and rolled" laterally and medially. This requires some countertraction on the artery with the left hand and gentle sweeping motions with the scissors in the right hand. Most of the fibrinous adhesions of the nodal tissue to the artery surface are incised sharply without cautery. This dissection moves distally to the external iliac artery. As the peritoneum and fibrofatty tissue are dissected distally along the external iliac artery, the vas deferens will be encountered, which is ligated using bipolar cautery or clips. The peritoneal incision is extended distally, lateral to the medial umbilical ligament to reveal the node of Cloquet which is the distal extent of the dissection. Locking clips or laparoscopic metal clips are used to secure small lymphatics here to prevent excessive lymph leak.

As this tissue is removed, retraction of the node packet is facilitated with a combination of the surgeon's thirrd working arm and the bedside assistant's laparoscopic suction irrigator or atraumatic graspers to provide countertraction to aid in the dissection. The genitofemoral nerve may be visualized lateral to the external iliac artery and identifies the lateral extent of lymphatic tissue removal. The distal aspect of the dissection is at Cooper's ligament and the pubic bone.

Tissue is rolled laterally off the external iliac artery and dissection proceeds along the pelvic sidewall behind the vessels. Much of the pelvic node dissection is performed from behind the vessels, allowing better visualization of the lateral borders of the dissection. The external iliac vein is immediately identified behind the artery and again the tissue on the anterior surface of the vein (but visualized behind the artery) is incised and split and rolled medially and laterally. Again, the tissue is sharply incised if directly on the surface of the vessel. There may be small perforating venous branches which can be ligated with clips or bipolar cautery. Using blunt dissection through this fibrofatty tissue will help to identify the obturator nerve, which is carefully separated from the packet without the use of electrocautery. We take care to attempt to remove the nodal tissue deep to the nerve as well, using clips to ligate the tissue. Obturator vessels are commonly seen running alongside this nerve (Figure 89.7).

As the dissection moves proximally, the internal iliac artery is identified. The tissue over the internal artery is often more adherent than that over the external artery. Again, the tissue directly over the internal artery is ligated with bipolar current and the tissue lateral is rolled off to reveal the obturator nerve. The dissection continues

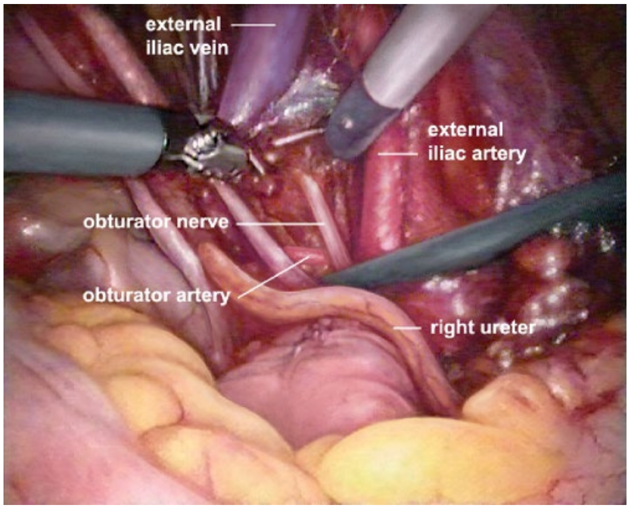

**Figure 89.7** Identification of the obturator nerve at its proximal course after separating the external iliac artery and vein (right side). *Source:* Feicke A, Baumgartner M, Talimi S et al. Robotic-assisted laparoscopic extended pelvic lymph node dissection for prostate cancer: surgical technique and experience with the first 99 cases. *Eur Urol* 2009 Apr;55(4):876–884. Reproduced with permission of Elsevier.

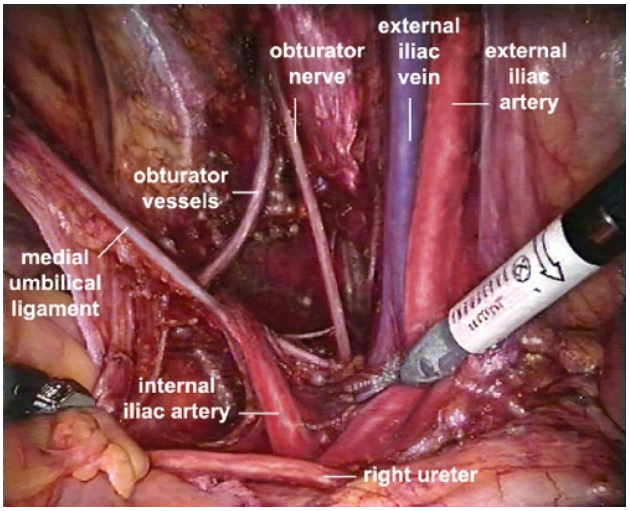

**Figure 89.8** Overview after completion of the extended pelvic lymph node dissection (right side). *Source:* Feicke A, Baumgartner M, Talimi S et al. Robotic-assisted laparoscopic extended pelvic lymph node dissection for prostate cancer: surgical technique and experience with the first 99 cases. *Eur Urol* 2009 Apr;55(4):876–884. Reproduced with permission of Elsevier.

distally until the insertion of the medial umbilical ligament is identified into the internal iliac artery (Figure 89.8).

After completing the right pelvic node packet we begin the presacral lymph node dissection. The robotic third arm is used to aggressively retract the sigmoid and its mesentery to the left. The dissection is begun by first identifying the medial aspect of the right internal iliac artery. The tissue here is rolled medially, peeling it down to the presacral area and identifying the left common iliac vein as it crosses under the right common iliac artery. Blunt spreading here is crucial to avoid lacerating the vein. Once the vein is identified, the tissue just distal to the vein is peeled away from the sacral promontory. Again, generous use of metal or locking clips is advised as the tissue is quite vascular. A difficult aspect of this dissection is the demarcation of sigmoid mesentery with actual presacral node packet (anterior border of the presacrals). There is usually a subtle plane identifying the two layers, but it is challenging and the ability to identify the correct tissue improves with experience. The tissue is dissected to the left until the left internal iliac artery is identified, where the tissue is then ligated and removed.

A completed presacral dissection allows for relatively easy identification of the left common iliac and ureter under the sigmoid mesentery from the right side. A large aperture is created under the sigmoid mesentery, allowing for easy transfer of the left ureter to the right side.

The left side pelvic node dissection is then dissected in a similar manner. Often the sigmoid must be mobilized off the left sidewall to allow visualization of the ureter, which is identified and dissected distally, again incorporating the periureteral fatty tissue into the dissection. The sigmoid must then be retracted aggressively to the right to improve exposure to the left pelvic sidewall. In the case of the radical cystectomy, the ureter has already been identified, clipped, divided, and placed proximally out of harm's way. In a similar procedure to the patient's right pelvic lymph node dissection, the fibrofatty tissue overlying the left common and external iliac arteries is incised. This tissue is split and rolled off the artery and dissection proceeds distally. The vas deferens is encountered and ligated. After incising the peritoneum lateral to the medial umbilical ligament, the pubic bone and Cooper's ligament are encountered and the lymphatic vessels distal to Cloquet's node are clipped and divided. The tissue lateral to the artery is first dissected back proximally to the common iliac, clipped and ligated. The remaining pelvic nodal tissue is then approached from behind the vessels and separated from first the external vein, and then the sidewall itself. Again much of the dissection is done from behind the vessels, allowing for improved visualization of the obturator nerve and external iliac vein. The obturator fossa is encountered and dissection is carried to the pelvic sidewall. The obturator nerve and accompanying vessels are identified. Fibrofatty tissue in the internal iliac packet is dissected and clipped. Both pelvic lymph node packets are placed in a specimen bag for removal at the conclusion of the procedure.

## Complications

Intraoperative complications directly related to pelvic lymph node dissection include damage to pelvic vasculature and nerve damage to the obturator nerve. Specifically, in the pelvis, injury may occur to the common iliac, external iliac, and internal iliac vessels, as well as their branches. Depending on the nature of these injuries, there should be consideration for a vascular surgery consult. Many vascular injuries can be repaired primarily using robotic intracorporeal suturing techniques. We use a 5-0 prolene cut to 12.7 cm, which is our "rescue suture" (i.e. always opened on the backtable in the event that vascular repair is necessary). If immediate vascular control and visualization of the injury is not obtained, then conversion to an open repair is mandatory. The obturator nerve may be injured via thermal energy or crush, especially if this structure has not been well defined. In particular, the obturator can be inadvertently clipped proximally near the bifurcation of the iliac vessels. It needs to be visualized at all times when clipping in the area.

Postoperative complications from a pelvic node dissection can include ileus, small bowel obstruction, lower extremity deep venous thrombosis (DVT), wound infection, and lymphocele. Lymphoceles are usually managed conservatively. However, if large, they may cause a DVT from compression of pelvic veins, may compromise the urethrovesical anastomosis, or may become secondarily infected. Treatment options include percutaneous drainage or creation of a peritoneal window. In an extended lymph node dissection during a radical prostatectomy, the ureter may be injured as it crosses the common iliac. Thus it should be identified prior to beginning the dissection and kept out of harm's way (see Video 89.1).

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# 90

# Endoscopic Subcutaneous Modified Inguinal Lymph Node Dissection for Squamous Cell Carcinoma of the Penis

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## Introduction

The presence and extent of metastatic disease to the lymph nodes is the most important prognostic indicator of survival in patients with squamous cell carcinoma of the penis and has significant clinical application for cutaneous melanoma and vulvar cancer. Lymphadenectomy is often required in these disease processes for cancer staging and can also be curative when cancer is isolated to the penis and regional nodes. Serious life-altering complications have been associated with inguinal lymph node dissection. Due to the substantial morbidity caused by inguinal lymphadenectomy, controversy surrounds the utility of bilateral and prophylactic dissection.

In 2002 Ian M. Thompson MD conceived the idea of applying laparoscopic techniques in an endoscopic approach to the inguinal lymph nodes, with the hope of decreasing the morbidity associated with open surgery by preserving the continuity of the lymphatic and vascular supply to the overlying skin. Working together, we combined various techniques from subcutaneous endoscopic brow lift and saphenous vein harvest to formulate an approach using laparoscopic instruments for inguinal node dissection in staging penile cancer. The result of our work was the endoscopic subcutaneous modified inguinal lymphadenectomy (ESMIL) procedure, which mimics the same oncological approach traditionally performed through an open incision.

We first explored the feasibility of this new procedure in several fresh cadaver studies and then finally in 2003 a patient with T3 N1 M0 squamous cell carcinoma of the penis underwent the first ESMIL procedure [1]. Since our initial report, others have used the technique with great success and have applied the same technique to penile and other cancers requiring inguinal node dissection [2–7]. Each series demonstrated reduced skin necrosis, reduced lymph edema, and fewer infections when compared to open surgery.

The key points of ESMIL are summarized in Box 90.1.

## Indications/contraindications

ESMIL is indicated when traditional inguinal lymphadenectomy would be required for staging squamous cell carcinoma of the penis. Patients with nonpalpable nodes or small (<1 cm) mobile nodes at high risk for inguinal node involvement are considered good candidates for endoscopic node dissection. Patients with pTa and pT1 grade 1 penile tumors will have positive nodes approximately 10% of the time, when inguinal nodes are not enlarged. Fifty percent of patients with pT2 tumors and G3 tumors will demonstrate positive inguinal lymph nodes.

Both stage and grade are predictive of nodal involvement. Verrucuous carcinoma and carcinoma in situ are both associated with a low risk for nodal metastasis. However, 70% of stage T2 cancers have positive nodes. Grade I tumors have a 30% chance of spread to lymph nodes, while approximately 85% of patient with grade III tumors have inguinal node involvement [8]. Because cross-drainage from the affected side to the contralateral side is a well-known occurrence, bilateral dissection is indicated in patients at high risk for metastatic disease (stage T2 or greater or grade II–III tumors).

Patients with large, fixed inguinal lymph nodes have a relative contraindication to ESMIL. In these patients it can be very difficult to dissect the superior aspect of fixed, matted lymph nodes with an endoscopic technique and as a result they are better candidates for traditional open surgery.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

**Box 90.1 Key points in ESMIL.**

- Using an illuminated instrument or the light directed from the laparoscope will improve visualization of the initial dissection and help with establishment of the correct tissue planes during placement of the first two trocars.
- Entry into the correct plane of dissection with scissors facilitates dissection after trocars have been placed.
- Continuous flow of $CO_2$ allows rapid clearing of water vapor or smoke during dissection in the small working space.
- A working pressure of 5 mmHg is sufficient to maintain visualization while avoiding spontaneous infiltration beyond the boundaries of dissection.
- Key landmarks are readily identified and transillumination of the skin facilitates orientation.
- Following the saphenous vein helps with identification of landmarks but as many branches as possible should be preserved to decrease lymph edema in the lower extremity.
- All tissue should be divided with ultrasonic energy or electrocautery to decrease the incidence of lymphatic leak.
- For further details see Video 90.1.

## Preoperative preparation and evaluation

A complete metastatic evaluation should be performed prior to biopsy of the presenting penile lesion or partial penectomy when indicated. The presence of carcinoma of the penis is established with biopsy to determine the diagnosis, extent of invasion, presence of vascular invasion, and grade of the lesion prior to lymphadenectomy. Distant metastatic disease without lymph node involvement is rarely seen. However, distant metastatic spread to bone, brain, liver, and lung should be considered as part of the overall work-up for penile cancer. Computerized tomography of the pelvis and inguinal region can be helpful in determining the presence of large pelvic and inguinal nodes, especially in the obese patient.

Waist-high elastic stockings should be fitted and obtained prior to surgery. Preoperative intravenous antibiotics for skin flora coverage are given 60 minutes prior to the skin incision. A sterile prep of the area is performed in the usual fashion.

## Operating room configuration and patient position

The operating room (OR) is configured so that all of the staff can view the procedure. The surgeon's monitor is placed on the contralateral side of the dissection, near the shoulder and arm of the patient. A second monitor is placed on the opposite side in the case of bilateral dissection or as needed for viewing by the entire team (Figure 90.1).

The patient is placed in a supine position, with the ipsilateral knee flexed and hip abducted. The foot on the side of dissection is secured to the contralateral leg in a unilateral dissection or both feet secured together in the case of a bilateral procedure. A pad placed under the bent knee will help maintain the correct position (Figure 90.2).

## Trocar placement

Before placing the first trocar, the limits of the dissection are marked on the skin to preserve the orientation once the skin is distorted from the insufflation used to create the working space. A line is drawn from the pubic tubercle to the anterior superior iliac crest. The width of the area of dissection is approximately 11–12 cm and the length 15 cm down the medial thigh and 20 cm down the lateral thigh (Figure 90.3).

Trocar placement is the same for the left and right sides. The trocars are placed just outside the delineated area of dissection. Initially, a 2.5 cm incision is made over the saphenous vein 15 cm below the pubic tubercle. It is important to avoid making the incision any larger than 2.5 cm to prevent $CO_2$ escape during the procedure once the trocar is inserted and the subcutaneous cavity insufflated. Sharp, fine scissors are used to develop the plane of dissection elevating the skin from the deep membranous fascia and Scarpa's fascia toward the area of dissection drawn on the skin for as far as the surgeon can see inside the lighted cavity. The laparoscope provides an excellent light source for the initial dissection. A blunt-tipped trocar is placed in the incision to create an airtight seal. The blunt-tipped trocar (USSC, Norwalk, CT, USA) is ideal for this procedure since its unique internal balloon and foam collar create an excellent seal and leaves a very small profile inside the area of dissection. This trocar will become the medial working trocar, and since it is 10 mm it can accommodate a retrieval sac to remove lymph node packets during the procedure. If a large nodal packet is placed in the sac and cannot be

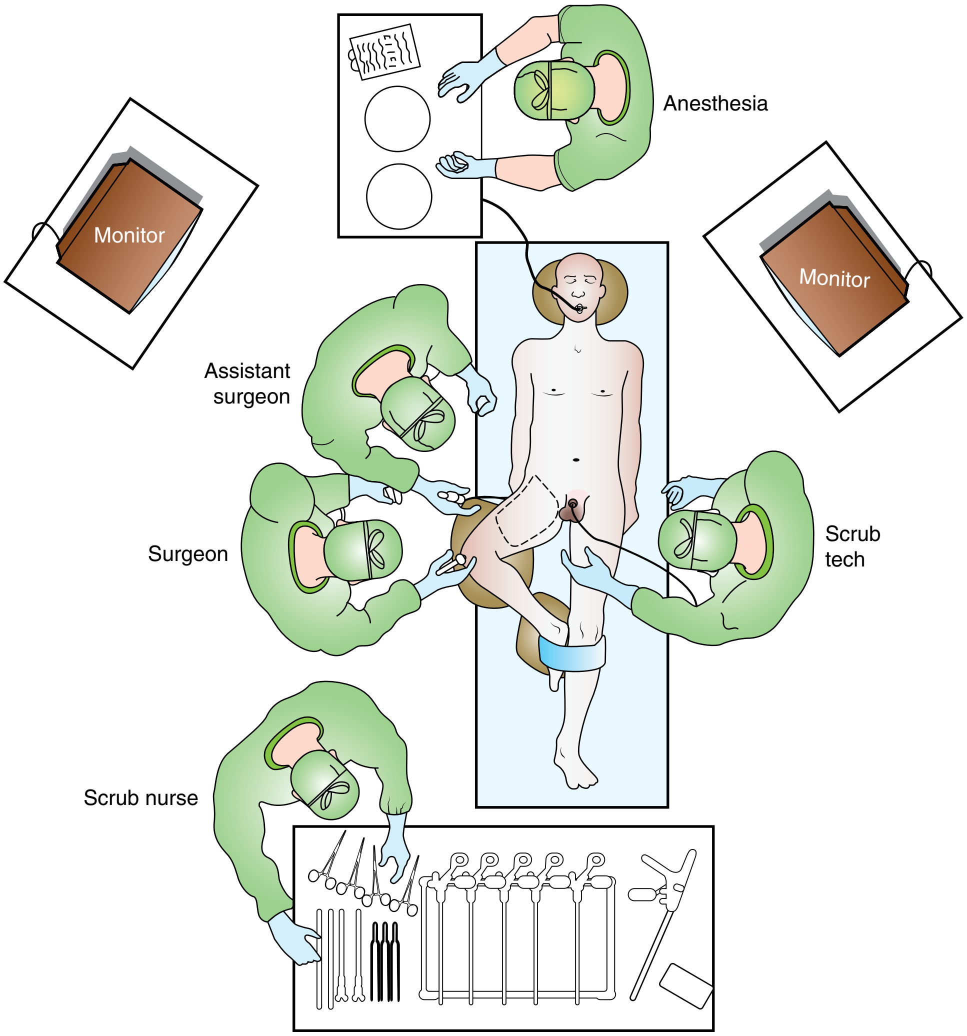

**Figure 90.1** The operating room is configured so that all of the staff can view the procedure. The surgeon's monitor is placed on the contralateral side of the dissection, near the shoulder and arm of the patient. A second monitor is placed on the opposite side in the case of bilateral dissection or as needed for viewing by the entire team.

extracted through the trocar, the balloon on the trocar can be deflated and the packet (secured inside the retrieval bag) can be extracted directly through the incision. In order to prevent seeding the trocar site, fatty and lymphatic tissue specimens should not be extracted directly through the skin incision without being placed inside an extraction sac.

A second 2.5 cm incision is placed outside the area of dissection approximately 16 cm inferior to the middle of the inguinal ligament. Scissors are used to establish the correct plane of dissection toward the first trocar until the two planes of dissection are joined and a second blunt-tipped trocar is placed. The laparoscope is usually placed through the second trocar during the procedure. The working space is insufflated to a pressure of 5 mmHg.

A pair of endoscopic scissors or ultrasonic or bipolar cautery shears are used to dissect the inferior skin margin toward the edge of the surgical field so that the third trocar can be placed. A 5 mm threaded trocar is placed outside the area of dissection approximately 15 cm below the iliac crest (Figure 90.4).

## Procedure

Inguinal lymph nodes are divided into superficial and deep nodes. The superficial nodes are those located anterior to the fascia lata and the deep nodes posterior to the fascia lata. Inguinal lymph nodes dissection is carried out 2 cm above the inguinal ligament superiorly, lateral to the sartorius muscle and medial to the

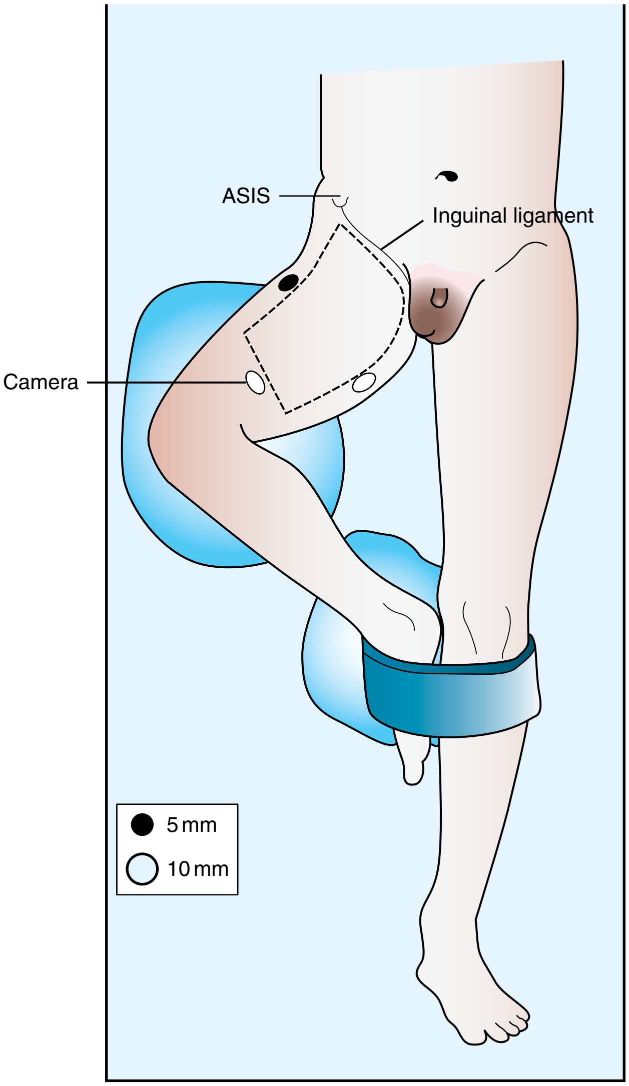
ASIS
Inguinal ligament
Camera
● 5 mm
○ 10 mm

**Figure 90.2** The patient is placed in a supine position, with the ipsilateral knee flexed and hip abducted. The foot on the side of dissection is secured to the contralateral leg in a unilateral dissection or both feet secured together in the case of a bilateral procedure. A pad placed under the bent knee will help maintain the correct position.

adductor longus. The superficial nodes are located in four quadrants centered around the saphenofemoral junction: (i) nodes in the area of the superficial circumflex iliac vein; (ii) nodes in the area of the superficial epigastric vein and the superficial external pudendal vein; (iii) nodes located in the inferomedial quadrant around the saphenous vein; and (iv) nodes around the insertion of the superficial circumflex iliac vein and the lateral accessory saphenous vein (Figure 90.5).

The deep inguinal lymph nodes include the most cephalad node, known as the node of Cloquet, which is

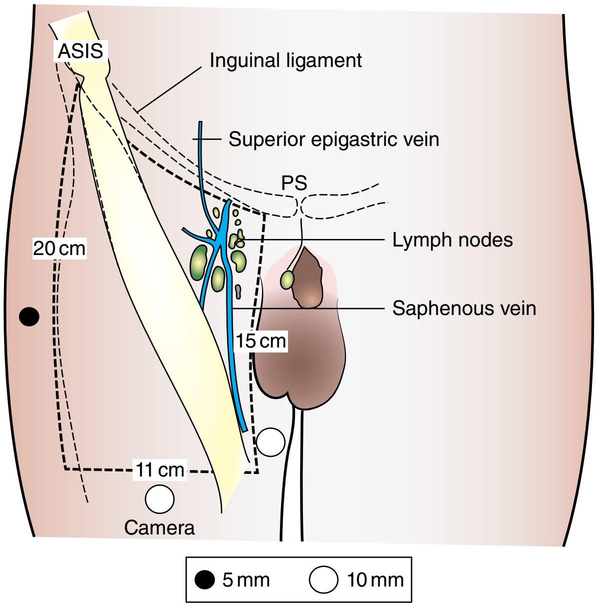
ASIS
Inguinal ligament
Superior epigastric vein
PS
Lymph nodes
20 cm
Saphenous vein
15 cm
11 cm
Camera
● 5 mm
○ 10 mm

**Figure 90.3** The limits of dissection are drawn on the skin.

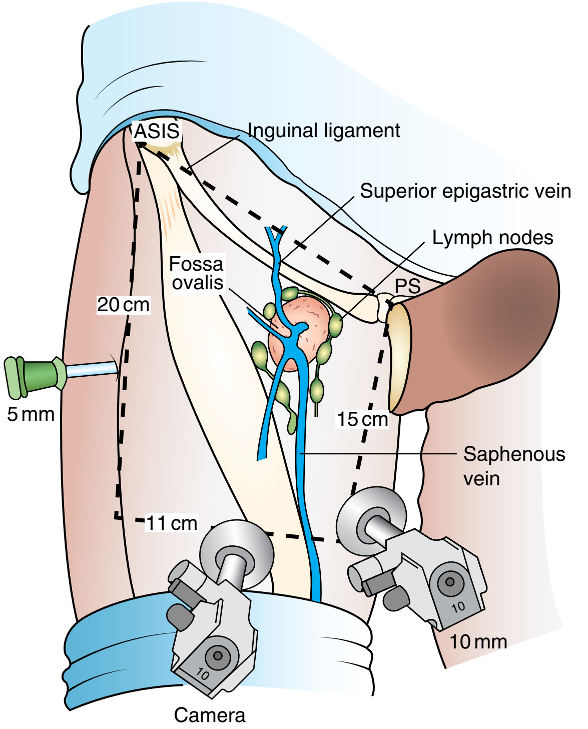
ASIS
Inguinal ligament
Superior epigastric vein
Lymph nodes
Fossa ovalis
PS
20 cm
5 mm
15 cm
Saphenous vein
11 cm
10
10
10 mm
Camera

**Figure 90.4** The trocars are placed just outside the delineated area of dissection. The first is placed approximately 15 cm below the pubic tubercle over the saphenous vein. A blunt-tipped trocar is placed in the incision to create an airtight seal. A second 2.5 cm incision is placed outside the area of dissection approximately 16 cm inferior to the middle of the inguinal ligament and a second blunt-tipped trocar is placed. The laparoscope is usually placed through the second trocar during the procedure. A 5 mm threaded trocar is placed outside the area of dissection approximately 15 cm below the iliac crest. ASIS, anterior superior iliac spine; PS, pubic symphysis.

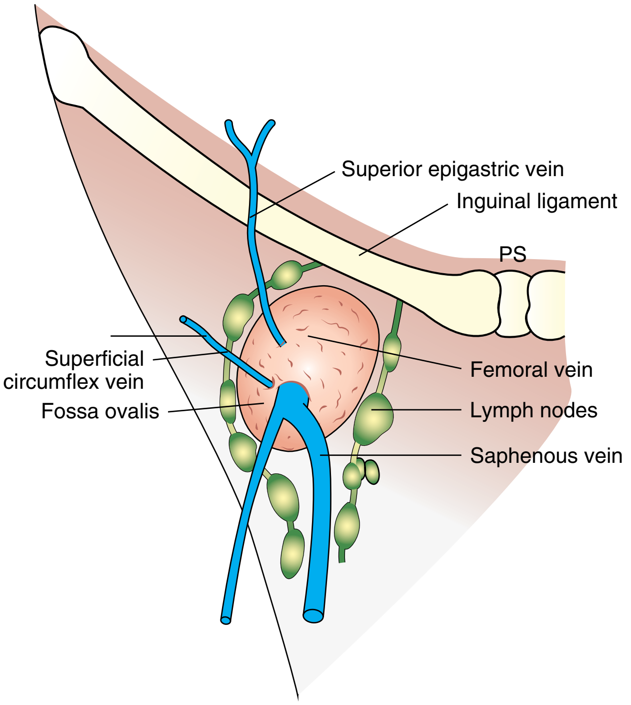

**Figure 90.5** The superficial nodes are located in four quadrants centered around the saphenofemoral junction (see text). PS, pubic symphysis.

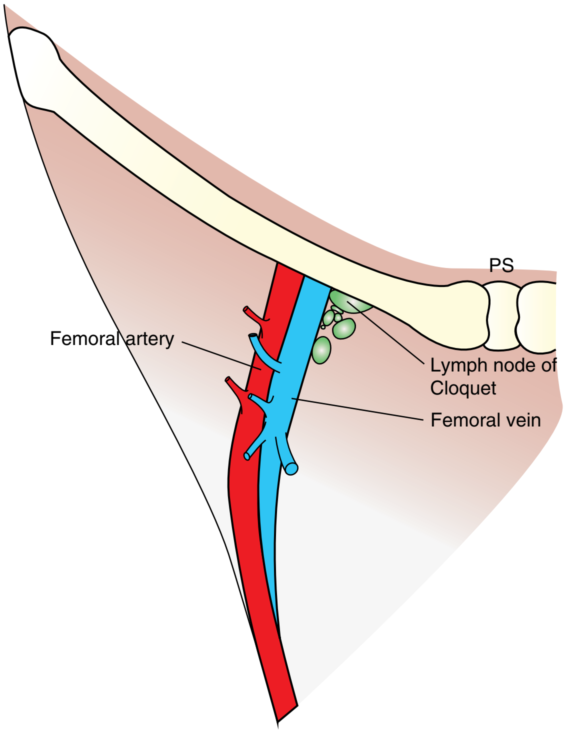

**Figure 90.6** The deep inguinal lymph nodes are located under the fascia lata and include the most cephalad node known as the node of Cloquet, which is located in the area of the femoral vein and the lacunar ligament. PS, pubic symphysis.

located in the area of the femoral vein and the lacunar ligament (Figure 90.6).

The dissection begins above Scarpa's fascia anteriorly, removing the tissue located between the skin and the fascia lata. Early in the dissection, the saphenous vein should be identified and preserved. If possible, it is helpful to identify the borders of dissection medially at the adductor longus and laterally at the sartorius muscle edges. In some patients it can be difficult to identify these landmarks without opening the fascia lata, but the margins marked on the skin will help in the dissection of the superficial nodal tissue. Subcutaneous vessels and saphenous branches can be divided using ultrasonic energy or electrocautery. Lymph node-bearing tissue is dissected from the fascia lata to the fossa ovalis.

As the dissection progresses toward the inguinal ligament, the external ring is identified and the fat and lymphatics in the area of the cord to the base of the penis medially are removed. The lymph node dissection is continued for 3–4 cm superior to the inguinal ligament. Once the nodal tissue and fat are removed from the external oblique and the inguinal ligament, the femoral vessels can be identified inside the femoral sheath.

To gain access to the deep nodes, the fascia lata is opened to the edge of the adductor longus medially and the sartoris muscle laterally. The triangular-shaped lymph packet within the femoral triangle is carefully removed. Opening the femoral sheath down toward the apex of the triangle will reveal the deep lymph nodes. Medial dissection will free the node of Cloquet. Any residual tissue between the femoral artery and vein is removed. Care is taken to prevent injury to the femoral nerve by limiting the lateral dissection to the femoral artery.

If the skin overlying the exposed vessels seems compromised in any way, the sartorius can be mobilized from the anterior superior iliac crest using ultrasonic or bipolar cautery and transferred over the exposed vessels. Three or four size 2-0 polydioxanone sutures are used to attach the sartorius muscle to the inguinal ligament.

At the end of the procedure a 7 mm Jackson–Pratt drain is placed inside the cavity to ensure drainage at the most dependent site of dissection. This can be placed through the 5 mm trocar sit or a new site chosen as needed. The two 10 mm trocar sites are closed with skin adhesive or subcuticular sutures. Once the skin adhesive is dry, a circular bandage is placed around the surgical area and held in place with an elastic bandage for 24 hours.

## Postoperative management

Waist-high elastic stockings are placed and the patient kept on bedrest for 5–7 days with the lower extremities elevated. Low molecular weight heparin or enoxaparin (Lovenox®, Sanofi-Aventis, Bridgewater, NJ, USA) is started after surgery and continued until the patient is fully ambulatory. The subcutaneous drain remains in place until daily output is less than 30 ml.

## Complications

The diagnostic and therapeutic benefits of early inguinal lymphadenectomy should be measured against the potential morbidity associated with the procedure. Patients should be aware of the minor and major postoperative complications associated with this procedure (Box 90.2).

**Box 90.2 Minor and major postoperative complications associated with ESMIL.**

**Minor postoperative complications**

- Local wound debridement in clinics
- Mild to moderate leg edema
- Seroma formation not requiring aspiration
- Minimal skin edge necrosis requiring no therapy
- Scrotal edema

**Major complications**

- Wound infection
- Severe leg edema interfering with ambulation
- Skin flap necrosis requiring skin graft
- Deep venous thrombosis
- Re-exploration or other invasive procedure performed in the OR
- Death

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# 91

# Laparoscopic and Robotic Retroperitoneal Lymph Node Dissection

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## Introduction

The management of patients with clinical stage I nonseminomatous germ cell tumors (NSGCT) of the testis remains controversial. Treatment options include retroperitoneal lymph node dissection (RPLND), surveillance, and primary chemotherapy. Fortunately, the survival rate is in the range of 95–99% with each treatment modality [1–3]. Therefore, the patient's perception of treatment toxicities and quality of life, without compromising cancer control, has become of paramount importance in decision-making when choosing therapy.

Open RPLND (O-RPLND) has been the standard of care for the surgical management of clinical stage I NSGCT. The approach provides both diagnostic information on the stage of the tumor and is curative in 75–80% of patients with low-volume retroperitoneal disease. With refinements in surgical technique to preserve the postganglionic sympathetic nerves, retrograde ejaculation has been minimized [4]. Nevertheless, there can be significant morbidity from O-RPLND, with associated bowel dysfunction, prolonged hospitalization, and delay in resumption of daily activities and work [5, 6].

The National Cancer Comprehensive Network (NCCN) guidelines for the treatment of stage I NSCGT include surveillance, 1–2 cycles of chemotherapy, or primary RPLND, with surveillance being preferred for low-risk patients [7]. In practice, the role of RPLND as a primary treatment for stage I NSGCT has diminished, and the European Association of Urology Guidelines for NSGCT does not recommend RPLND as a treatment option for even high-risk clinical stage I disease [8]. There are probably several factors contributing to the decline in RPLND, including the significant morbidity associated with O-RPLND. Young men with high-risk NSGCT (evidence of lymphovascular invasion and >50% embryonal cancer) given the choice between two cycles of chemotherapy or an O-RPLND, will usually choose chemotherapy. In addition, as surveillance becomes more prevalent, many urologists may not feel comfortable performing RPLND and chemotherapy then becomes the natural progression of surveillance.

In an attempt to make RPLND less morbid, several investigators have applied minimally invasive techniques to RPLND [9–12]. The effort initially began with laparoscopic RPLND (L-RPLND) and more recently has evolved to include the robot-assisted surgical platform that has gained prevalence with other urologic procedures. This review will highlight the current role of both laparoscopic and robotic RPLND (R-RPLND) in the management of patients with testicular cancer. The goal of this review is to provide a framework for urologists to perform minimally invasive RPLND (MI-RPLND), and at the same time maintain the current standard of cancer care while reducing surgical morbidity for these patients.

## Indications for minimally invasive RPLND

The goal of treating patients with stage I NSGCT should be the timely recognition and treatment of those men with metastatic disease. To avoid overtreatment this goal is best accomplished by the availability of accurate staging information. Of the three treatment options commonly employed for patients with NSGCT, surveillance, chemotherapy, and RPLND, the latter meets these criteria better than the other two options. O-RPLND provides accurate staging information and is curative in 75–80% of patient with stage II disease. MI-RPLND has the potential to provide the same benefits of O-RPLND but with a marked reduction in morbidity. Thus, MI-RPLND

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Companion website: www.wiley.com/go/smith/textbookofendourology

could provide the diagnostic and therapeutic advantages of O-RPLND but with a marked reduction in morbidity.

The indications for L-RPLND and R-RPLND are the same. Patients with NSGCT found on radical orchiectomy (T1–3) with no evidence of nodal involvement on computed tomography (CT) of the abdomen, no signs of lung involvement on CT of the chest, and negative or normalized tumor markers are appropriate candidates for MI-RPLND. In select patients with small-volume nodal involvement in the abdomen (stage IIa) and predominantly teratoma on orchiectomy, MI-RPLND can be considered depending on the marker status. Patients are counseled regarding all treatment options for NSGCT, including O-RPLND, surveillance, and primary chemotherapy.

As experience has been gained with MI-RPLND, the indications have expanded to patients with residual masses after primary chemotherapy. Masses greater than 1 cm in patients with negative tumor markers may be candidates for MI-RPLND with the caveat that larger masses (N3) and tumors involving renal hilum may be better addressed with O-RPLND.

Contraindications to MI-RPLND include pure seminoma, patients with elevated tumor markers despite negative nodes on CT scan and patients who have had prior abdominal radiation. Relative contraindications include extreme obesity (body mass index >40), prior episodes of peritonitis, and coagulopathy. Patients with prior abdominal surgeries can usually undergo successful MI-RPLND after takedown of adhesions.

## Patient preparation

Patients being considered for MI-RPLND should undergo complete staging of the disease with radiographic imaging of the chest and abdomen, and tumor marker assessment including alpha-fetoprotein, beta-human chorionic gonadotropin, and lactate dehydrogenase. If there is a delay of more than six weeks from the initial CT scan of the abdomen to the time of surgery, it is prudent to repeat the CT to look for evidence of nodal enlargement as this may affect the clinical stage of the disease and the operative plan. Patients should be counseled that there is a possibility of conversion to open surgery due to vascular or bowel injury and this should be clearly stated in the informed consent. This is especially important in patients undergoing a postchemotherapy MI-RPLND, where there can be significant fibrosis and scarring between the tumor and great vessels. The patient should also be informed of the possibility of nephrectomy as this is sometimes necessary due to tumor involvement of the renal hilum. They should be aware of the risk of blood transfusion. We routinely counsel patients that they will be on a low-fat diet (20 g of fat per day) for two weeks after the procedure to decrease the risk of developing chylous ascites that may require bowel rest with total parenteral nutrition and reoperation if it does not resolve. Finally, we encourage patients to bank sperm prior to surgery in the event of retrograde ejaculation.

To decrease the size of the intestines and provide more working space for MI-RPLND, patients are asked to undergo a modified bowel preparation the day prior to surgery with a clear liquid diet and magnesium citrate orally. We request that patients avoid platelet inhibitors such as aspirin and nonsteroidal anti-inflammatory medications for seven days prior to the procedure. Patients are typed and crossed for blood in the event of acute hemorrhage during the procedure.

## Preoperative preparation

### Anesthesia and patient position

Patients undergoing both L-RPLND and R-RPLND require general endotracheal anesthesia with continuous attention by the anesthesiologist to deep paralysis to maintain adequate pneumoperitoneum. A Foley catheter and orogastric tube are placed prior to positioning the patient to decompress the bladder and stomach and decrease the risk of injury during port placement as well as to provide more room in the peritoneal space for the procedure. Sequential compression stockings are placed on the lower extremities and a cephalosporin antibiotic is administered just prior to making the incision.

For L-RPLND and R-RPLND using the lateral approach patients are placed in a 60° modified flank position with the side of prior orchiectomy up (Figure 91.1). The patients are well padded on a gel pad and the legs are supported with pillows. The arms are placed on an arm board with pillows placed between the arms, although we sometime place the arms in a “prayer” position for patients undergoing R-RPLND. For R-RPLND using the supine approach, patients are placed supine with the arms padded and tucked by the sides and the legs are straight with sequential compression stockings (Figure 91.2). Because the patient is placed in a slight Trendelenburg position, a full body gel pad is placed between the patient and operating table to prevent patient movement. As with the lateral position, Foley catheter, orogastric tube, and pre-incision antibiotics are employed.

### Operating room setup and equipment: L-RPLND

L-RPLND is routinely accomplished with two assistants and a scrub nurse helping the primary surgeon (Figure 91.3). The room configuration for L-RPLND

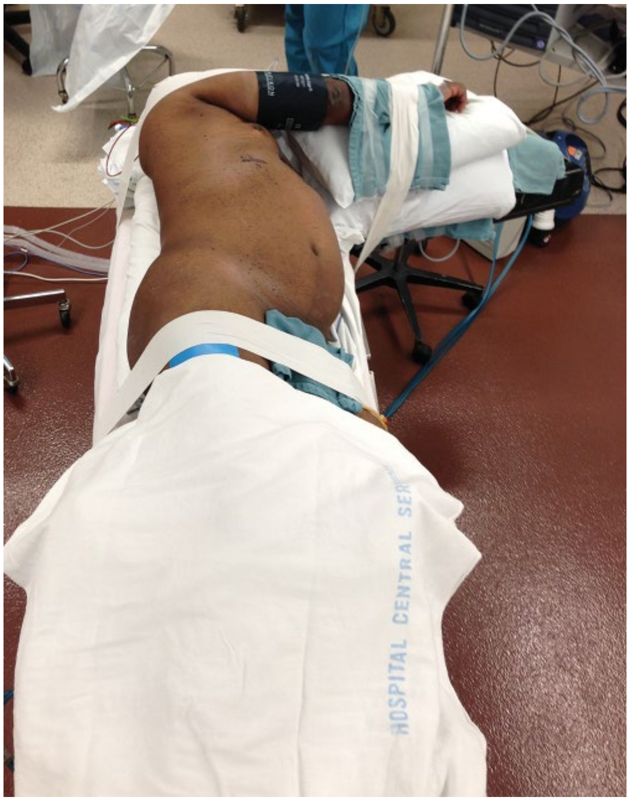

**Figure 91.1** Lateral modified flank position for minimally invasive retroperitoneal lymph node dissection with arms on arm board.

requires the primary surgeon and the first assistant to be standing on the side contralateral to the side of prior orchiectomy. The second assistant and scrub nurse stand on the side opposite the primary surgeon and first assistant. The anesthesia team is at the patient's head with full access to the airway and face. Video monitors are located on both sides of the patient to allow all involved personal to have an optimum view of the operative field. The first assistant's primary role is to hold the endoscope and maintain a steady operative view. The second assistant usually controls a grasping device or retractor to provide tissue exposure.

Laparoscopic instruments routinely used during L-RPLND include endoscopic scissors, graspers, clip appliers, and blunt dissectors. A 30° endoscope is usually used. In the event of vascular injury, laparoscopic needle drivers should be available along with a "rescue stitch" to allow rapid control of bleeding if this is encountered. A rescue stitch in our experience is a 4-0 polypropelene suture cut to 12 cm with a polymer clip on the end of the suture opposite the needle. This allows multiple throws of the needle without the need to tie the suture, although the clip can be removed and the sutured tied once bleeding is controlled if this is the surgeon's preference. Lymph nodes are removed with the aid of an endoscopic retrieval bag that decreases the risk of potential tumor cells coming into contract with the abdominal wall or an extraction port. Hemostatic agents are used at the end of the procedure to aid in the sealing of lymphatic changes that

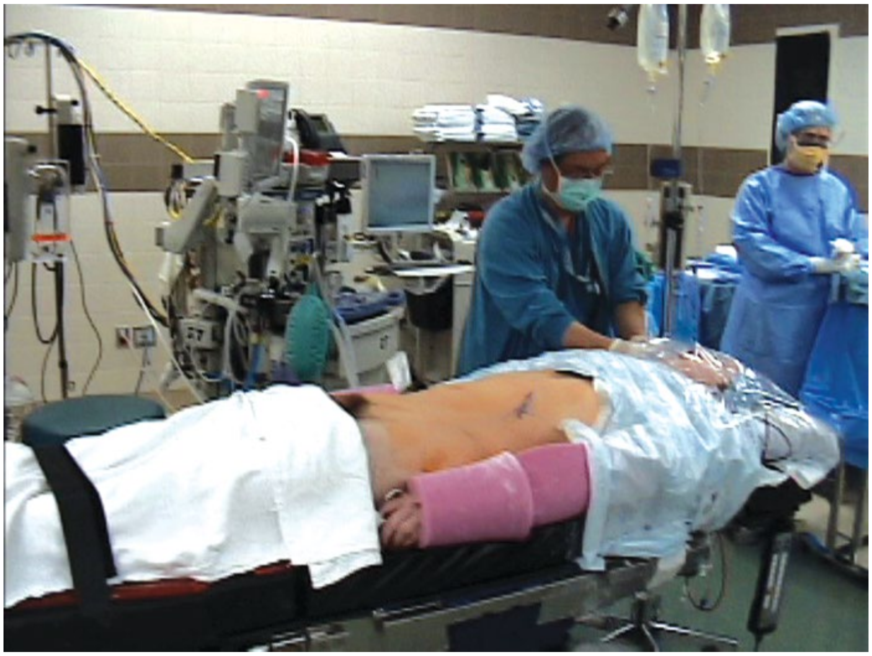

**Figure 91.2** Supine position with arms padded and tucked at sides.

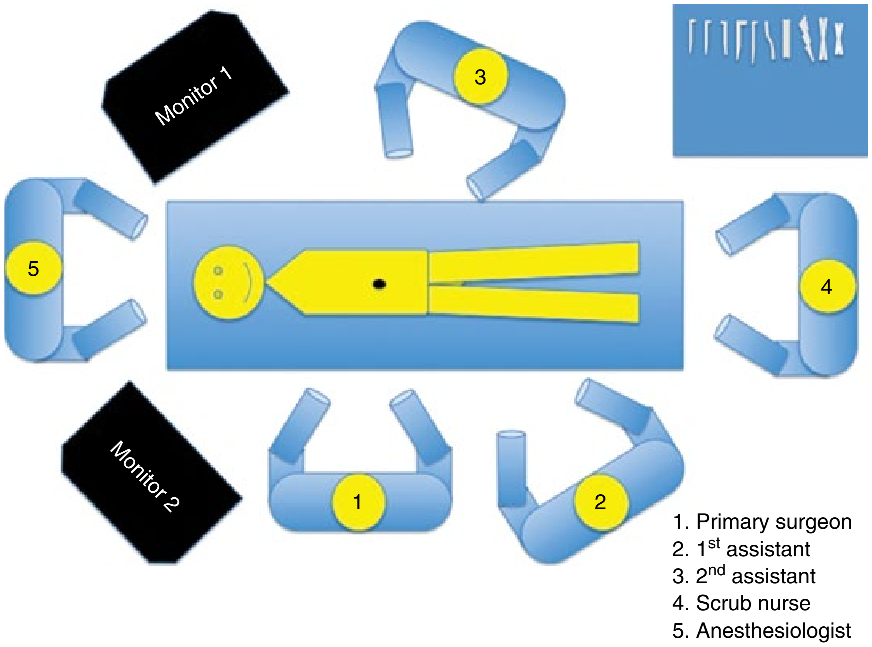
Monitor 1
3
5
4
Monitor 2
1
2
1. Primary surgeon
2. 1st assistant
3. 2nd assistant
4. Scrub nurse
5. Anesthesiologist

**Figure 91.3** Room configuration for left laparoscopic retroperitoneal lymph node dissection.

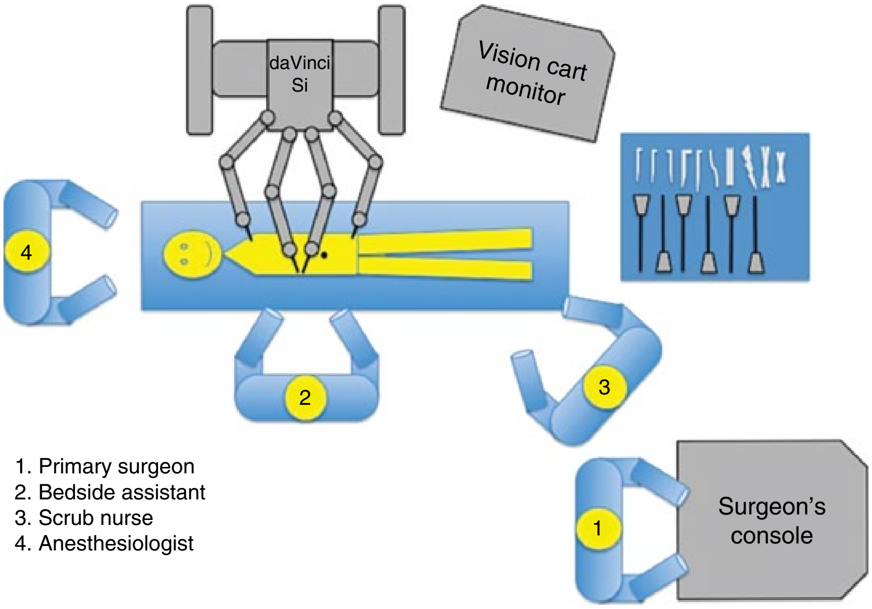
daVinci Si
Vision cart monitor
4
2
3
1
Surgeon's console
1. Primary surgeon
2. Bedside assistant
3. Scrub nurse
4. Anesthesiologist

**Figure 91.4** Room configuration for left robotic retroperitoneal lymph node dissection with da Vinci Si and the lateral approach. Robot is docked over the patient's back.

may remain open after lymph node removal. As with any laparoscopic procedure an open laparotomy set is in the room, opened and prepared in the event of rapid conversion to open surgery.

## Operating room setup and equipment: R-RPLND

The robotic setup will depend on whether the lateral or supine approach is used or whether the da Vinci® Si or Xi (Intuitive Surgical, Inc., Sunnyvale, CA, USA) is employed. For the lateral approach with the da Vinci Si the robot is docked over the patient's back on the side of the bed ipsilateral to the orchiectomy (Figure 91.4). The bedside assist and scrub nurse are on the side opposite the robot and the primary surgeon resides at the surgeon's console. The anesthesia team is again located at the patient's head. A second assistant is not routinely used during R-RPLND. For the supine approach using the da Vinci Si, the robot is docked over the patient's left shoulder after the patient is placed in a 15–20° Trendelenburg position (Figure 91.5). The bedside assistant stands on the patient's right directed toward the head of the patient and the scrub nurse is usually on the

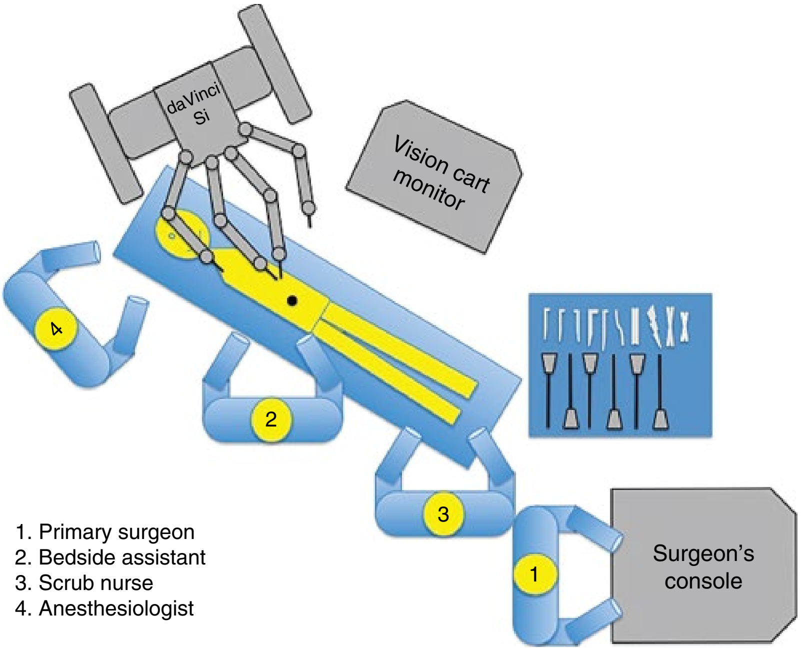
daVinci Si
Vision cart monitor
4
2
3
1
Surgeon's console
1. Primary surgeon
2. Bedside assistant
3. Scrub nurse
4. Anesthesiologist

**Figure 91.5** Room configuration for robotic retroperitoneal lymph node dissection with da Vinci Si in the supine approach. Robot is docked over left shoulder of patient.

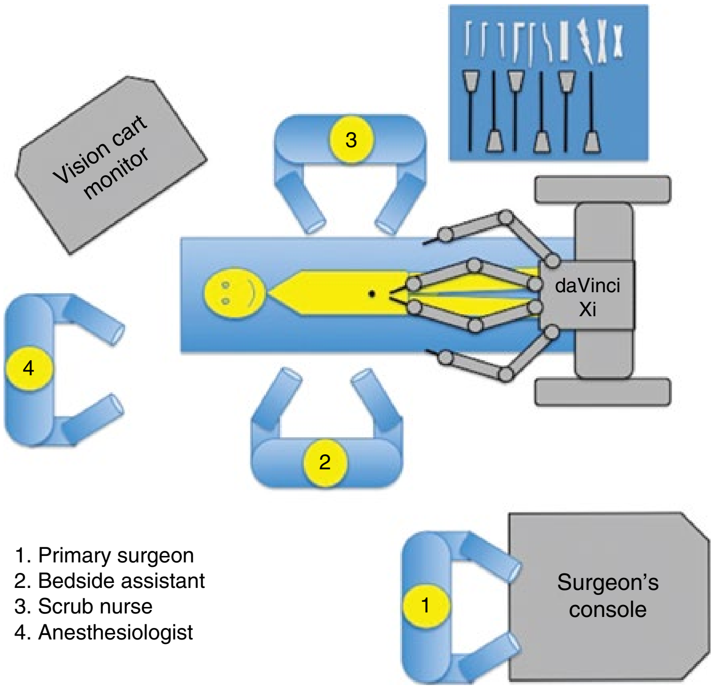
Vision cart monitor
3
daVinci Xi
4
2
1
Surgeon's console
1. Primary surgeon
2. Bedside assistant
3. Scrub nurse
4. Anesthesiologist

**Figure 91.6** Room configuration for da Vinci Xi retroperitoneal lymph node dissection using supine approach. Robot is docked over the patient's foot.

same side. The anesthesiologist will be on the right side of the patient's head opposite the robot. The patient side vision cart holds the insufflator, electrosurgical unit, light source, and accessory energy components and can be placed in the optimum position depending on room size and configuration specific to the room.

The da Vinci Xi is designed to allow docking from any position due to the presence of a rotating boom. This permits the robot to be brought in from any direction depending on the side of the dissection and thereby simplifies patient position and room configuration. It is also designed to allow extended reach of the robotic arms and allows multi-quadrant access in the abdomen and is ideal for RPLND. Given these advantages, the da Vinci Xi is our preferred platform for R-RPLND and we have abandoned the lateral position and da Vinci Si for R-RPLND.

For a left-sided R-RPLND using the da Vinci Xi the patient is placed in the Trendelenburg position and the robot can be brought in on the patient's left side, right side or over the foot of the patient as shown in Figure 91.6.

The bedside assistant stands on the right side directed up toward the head and the scrub nurse is on the patient's left. The mirror image configuration is used for a right-sided R-RPLND.

The instrumentation used for R-RPLND is much the same irrespective of the approach or which model robot used. The monopolar scissors are used in the right robotic arm, fenestrated bipolar in the left arm, and atraumatic grasper in the fourth robotic arm. For the lateral approach with the da Vinci Si, a 0° lens is used in the lateral camera position. For the supine approach with da Vinci Si or Xi, a 0° lens is used initially during exposure of the retroperitoneum and then switched to a 30° down lens during dissection of the lymph nodes. Other robotic instruments routinely used during R-RPLND include the robotic needle drivers and the robotic clip applier. The robotic clip applier is an important aid for R-RPLND as it allows clips to be applied in tight spaces and with angles that cannot be accomplished by the bedside assistant. The bedside assistant uses a suction-irrigation device throughout most of the procedure, but may be called upon to apply clips with a laparoscopic clip applier. Similar to the laparoscopic procedure we have a "rescue stitch" prepared and ready for vascular control. Lymph nodes are extracted with an endoscopic retrieval sac and hemostatic agents are applied to the dissection bed to decrease the risk of lymphatic leakage.

## Technique

### Access and port placement: L-RPLND

Once the patient has been sterilely prepped and draped, pneumoperitoneum is established by either an open technique using a Hasson port or a closed technique using a Veress needle. If a Veress needle is used this is usually placed in the midclavicular line below the ipsilateral costal margin to avoid the midline great vessels. For a right-sided L-RPLND a five-port configuration is used as shown in Figure 91.7. A 12 mm camera port is placed in the midline midway between the xiphoid and umbilicus. A second 12 mm port is used for the right hand to allow clip appliers and possibly a stapling device if necessary. The remaining ports are 5 mm located in the mid rectus muscle for the left-hand instruments, laterally for assistance with retraction, and just below the xiphoid for liver retraction. The key for L-RPLND is to move the ports medial relative to laparoscopic renal procedures to allow access to the midline structures such as the vena cava and aorta. A four-port configuration is used for a left-sided L-RPLND as there is no need for a liver retractor.

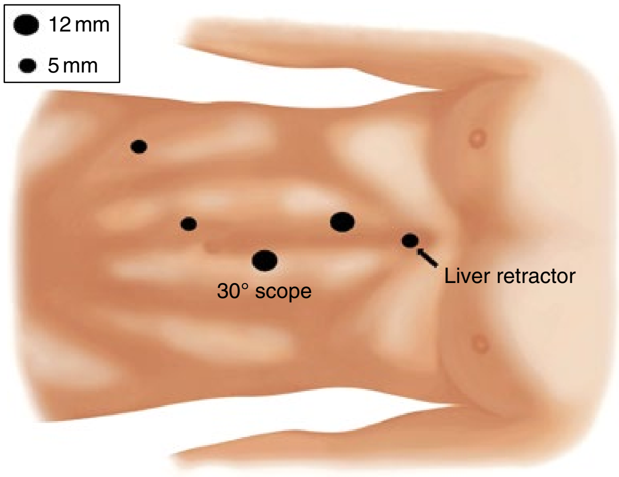

**Figure 91.7** Right laparoscopic retroperitoneal lymph node dissection port configuration.

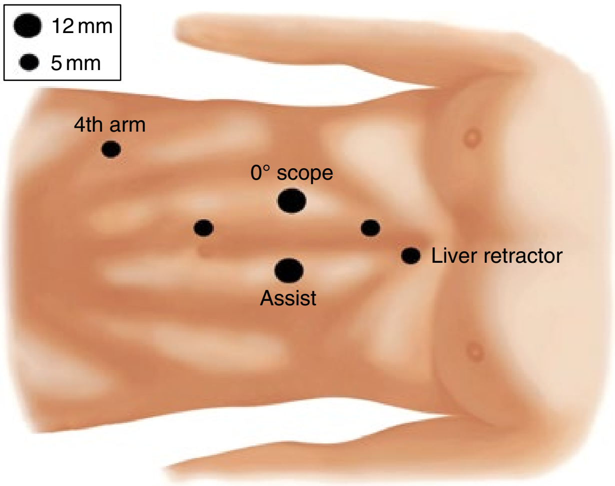

**Figure 91.8** Right robotic retroperitoneal lymph node dissection lateral approach port configuration with da Vinci Si.

### Access and port placement: R-RPLND

Access for R-RPLND is the same as for L-RPLND and port placement varies depending on approach or which model da Vinci robot is being used. For a right lateral R-RPLND using the da Vinci Si a six-port configuration is used with the 12 mm camera port placed midway between the umbilicus and xiphoid in the mid rectus muscle (Figure 91.8). In contrast to the lateral approach for L-RPLND, the camera for R-RPLND is placed lateral to the other ports to decrease external arm collision and allow more room for the bedside assistant. The left and right robotic arms are placed near the midline and the assistant is placed just medial to the line created by these two ports. The fourth robotic arm is placed laterally near the ipsilateral anterior superior iliac spine and is essential for R-RPLND to allow retraction and to facilitate dissection behind the great vessels. A 5 mm

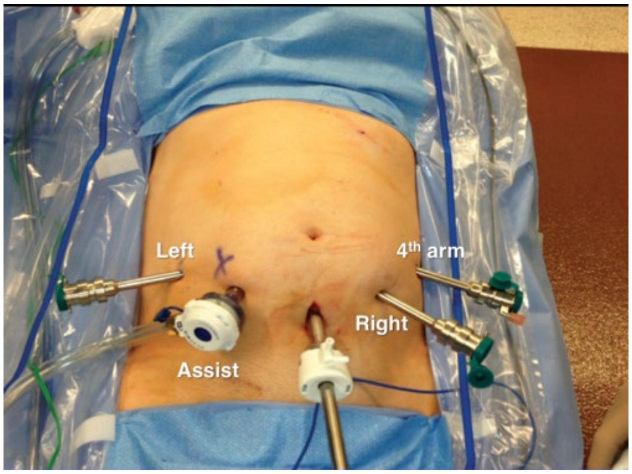

**Figure 91.9** Supine robotic retroperitoneal lymph node dissection port configuration with da Vinci Si.

subxiphoid port is placed to allow retraction of the liver. The mirror image port configuration for left-sided R-RPLND is performed with the exception of the liver retractor, which is not necessary on the left side.

For supine R-RPLND the port configuration depends on which model da Vinci is being employed. A five-port fan configuration is utilized for da Vinci Si with the 12 mm camera port in the midline approximately 4 cm below the umbilicus (Figure 91.9). The 8 mm right robotic arm and fourth arm are placed on the patient's left and the 12 mm assistant port is placed between the camera and the 8 mm left robotic port. This port configuration is used for both left- and right-sided supine R-RPLND using the da Vinci Si.

The robotic arms on the da Vinci Xi are designed to avoid external arm conflict by placing the ports in a linear configuration without the need for port offset as commonly employed with the da Vinci Si. The right-sided da Vinci Xi port configuration is shown in Figure 91.10a. The ports are placed linear at a slight angle to allow room for the assistant in the left lower quadrant. The camera port and the right robotic arm port are placed on either side of the medial umbilical ligaments. The ports are placed approximately 6–7 cm apart to allow freedom of movement and avoid conflict. The robot is docked from the right side and the 30° lens is used after exposure is created. The left-sided da Vinci Xi approach is shown in Figure 91.10b. For a full bilateral approach with the da Vinci Xi, as in the setting of postchemotherapy RPLND, the linear port configuration is not angled but placed at a right angle to the midline to allow access to both the right and left distal ureters.

## Boundaries of dissection: L-RPLND

The right-sided template dissection performed during L-RPLND begins with complete mobilization of the right colon and duodenum, exposing the retroperitoneum and great vessels. The gonadal vessels are clipped and dissected down to the internal inguinal ring where the entire cord is removed along with cord stump as indicated by retained suture. The renal pedicle establishes the upper limit of dissection while the inferior mesenteric artery is the lower limit of resection medially. The lower limit of dissection laterally is the crossing of the ureter over the right common iliac artery. The modified unilateral template dissection on the right side includes removal of the precaval, paracaval, retrocaval, interaortacaval, and preaortic node packages with extension to the left paraaortic nodes. The postganglionic sympathetic nerve fibers are identified coming off the sympathetic chain and are traced under the inferior vena cava on their way to the hypogastric plexus. These fibers are preserved within the template. The split and roll technique is used

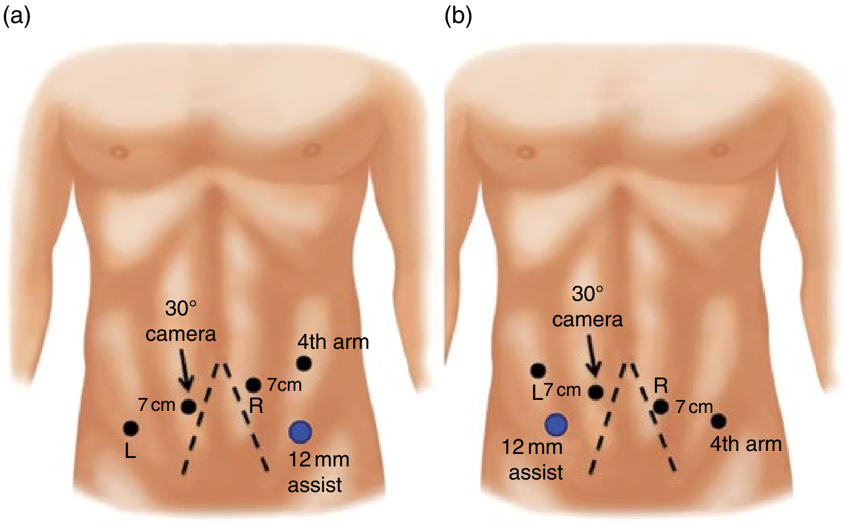

**Figure 91.10** Right (a) and left (b) supine robotic retroperitoneal lymph node dissection port configuration with da Vinci Xi. For bilateral dissection the linear port array is placed horizontally below umbilicus.

to remove retrocaval nodal tissue, which includes nodal tissue posterior to lumbar vessels. Care is taken to clip all lymphatic channels to prevent lymph leakage, especially the lymphatic channels crossing over the left renal vein. For the left-sided L-RPLND the descending colon is mobilized from the splenic flexure to the iliac vessels and medially to expose the great vessels. The gonadal vessels are once again mobilized and clipped at their proximal origin and dissected down into pelvis to remove the entire cord stump. Dissection of the paraaortic lymph nodes begins at the renal hilum and extends to the where the left ureter crosses over the common iliac artery. The postganglionic fibers on the left side are not as large as the right and can be difficult to identify and maintain. The preaortic and interaortocaval nodes are dissected from the renal hilum to the inferior mesenteric artery, which is spared.

Excised tissues are removed in organ entrapment bags and sent for immediate frozen section analysis. Patients with positive lymph nodes and stage IIA or stage IIB disease are repositioned for contralateral L-RPLND with nerve sparing. In patients found at surgery to have stage IIC disease, the procedure is terminated after unilateral dissection and the patient is scheduled for post-RPLND chemotherapy.

### Boundaries of dissection: R-RPLND

The dissection performed for the lateral robotic approach is the same as described for L-RPLND, with the need to reposition and redrape the patient if positive nodes are found on frozen section. For supine R-RPLND the dissection is the same with the da Vinci Si or Xi but is modified depending on the stage of the patient. To begin the dissection the retroperitoneum is exposed by incising the posterior peritoneum medial to the cecum and extending this incision toward the ligament of Trietz. The cut edge of the posterior peritoneum is sutured to the right side of the anterior abdominal wall to provide exposure of the great vessels and retroperitoneum. The left side of the cut edge of the posterior peritoneum is likewise sutured to the left side of the anterior abdominal wall, creating a hammock-like barrier preventing the small bowel from falling into the retroperitoneum. The combination of the suspension sutures and the Trendelenburg position provides excellent exposure. Although the suspension sutures provide the distal exposure of the retroperitoneum, the fourth robotic arm, using an atraumatic grasper, is used to retract the duodenum proximally and create proximal exposure.

Patients with clinical stage I NSGCT undergo a unilateral template dissection with nerve sparing as described for L-RPLND. Lymph nodes are sent for frozen section analysis and, if positive, a full bilateral dissection is performed. For patients with postchemotherapy residual masses, a full bilateral dissection with nerve sparing is performed, including complete removal of the ipsilateral spermatic cord. With the da Vinci Si, this is accomplished by repositioning the robot parallel to the ipsilateral leg, providing access to the spermatic cord and internal inguinal ring. Dissection is then carried out caudally, excising the spermatic cord out of the internal inguinal ring until the remnant suture from radical orchiectomy is removed. With the da Vinci Xi, the spermatic cord is fully accessible without the need to reposition the robot.

## Results

The experience with MI-RPLND began with L-RPLND as case reports and then larger single and multi-institutional series. The most extensive analysis of L-RPLND was a review article authored by Rassweiler et al. that evaluated over 800 patients in 34 publications [13]. The majority of the patients underwent a modified template dissection and the mean number of lymph nodes removed across all studies was 16. Operative times were longer for L-RPLND as compared to O-RPLND, 208 versus 186 minutes, and complications for L-RPLND were 15.6% with a 1.7% re-intervention rate, both of which are comparable to O-RPLND. Oncologic outcomes for L-RPLND were determined from five studies with 557 patients and a mean follow-up of 63 months. The vast majority of patients (126 out of 140) with positive nodes after L-RPLND received chemotherapy, and of the 14 patients who were followed, 2 patients had recurrences and were successfully salvaged with chemotherapy. Despite the large number of patients, there were no infield retroperitoneal recurrences in the area of the template dissection, although 1.4% of patients had recurrences out of the area of dissection and 3.3% of patients developed distant recurrences. There was one port site recurrence noted. Compared with O-RPLND, there was no difference in relapse rates, percentage of patients receiving chemotherapy (29% vs. 31%), rate of salvage surgery (1.2% vs. 1.5%), and patients with no evidence of disease (NED; 100% vs. 99.7%). The authors concluded that L-RPLND offers accurate staging and long-term outcomes similar to O-RPLND and that further studies should be performed to determine the therapeutic benefit of L-RPLND in patients with low-volume retroperitoneal disease.

A multi-institutional retrospective review of L-RPLND from four centers of excellence was reported by Nielsen et al. [14]. The study group included 120 patients with clinical stage I NSGCT who underwent primary RPLND employing a template dissection. Pathologically, 74 patients had stage I disease and 46 had positive lymph nodes with stage II disease. Median lymph node count was 20 with a median count of 22 for patients with negative lymph nodes and 15.5 for patients with positive lymph nodes. Thirty-six of 46 (78%) with stage II disease received chemotherapy while 10 patients were observed. Of the 10 stage II patients observed, 2 had recurrence of disease, both at eight months after surgery. Both were successfully treated with chemotherapy. Of the 74 pathological stage I patients, 7 (9%) developed recurrence at a mean follow-up of 36.4 months, with 4 pulmonary, 2 pelvic, and 1 marker recurrence. All patients were salvaged with chemotherapy and surgery was performed for the patients with pelvic recurrence. With a median follow-up of 29 months, there was no evidence of retroperitoneal recurrence in the region of dissection. The authors concluded that in experienced hands, L-RPLND can be performed safely and with outcomes comparable to O-RPLND based on intermediate-term follow-up.

The most recent experience with primary L-RPLND for clinical stage I NSGCT was published by Hyams et al. from Johns Hopkins who reported on 91 patients over a 15-year period [15]. The majority of patients had high-risk features, with 66% having lymphovascular invasion and 60% with greater than 40% embryonal carcinoma in the orchiectomy specimen. The median blood loss was 200 ml and two patients received transfusions. Operative times were not reported. There were 4 (4.3%) open conversions and 4 (4.3%) intraoperative complications, including a renal vein injury and an aortic injury that were converted to open surgery. The remaining two intraoperative complications were a renal artery injury and a serosal injury both of which were repaired laparoscopically. The mean length of stay was 2.1 days and there were 9 postoperative complications, 3 of which were related to lymphatic fluid leakage. Four patients experienced retrograde ejaculation. The mean lymph node count was 26.1 and 28 out of 91 patients had positive lymph nodes. Seven of these patients were pN2 status and received chemotherapy, while the remaining 21 were pN1. Fourteen of the pN1 patients elected to receive postoperative chemotherapy and 7 were followed with no evidence of recurrence. At a median follow-up of 38 months, no patient demonstrated a retroperitoneal recurrence and 5 of the pN0 patients developed systemic recurrence and were treated with chemotherapy.

Although there a few select centers still performing L-RPLND, the majority of MI-RPLND has evolved to the robotic approach due to improved visibility, better access to the retroperitoneum, and more comfort in controlling bleeding encountered during dissection around the great vessels. The first report of R-RPLND was presented by Davol et al. and demonstrated that it was technically feasible [16]. A case series of three patients with NSGCT undergoing primary R-RPLND was reported by Williams et al. in 2011 [17]. Patients were placed in the lateral position and the technique described was an extension of the laparoscopic approach using the robot. All three patients underwent unilateral template dissections without complications and no positive lymph nodes.

A series demonstrating the supine approach for R-RPLND was recently published by Cheney et al. from the Mayo Clinic [18]. They reported on 18 patients, 9 with primary testicular cancer, 8 with residual masses after chemotherapy, and 1 with paratesticular rhabdomyosarcoma. The supine approach was successful in 15 of the 18 patients with open conversion performed for hemorrhage, poor exposure, and robotic malfunction in three cases. Mean operative time was 311 minutes for primary R-RPLND and 369 minutes for postchemotherapy R-RPLND ($P = 0.03$). Mean estimated blood loss was 100 ml for primary R-RPLND and 313 ml for the postchemotherapy group ($P = 0.13$). Mean length of stay was 2.4 days and there were three minor (Clavien II) complications (17%). Mean lymph node count was 20 and lymph nodes were positive in 8 of 18 patients (44%), including 5 of 8 patients with postchemotherapy tumors and 3 of 10 patients undergoing primary R-RPLND. No patient received adjuvant chemotherapy, and at a mean follow-up of 22 months, there were no retroperitoneal recurrences, although two patients required salvage chemotherapy for pulmonary recurrence. This study highlighted the utility of the supine approach for R-RPLND and demonstrated that a full bilateral dissection could be performed without the need for reprepping and redraping the patient.

Our group recently reviewed our experience with R-RPLND using both the lateral and supine approaches [19]. Our initial experience was an extension of our laparoscopic procedure and we quickly recognized that the robotic platform offered several advantages over the laparoscopic approach. The advantages include 3D vision with improved visibility, enhanced instrument dexterity, and most importantly, better control of major vascular bleeding. A major limitation of the lateral approach was the inability to perform a full bilateral dissection in the event of positive nodes or in patients with postchemotherapy residual masses. The supine approach using the da Vinci robot addresses this issue and allows a full bilateral dissection without redocking or repositioning the patient. It also permits a superior view of the postganglionic sympathetic fibers in those patients undergoing nerve-sparing R-RPLND. Our experience includes 19 patients who underwent 20 procedures with 11 clinical stage I, 6 clinical stage II, and 3 clinical stage III patients. There were 16 primary and 4 postchemotherapy procedures with 11 lateral and 9 supine approaches. Median operative time for the group was 293 minutes, but was 259.7 minutes for unilateral dissections and 313 minutes for bilateral procedures. Median estimated blood loss was 50 ml and no patient required transfusion or conversion for bleeding. The median length of stay was 1 day with 14/20 (70%) of patients being discharged in less than 24 hours. Median lymph node count was 19.5. Eleven patients had pathologic stage I disease and 8 patients had pathologic stage II. One of the 8 with retroperitoneal disease had clinical stage I, 6 had clinical stage II, and 1 had clinical stage III disease preoperatively. Teratoma was found in 3 patients: 2 with clinical stage II disease and 1 with clinical stage III disease. There has been no evidence of recurrence in these patients. Embryonal carcinoma was found in 5 patients, 4 of whom had pathologic stage IIA, and 1 pathologic stage IIC disease. Two of these 5 patients received chemotherapy: 1 with pathologic stage IIC disease, and 1 with pathologic stage IIA disease who was followed and found to have a lung recurrence at four months after surgery. Three patients with pathologic stage IIA disease did not receive chemotherapy and have been followed expectantly; they have not required systemic therapy at follow-up of 46, 47, and 91 months. There has been no evidence of retroperitoneal disease recurrence in any patient in the series at a median follow-up of 49 months. There was one complication in the series. A ureteral transection occurred due to tumor involvement during a left-sided R-RPLND in clinical stage II patient. The ureter was repaired over a stent and remains patent after stent removal. Two patients who underwent bilateral R-RPLND suffered ejaculatory dysfunction.

A recent comparative analysis between L-RPLND and R-RPLND was reported by Harris et al. in *BJU International* in 2015 [20]. They compared 21 L-RPLND with 16 R-RPLND performed by a single surgeon. The series represented a mature experience with L-RPLND as compared to the early learning curve with R-RPLND. Despite this difference in experience, the outcomes for the two MI-RPLND techniques were essentially the same. The R-RPLND operative time was 270 minutes versus 294 minutes for L-RPLND, representing a difference of 24 minutes that was not statistically significant. Median estimated blood loss was 125 ml for L-RPLND and 75 ml for R-RPLND ($P = 0.16$). Median lymph node yield was 22 for L-RPLND and 30 for R-RPLND ($P = 0.13$). There were 2 (9.5%) postoperative complications in the L-RPLND group and 1 (6.3%) complication in the R-RPLND cohort. Follow-up for both groups was too short to make any meaningful statements about oncologic outcomes. The authors concluded that R-RPLND appears comparable to L-RPLND but at this stage it is unclear whether R-RPLND offers any tangible benefits over standard laparoscopy.

## Conclusions

MI-RPLND has undergone an evolution with regard to both technique and intent of the procedure. Initially, L-RPLND was performed as a staging procedure to direct adjuvant treatment in those patients with positive nodes, but with growing experience the procedure was carried out with therapeutic intent. To date, there have been many young men with pathologic stage II disease who have been cured with L-RPLND and have avoided the sequelae of chemotherapy including neuropathy, cardiovascular disease, infertility, and secondary cancers. There have been no recurrences reported in the retroperitoneum when L-RPLND was performed with care to remove the retrocaval and retroaortic tissues. Multiple studies have demonstrated that L-RPLND is feasible, safe, and reproducible, with reduced surgical morbidity compared to O-RPLND.

The application of robotics to RPLND has addressed the major hurdle of L-RPLND – the control of major vascular bleeding. In addition, the robotic platform has facilitated the development of the bilateral approach in patients with positive lymph nodes and opened the door for the safe application of minimally invasive surgery to postchemotherapy masses. R-RPLND is the future of MI-RPLND. There will be and should be continued scrutiny of MI-RPLND, as the current standards set by O-RPLND need to be adhered to and not compromised in the effort to reduce patient morbidity.

See accompanying Video 91.1.

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## 92

# Laparoscopic Radical Nephrectomy

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## Introduction

Laparoscopic surgery is a standard technique for the management of benign and malignant renal conditions. The first (pure) laparoscopic radical nephrectomy (LRN) was performed in 1991 by Clayman et al. [1]. Since its inception, modifications have been made to the technique to improve perioperative, short- and long-term functional and oncological outcomes. These modifications include retroperitoneal approach, hand-assisted and robotic-assisted techniques [2, 3]. The introduction of robot-assisted laparoscopic surgery was rapidly adopted by urologists largely because of the improved learning curve. Although laparoscopic techniques have evolved, allowing urologic surgeons to perform minimally invasive partial nephrectomies for smaller yet complex renal masses (see Chapter 93), LRN remains the gold standard for clinically localized renal masses. This chapter will review the indications, techniques, and results for laparoscopic radical nephrectomy, including hand- and robotic-assisted approaches.

## Indications for and contraindications to laparoscopic radical nephrectomy

The most common indication for radical nephrectomy is kidney cancer, which accounts for 3–5% of all adult malignancies [4]. Most clinical practice guidelines, including the American Urological Association and European Association of Urology guidelines, recommend radical nephrectomy (RN; surgical removal of the entire kidney, including Gerota's fascia, ± the ipsilateral adrenal gland) in patients with clinical stage T2, T3, or T4 renal cancer or in patients with multifocal ipsilateral renal masses without genetic predisposition [5, 6]. Although nephron-sparing surgery is recommended for T1 renal masses, RN may be performed in certain situations such as patient's preference or surgeon's inexperience (see Chapter 93). Whenever possible, however, partial nephrectomy should be performed for T1a renal masses [7]. The increased risk of cardiovascular mortality associated with decreased glomerular filtration rate (GFR) has been well documented [8]. This reduction in GFR has also been demonstrated in those who undergo radical nephrectomy for T1b lesions when compared to those who underwent partial nephrectomy [9]. Decreasing the risks associated with a compromised GFR, coupled with the sound oncologic data for nephron-sparing surgery, has led to the recommendation for partial nephrectomy for complex or T1b renal masses [10–14]. If not amenable to minimally invasive techniques, an open partial nephrectomy should be considered [15].

LRN with or without hand or robotic assistance can be utilized for clinically localized T2 disease. Recently, these techniques have been successfully modified and popularized for advanced T3 or T4 disease [16–19]. Finally, LRN or RLRN may also be used in the setting of cytoreductive nephrectomy to reduce the overall tumor burden when the metastatic disease burden is smaller in size than tumor burden within the kidney [20].

Contraindications are the same as for open radical nephrectomy and those specific to laparoscopy in general. Patients with significant coagulopathy or comorbidities that preclude them from undergoing general anesthesia or major surgery should not be subjected to LRN. LRN is also contraindicated in patients with inability to tolerate pneumoperitoneum, such as in chronic obstructive pulmonary disease (COPD) or morbid obesity. Although previous surgery at the same site has demonstrated increased operative time and hospital stay, it is not an absolute contraindication to performing laparoscopy [21]. Previous abdominal surgery may increase risk of either

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Companion website: www.wiley.com/go/smith/textbookofendourology

complications or need for conversion to open surgery. Recent reports have been published regarding the minimally invasive management of a renal vein, inferior vena cava (IVC), or atrial thrombus, but this is limited and should only be performed in highly experienced centers [22]. Finally, advanced age is not an absolute contraindication to LRN [23].

## Preoperative evaluation and patient preparation

In general terms, the preoperative work-up for a patient with a renal mass is no different for an LRN than that for an open radical nephrectomy (see Chapter 77 for details on patient preparation). Briefly, this includes a detailed history and physical examination, a complete blood count, serum electrolytes, coagulation profile, calcium, and alkaline phosphatase. A chest X-ray or chest computed tomography (CT) scan is required to screen for pulmonary metastases. A bone scan is unnecessary in the absence of bone pain or an elevated alkaline phosphatase. A head CT scan is indicated in the presence of neurological symptoms. If the serum creatinine is elevated, a 24-hour urine creatinine level and possibly a MAG3 or DMSA renal scan may be needed to assess differential renal function. Usually the patient presents with abdominal imaging demonstrating a renal mass. If abdominal imaging is inadequate, a three-phase CT or magnetic resonance imaging (MRI) is required to document enhancement of the renal mass. Abdominal imaging may also inform operative planning and approach if multiple renal arteries are identified, for example. If there is concern for a renal vein or caval thrombus, an MR venogram should be obtained. Finally, although the evidence for lymphadenectomy in renal cell carcinoma remains inconclusive, careful attention should be paid on imaging to regional and retroperitoneal lymphadenopathy. Despite the European Organization for Research and Treatment of Cancer (EORTC) trial demonstrating no improvement in survival in those who underwent lymphadenectomy for localized renal cell carcinoma [24], others have demonstrated improved staging capability [25–27] and, in certain situations, improved survival with lymph node dissection for clinically detected lymphadenopathy [28]. The patient is kept nil per os after midnight the evening before surgery. The use of a mechanical bowel preparation is optional. Some prefer to use a bowel preparation in order to decompress the colon and small bowel for improved visualization and working space within the abdomen. A single dose of an antibiotic agent is given 30–60 minutes prior to the first incision to cover skin flora. Venous sequential compression devices are placed around the calves of the patient and initiated prior to the induction of general anesthesia. A prophylactic dose of subcutaneous heparin may be administered.

## Laparoscopic transperitoneal nephrectomy

### Patient positioning

The patient is placed in the supine position upon arrival in the operating room. After induction of general endotracheal anesthesia, an orogastric tube and bladder catheter are inserted to decompress the stomach and bladder respectively. The location of the extraction site, usually a Pfannenstiel or an infra-umbilical midline incision, is marked on the patient's skin to ensure a straight incision after the patient is positioned. The patient is then carefully placed in a modified lateral decubitus position, angled at approximately 30° from the ground. The patient's flank overlays the kidney rest, an axillary role is placed, and an additional roll is placed longitudinally along the patient's back to support the thoracolumbar spine. The two legs are kept straight with a pillow or other padding placed behind the knees for support. Thick (silk or cloth) tape is used to secure the patient to the table (with paddings) at several points in order to prevent the patient from sliding off the table during the procedure should the table require rotating (Figure 92.1). Finally, the abdomen is prepped and draped in a sterile fashion, along with the corresponding flank in case the need arises to convert to an open procedure.

### Access

This can be achieved in a variety of ways, including but not limited to the Veress needle or Hasson cut-down technique, depending on the experience or comfort of the surgeon. The Hasson cut-down technique is preferred by some surgeons, especially in cases of previous abdominal surgeries, although the utilization of Veress needle access is documented to be safe in this patient group as well [15]. The abdomen is insufflated to a pressure of 15–20 mmHg. Once sufficiently insufflated, a 10 mm reusable screw or a 12 mm disposable trocar is placed into the abdomen at the level of the umbilicus for the camera. The position of this trocar may be shifted proximal or lateral depending on the abdominal girth after sufficient pneumoperitoneum is achieved. A 0° or 30° lens is utilized depending on surgeon's preference. The abdominal contents are inspected for any injury during access or from introduction of the first trocar. A second 12 mm trocar is placed at the level of the

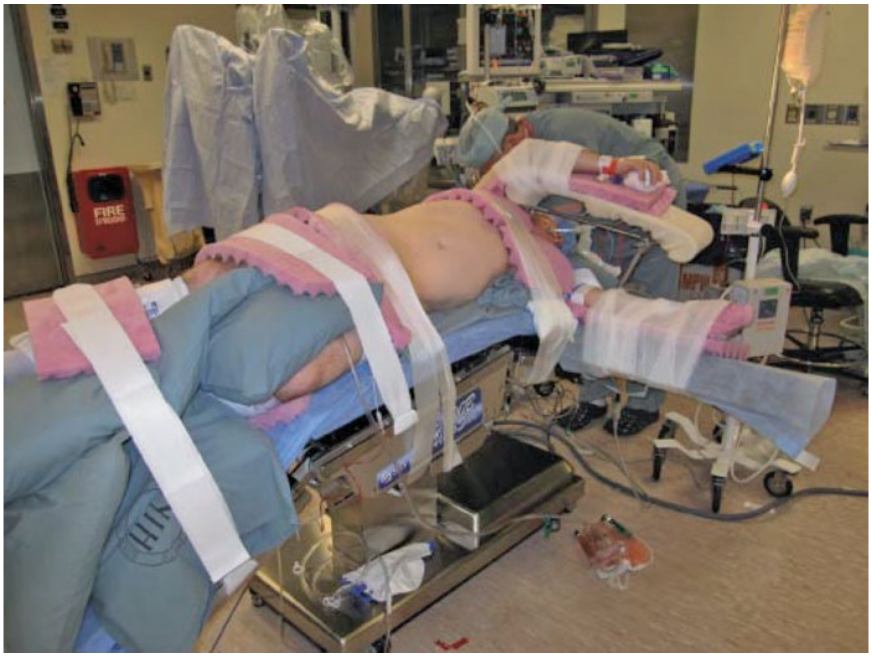

**Figure 92.1** Patient position for a transperitoneal laparoscopic or robot-assisted radical nephrectomy.

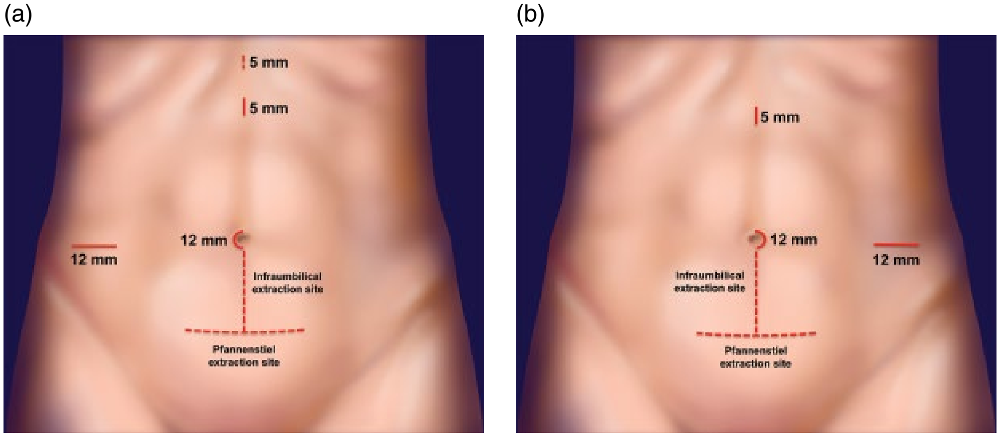
(a)
5 mm
5 mm
12 mm
12 mm
Infraumbilical extraction site
Pfannenstiel extraction site
(b)
5 mm
12 mm
12 mm
Infraumbilical extraction site
Pfannenstiel extraction site

**Figure 92.2** Port placement for a laparoscopic (a) right and (b) left radical nephrectomy. The extra (dotted line) 5 mm port may be utilized for liver retraction. *Source:* Visible Health, Inc., USA. Reproduced with permission of Visible Health, Inc.

umbilicus in the anterior clavicular line. A valveless (AirSeal®, ConMed, Utica, NY, USA) trocar system is preferred by some surgeons at this site, because of the documented stability of insufflation pressure during aggressive suctioning and reduction in $CO_2$ consumption [29, 30]. A third, 5 mm trocar is placed approximately 8 cm cephalad to the umbilical trocar in the midline. For a right nephrectomy, an additional 5 mm port may be placed inferior to the subxiphoid process to assist with liver retraction (Figure 92.2). Again, if the patient is obese, all respective port positions may need to be placed laterally and superiorly in order to account for abdominal wall distortion. Further, for large renal masses, a 12 mm port should be considered in place of the 5 mm port to allow for maximum versatility in passing a greater variety of instruments through any port location. Finally, if an additional port is needed for retraction, an ideal placement is in the previously marked Pfannenstiel or infra-umbilical midline incision line. At the completion of the case, the extra port incision is extended and used to extract the specimen.

## Procedure

The white line of Toldt is incised sharply. If electrocautery is utilized for this incision, care must be taken to avoid the risk of bowel injury from thermal spread. A plane is developed between the posterior mesenteric and anterior perirenal fat using a combination of blunt and sharp dissection. The respective colon is mobilized medially from the iliac vessels to the respective hepatic or splenic flexure. For a right nephrectomy, the hepatic flexure is released by dividing the renocolic ligament. This allows for further medial mobilization of the colon. The duodenum is mobilized using sharp dissection. Minimal use of blunt dissection is encouraged around the duodenum to avoid inadvertent serosal injuries. Duodenal mobilization is completed after gaining adequate exposure to the IVC (also referred to as a Kocher maneuver). In the case of a left nephrectomy, the left colon is mobilized similarly with a combination of blunt and sharp dissection. The splenorenal ligament and splenophrenic attachments are divided in order to mobilize the spleen medially, en bloc with the splenic flexure, which provides medial reflection of the tail of the pancreas. This maneuver is important to minimize the risk of injury to the tail of the pancreas during left hilar dissection. Complete splenic mobilization often requires visualizing the stomach above the spleen. Finally, mobilization of the left colon is complete once the aorta is exposed. Once Gerota's fascia is exposed, the psoas is identified, anterior to which is the ureter. Alternatively, the mid ureter can be found posterior and medial to the gonadal vein. This relationship is particularly important when tracing the ureter to the renal hilum in the case of a right nephrectomy. Care is taken to sweep the gonadal vein medially, separating it from the ureter and avoiding the risk for avulsing it from the vena cava. The ureter is kept intact, which allows it to be used as a handle for anterior and cephalad retraction of the kidney later in the case. At this point the lower pole of the kidney is mobilized within Gerota's fascia. This has the potential for causing significant bleeding in the case of large, lower pole masses or if multiple parasitic vessels are encountered. To help facilitate lower pole mobilization with adequate hemostasis, electrocautery, any of a number of ultrasound-based coagulation devices, or the LigaSure® (Valleylab, Boulder, CO, USA), which uses an electrical current to fuse blood vessels, may be utilized. Prior to the start of dissection, some surgeons recommend placing a small lap pad into the patient. In the event of unexpected bleeding, this can be used to improve visualization, or in the worst case scenario, tamponade bleeding to allow time for open conversion.

With the lower pole of the kidney mobilized, the ureter can be traced cephalad to the renal hilum. Care needs to be taken when dissecting toward the renal hilum in the event of a lower pole accessory vessel that was not visible on preoperative imaging. Retracting anteriorly and cephalad on the kidney allows for better exposure to the renal vein and artery. Judicious use of energy-based dissection may be required to divide the fibrous lymphatic tissue often surrounding the renal artery.

For a left nephrectomy, ensuring the left renal artery is positioned posterior to the exposed renal vein ensures that the superior mesenteric artery is not mistaken for the left renal artery. Next, when the left renal vein is isolated, the gonadal vein can be clipped and divided if necessary. Caution should be exercised at this point to prevent avulsing a potential lumbar vein draining into the posterior surface of the left renal vein.

If the adrenal gland is to be taken, the left adrenal vein can be clipped and divided at this point. Once the renal artery and vein are isolated, an endovascular stapler or clips are used to secure the artery and vein. Once the artery has been divided, if the renal vein does not decompress as expected, thus raising the concern for a renal vein thrombus, or if there is a known renal vein thrombus preoperatively, laparoscopic ultrasound is employed to ensure the thrombus has retracted completely before dividing the vein. After the artery, followed by the vein, has been divided, the decision is made whether to preserve the adrenal gland or to take it with the specimen. For large, central tumors or those located in the upper pole of the kidney, removing the adrenal gland with the kidney should be considered to ensure there are negative margins or if there is any evidence of metastatic or contiguous involvement of the adrenal gland.

In the case of a right nephrectomy, moving superiorly along the IVC will expose the short, right adrenal vein. Care should be taken to avoid avulsing the right adrenal vein, as this can lead to significant hemorrhage. Once divided, the use of energy-based dissection can facilitate expeditious mobilization of the kidney and adrenal gland from the surrounding attachments and renal fossa, while securing potential parasitic vessels feeding the tumor. Care is taken superiorly to avoid inadvertent injury to the diaphragm. At this point, the ureter is clipped and divided, completely freeing the specimen. When taking the left adrenal gland, either the left renal vein can be stapled proximal to the insertion of the adrenal vein, or the adrenal vein can be clipped and divided separately. In the case of an adrenal-sparing nephrectomy, energy-based dissection can be used to effectively dissect and coagulate any small feeding vessels between the kidney and the adrenal gland.

Current evidence does not suggest a benefit to performing a lymph node dissection for T1 or T2 disease in the absence of clinically positive nodes [24, h 31]. However, retrospective data suggest some benefit to improved staging in those with clinically detected nodal disease [25]. Adding to the argument in favor of extended lymphadenectomy, Pantuck et al. demonstrated improved survival in patients with metastatic disease who underwent cytoreductive nephrectomy and lymphadenectomy prior to immunotherapy compared to those who did not receive an extended lymphadenectomy [28].

Depending on the clinical situation and surgeon preference, the lymph node dissection can be performed either laparoscopically or robotically, and is not precluded based on a minimally invasive approach.

Finally, the specimen is entrapped in any commercially available laparoscopic organ retrieval device. The specimen, depending on the size of the tumor, can be removed through a small extension of either the lateral or umbilical trocar incisions, or through a separate Pfannenstiel or midline infra-umbilical incision. A few surgeons have advocated morcellation to minimize the size of the incision necessary for specimen extraction, but the potential for tumor spillage is theoretically higher [32].

## Laparoscopic retroperitoneal radical nephrectomy

### Advantages/disadvantages

The retroperitoneal approach to LRN may be useful in cases of prior abdominal surgeries. However, if the patient is particularly obese or has a large amount of retroperitoneal fat, proper orientation can be difficult. Improper orientation and loss of appropriate landmarks can lead to significant operative challenges and even inadvertent caval transection when mistaken for the renal vein [33]. Furthermore, previous renal surgeries or renal infections can lead to significant perirenal adhesions or scarring, making the retroperitoneal approach even more challenging. Finally, large renal masses with multiple parasitic vessels or those that may involve other organs should not be removed retroperitoneoscopically.

### Positioning

The patient is placed in the full flank position. After the axillary roll and appropriate anterior/posterior bolsters are placed, the table is flexed to extend the space between the 12th rib and the iliac crest. The patient is secured with thick silk or cloth tape to the operative table.

### Procedure

After the patient is prepped and draped sterilely, an incision is made off the tip of the 12th rib large enough to accommodate the surgeon's index finger. With the oblique muscles divided, the lumbodorsal fascia is incised and the retroperitoneum is entered. The surgeon's index finger is inserted into the retroperitoneum, and the psoas muscle and lower pole of the kidney are palpated. A commercially available balloon dilator that accommodates a 10 mm laparoscopic lens is inserted into the incision under direct vision. The potential retroperitoneal space is dissected with the dilating balloon to a volume of approximately 800 ml. After deflating and removing the balloon, a blunt-tipped trocar with a soft collar is placed into the incision. The soft collar on the inside of the incision helps maintain insufflation as well as prevent subcutaneous emphysema. Furthermore, this port does not project far into the working space, therefore not impairing the view of the kidney. The laparoscope is placed through this trocar. Two additional trocars are placed. A 12 mm trocar is placed lateral to the camera port and approximately 2 cm cephalad to the iliac crest. A second 5 mm trocar is placed off the tip of the 11th rib. Finally, an optional additional 5 mm port can be placed off the tip of the 10th rib. When placing the ports medial to the initial camera port, the peritoneal lining must be swept medially or inadvertent peritoneal entry and bowel injury may occur. After the 10 mm 30° lens is placed through the 12 mm inferior port, surgical orientation is achieved based upon the position of the psoas muscle and overlying ureter.

At this point, the psoas muscle and tendon are dissected free of all retroperitoneal fat. Anterior and medial to the tendon will be the ureter. As with the transperitoneal approach, the ureter is traced back to the renal hilum and is used for placing traction on the kidney and hilum. Care is taken at this point as the IVC (for a right nephrectomy) or the aorta (for a left nephrectomy) is medial and in close proximity to the ureter.

For a left nephrectomy, as the ureter is traced to the renal hilum, dissection should be performed bluntly with the suction irrigator in case an ascending lumbar vein is encountered entering the renal vein. If found, the vein is clipped and divided before proceeding to the renal hilum. The ureter is traced superiorly along the medial aspect of the psoas muscle. This helps to keep the dissection in proper orientation and posterior to the kidney. The renal hilum is identified based on pulsation of the renal artery. Gerota's fascia is incised over the pulsation to expose the renal artery and vein. The artery and vein are isolated and divided as described for the transperitoneal approach.

After the kidney has been completely freed from the renal fossa and the ureter divided, the kidney is placed in a laparoscopically deployed organ entrapment device. If the mass and kidney are small, the initial port can be extended in order to deliver the kidney. In cases where the specimen is large, a Pfannenstiel incision is made and the space of Retzius is entered. Matin and Gill described a modified Pfannenstiel incision that is lateralized to the side of the surgery [34]. Dissection is carried down to the anterior rectus fascia and a vertical incision is created along the lateral rectus border. With the fascia and rectus muscle retracted, the transversalis fascia is divided near the pubis and the extraperitoneal space is entered.

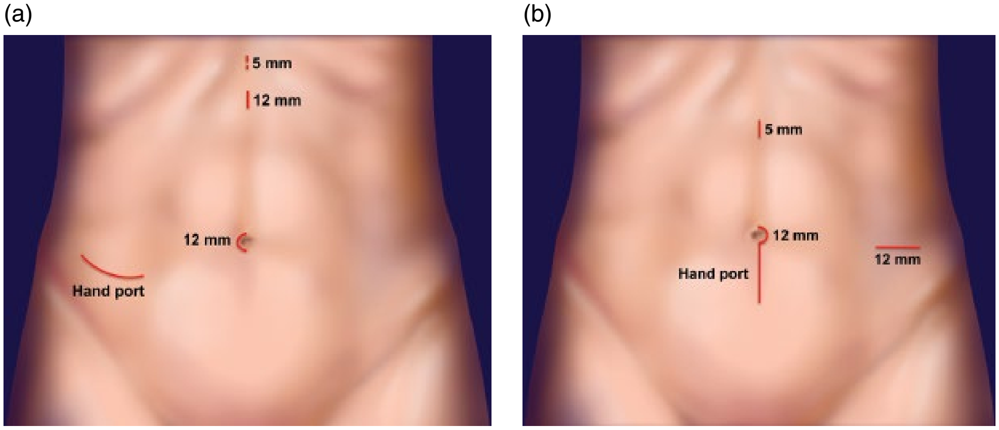

**Figure 92.3** Port placement for a hand-assisted laparoscopic (a) right and (b) left radical nephrectomy. The extra (dotted line) 5 mm port may be utilized for liver retraction. *Source:* Visible Health, Inc., USA. Reproduced with permission of Visible Health, Inc.

Careful blunt dissection into the retroperitoneum through the Pfannenstiel incision can allow for delivery of larger specimens through a lower abdominal incision [34].

See accompanying Video 92.1.

## Hand-assisted laparoscopic nephrectomy

### Advantages/disadvantages

Surgeons with limited experience in pure laparoscopy may find hand-assisted laparoscopic nephrectomy (HALN) advantageous. It is particularly helpful when large renal masses are encountered and significant risk for intraoperative bleeding is anticipated. HALN also allows for the use of tactile sensation, which is useful in cases where the anatomy is obscured. Finally, it may also be used as a technique to convert from a pure laparoscopic approach to open. One disadvantage of this approach, however, is that it often results in a cosmetically suboptimal incision compared to the Pfannenstiel incision when used for specimen extraction. Additionally, maintaining adequate pneumoperitoneum, and thus proper visualization, may be a challenge if the hand port leaks or if the incision for the port is too long.

### Position and trocar placement

Patient position is the same as for the laparoscopic approach. The details of trocar placement and nuances of various hand ports are beyond the scope of this chapter. Briefly, for a right nephrectomy, the hand port is placed in the right lower quadrant, a 12 mm trocar at the umbilicus, another 12 mm camera port in the midline approximately 8 cm cephalad to the umbilicus, and a 3 or 5 mm port immediately inferior to the subxiphoid process for a liver retractor (Figure 92.3a). For a left nephrectomy, the hand port is placed immediately below the umbilicus in the midline, followed by a 12 mm trocar 8–10 cm lateral to and at the level of the umbilicus. Finally, a third 12 mm port is placed 8 cm cephalad to the umbilicus for the camera (Figure 92.3b).

### Procedure

The white line of Toldt is incised sharply while the nondominant hand through the hand port places traction on the colon medially. After the correct plane between the colonic mesentery and Gerota's fascia is entered, the colon is swept medially with the nondominant hand and the suction irrigator. For a right nephrectomy, the renocolic ligament is divided while the nondominant hand retracts the hepatic flexure medially. This exposes the duodenum and Gerota's fascia. As with the pure laparoscopic approach, the duodenum is reflected sharply. At this point, a liver retractor may be placed through the subxiphoid port to elevate the liver and allow better access to the renal hilum. For a left nephrectomy, the splenorenal and splenophrenic ligaments are divided. The hand provides gentle medial traction on the spleen to allow for exposure to the upper pole. The psoas muscle is identified and the ureter and gonadal vessels are isolated. For a right nephrectomy, the ureter is retracted anteriorly with the hand while the gonadal vessels are swept medially with the suction irrigator. On the left, the vessels are taken with the ureter. The ureter is then traced toward the renal hilum.

At this point, the lower pole of the kidney is mobilized and retracted anteriorly and cephalad with the hand, while the renal vessels are dissected free with a combination of blunt and energy-based dissection. In cases where a large renal mass partially obscures the renal hilum, it may help for the surgeon to use an index finger to palpate the renal artery. After sufficient exposure of the vein and artery is achieved, the endovascular stapler or clips are used to divide the renal artery, followed by the vein, while maintaining exposure of the renal hilum with the surgeon's hand. At this point, the decision must be made whether to keep the adrenal or remove it with the kidney. On the right side, if the adrenal gland is to be taken with the kidney, the nondominant hand is used to retract the kidney laterally while the suction irrigator is used to bluntly dissect the adrenal vein. After the short adrenal vein is exposed, it can be clipped and divided sharply. Once divided, a combination of energy-based dissection and finger-fracturing of the surrounding renal attachments expeditiously mobilizes the kidney and adrenal gland. While doing this, the surgeon is also simultaneously palpating and securing parasitic vessels feeding the tumor.

Finally, the ureter is ligated and divided, completely freeing the specimen. If the decision is made to preserve the adrenal gland, dissection of the adrenal is performed by retraction on the adrenal with the off-hand and division of the adrenal gland from the kidney with energy-based dissection.

The remaining portion of the nephrectomy is completed as described above. We recommend the use of a laparoscopically deployed entrapment device for HALN. This helps protect the exposed incision from the unnecessary risk of tumor spillage/implantation.

## Robot-assisted laparoscopic radical nephrectomy

### Advantages/disadvantages

RLRN allows urologic surgeons with minimal laparoscopic skills to more easily transition open surgical techniques into a minimally invasive procedure. In addition, some surgeons prefer the use of robotic assistance in cases where hilar and/or retroperitoneal lymph node dissection is indicated. Disadvantages of this procedure include the lack of a haptic interface and the increased operating room costs imposed when using the robotic approach. Furthermore, operative time may be increased as a result of docking and undocking the robot [35]. The following will describe the use of the da Vinci robotic system (Intuitive Surgical, Inc., Sunnyvale, CA, USA) for a radical nephrectomy.

### Positioning

Robotic renal surgery can be performed both transperitoneally and retroperitoneally. For a transperitoneal approach, the robot is docked from the back of the patient at a 20° angle toward the head of the patient (Figure 92.4a). When performing retroperitoneal robotic renal surgery, the robot is docked directly over the head of the patient (Figure 92.4b). The patient is positioned in

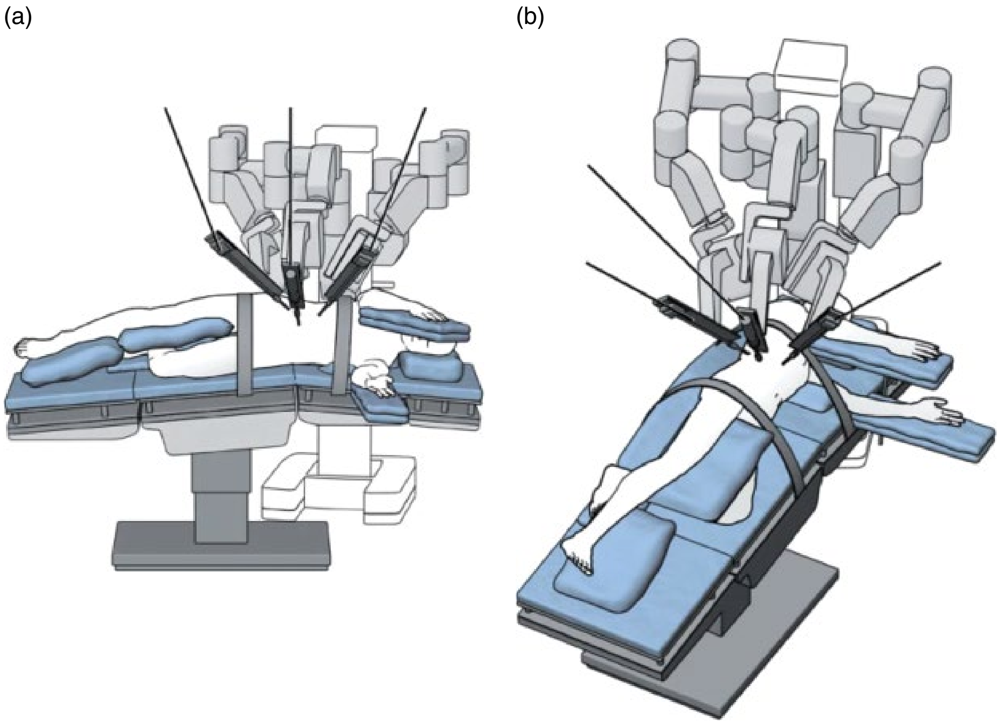

**Figure 92.4** Robot docking position for (a) transperitoneal and (b) retroperitoneal laparoscopic radical nephrectomy.

the modified lateral decubitus position as previously described for the transperitoneal approach with attention paid to the arm ipsilateral to the affected kidney. This arm should be positioned medial and cephalad, as it could limit the movement of the subcostal robotic instrument.

### Procedure

With the patient properly positioned, pneumoperitoneum is achieved to a pressure of 15–20 mmHg, as described above. A 12 mm umbilical trocar is placed and the abdominal contents are inspected for adhesions and to rule out bowel injury after establishment of pneumoperitoneum. Two additional 8 mm robotic trocars are placed, each 8 cm from the umbilical trocar and from each other. A 12 mm assistant trocar is placed approximately 8 cm inferior to the umbilical trocar. An additional 5 mm assistant trocar is placed superior to the umbilical port if needed for organ retraction. When using the standard system, the trocars need to be spaced out further to avoid robotic arm collisions. When using the da Vinci Xi robotic series, the slimmer profile of the robot allows the trocars to be placed in closer proximity to each other. Using the robotic Maryland forceps or fenestrated bipolar and electrocautery shears, the white line of Toldt is identified and incised sharply while the assistant is retracting medially on the bowel.

Once the proper plane between the mesocolon and Gerota's fascia is established, much of the bowel mobilization can be done bluntly. After adequate bowel mobilization, the ureter and gonadal vessels are exposed and lifted anteriorly to expose the psoas muscle. The assistant may retract anteriorly on the ureter, allowing the robotic surgeon to use both hands for additional dissection. An additional port for the robotic fourth arm could be placed and utilized for retraction.

For a right nephrectomy, the gonadal vessel needs to be swept medially in order to prevent inadvertent injury to or avulsion of the gonadal vein. Blunt dissection using both robotic arms for traction–countertraction sweeping movements is performed when progressing cephalad along the psoas toward the hilum. For a left nephrectomy, the spleen is mobilized as described for the pure laparoscopic approach. In the case of a right nephrectomy, the Kocher maneuver is performed exclusively with sharp dissection in the same manner as previously described. With the lateral attachments of the kidney left in place, exposure of the hilum and renal vasculature is performed. The Maryland dissector or the fourth arm (with a Prograsp installed) is used to retract the kidney laterally to place mild traction on the hilum for dissection. The bedside assistant may also be utilized for this. Electrocautery is often required to divide the dense lymphatic and fibrous tissue surrounding the renal artery. For large renal masses on the right, the robot may be helpful in dissecting an obscured renal artery from an interaortocaval approach. After the renal vasculature has been sufficiently exposed, the assistant inserts an endovascular stapler to divide the renal artery, followed by the renal vein. Alternatively, the assistant can ligate the vessels with clips. In addition, the robotic system allows the console surgeon to apply locking clips if the bedside assistant is unable to.

With the renal vasculature divided, an adrenal-sparing nephrectomy may be performed as indicated. After the kidney has been fully mobilized medially, it is freed from the surrounding renal fossa and lateral attachments. At this point, liberal use of electrocautery and bipolar energy through the Maryland forceps or fenestrated bipolar can help minimize bleeding from parasitic vessels. Finally, with the kidney completely free within the abdomen, the pneumoperitoneum is slowly dropped and the renal fossa observed for several minutes to inspect for bleeding. The robot is undocked and the specimen is removed through an extraction site that was marked previously on the patient.

## Results

Since the original description of laparoscopic nephrectomy in 1991, the minimally invasive approach to radical nephrectomy has gained wide acceptance throughout the urologic community and is now considered the treatment of choice for isolated renal masses not amenable to nephron-sparing surgery [32].

Compared to open surgery, laparoscopy has been shown to result in less postoperative pain, less analgesic requirement, early postoperative ambulation, faster return of bowel function, shorter hospital admissions, improved cosmesis, and overall decreased convalescence period [23, 36–40]. As urologic surgeons adopted LRN, multiple series published in the literature have reported oncologic outcomes comparable to those for open radical nephrectomy (Table 92.1). The longest current series runs over 11 years postoperatively. The overall, cancer-specific, and recurrence-free survival rates at 10 years in this group were 65%, 92%, and 86%, respectively. From this series, 71% of renal masses were T1, 15% were T2, and 10% were T3a [41]. Several series have also demonstrated equivalent oncologic outcomes when comparing HALN to the open approach. Though these studies were limited by their retrospective nature, their results are nonetheless compelling [39, 42, 43]. Although RLRN should have similar outcomes to LRN, there are limited follow-up data available.

**Table 92.1** Outcomes of hand-assisted laparoscopic (HALN), robotic-assisted laparoscopic (RALRN), pure laparoscopic (Lap), and open nephrectomies.

| Study | Cohort size | Surgical approach | Follow-up duration[a] | Recurrence-free survival (%) | Cancer-specific survival (%) |
|---|---|---|---|---|---|
| Chung et al. [39] | 54 | HALN | 47 months | 91 | 94 |
| Kawauchi et al. [42] | 123 | HALN | 41 months | 92 | 92 |
| Miyake et al. [43] | 63 | HALN | 38 months | 85 | 92 |
| Rogers et al. [44] | 34 | RALRN | 15.7 months | 100 | NR |
| Berger et al. [41] | 73 | Lap | 11.2 years | 86 | 92 |
| Colombo et al. [45] | 48 | Lap | 65 months | 91 | 91 |
| Permpongkosol et al. [46] | 67 | Lap | 73 months | 94 | 97 |
| Hemal et al. [47] | 132 | Lap | 56 months | 87 | 88 |
| Portis et al. [48] | 64 | Lap | 54 months | 92 | 98 |
| Saika et al. [49] | 181 | Lap | 40 months | 91 | 94 |
| Tsui et al. [50] | Stage I[b] 185 | Open | 47 months | NR | 91 |
| | Stage II[b] 57 | Open | 47 months | NR | 74 |
| Javidan et al. [51] | Stage I[b] 205 | Open | 64.5 months | NR | 95 |
| | Stage II[b] 53 | Open | 64.5 months | NR | 88 |

[a] Mean or median.
[b] Based on 1997 TNM Staging criteria.
NR, not reported.

## Conclusions

Significant advances have been made in the field of minimally invasive surgery for kidney cancer, leading to improvements in patient convalescence, while providing comparable or equivalent oncological outcomes for renal malignancies. With the development of robotic technology and incorporation into formal training programs, these advances can be adopted easily by those with limited laparoscopic skills, thus extending the reach of minimally invasive surgery to a greater number of patients.

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# Robotic Partial Nephrectomy: Advancements and Innovations

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## Introduction

Despite recent debate about whether partial nephrectomy (PN) confers any overall survival advantage over radical nephrectomy in patients with small renal masses [1, 2], the relevance and importance of nephron-sparing surgery remains unquestioned [3–7]. Minimally invasive techniques such as robotic PN provide oncologic and functional outcomes equivalent to those from open PN while decreasing patient morbidity [7], and have increased the utilization of PN surgery in the field.

Post-PN kidney function depends primarily on the volume and condition of the remnant renal parenchyma, and secondarily upon the duration of ischemic insult during PN [8]. To minimize renal damage during PN surgery, warm ischemia time is best restricted to less than 20–25 minutes [8, 9]. During PN surgery, the amount of kidney excised strongly correlates with the ischemia time required to achieve that excision and reconstruction. Almost always, the deeper, larger, and more complex a particular renal tumor, the longer the ischemia time required to excise that specific tumor and perform the necessary renal reconstruction; conversely, the smaller and simpler the renal tumor, the shorter the ischemia time needed to perform that particular PN. Thus, the volume of kidney excised/preserved during PN is inextricably interlinked with the ischemia duration. Recent surgical innovations seek to maximize PN outcomes by optimizing surgically modifiable factors, such as minimizing/eliminating global ischemia, performing tumor excision with a thin negative margin, meticulous point-specific parenchymal hemostasis, careful renorrhaphy, all to secure maximal preservation of vascularized, functional, normal kidney parenchyma [10]. Minimally invasive technique aside, the initial surgical innovations for reducing warm ischemic injury during PN were "early-unclamping" techniques, which then evolved to selective arterial clamping aimed at achieving only tumor-specific ischemia [11] and now zero-ischemia, unclamped techniques in an attempt to maximally retain global kidney function. While minimizing ischemia during the PN, surgical techniques such as sculpted tumor excision, with pinpoint suturing to achieve hemostasis, further minimize functional parenchymal loss [12].

In this chapter, advancements of robotic PN technique are described. These technical nuances minimize global renal ischemia, maximize normal kidney parenchyma preservation, and perform meticulous sutured renal reconstruction with minimal blood loss and complications. We also discuss imaging modalities that assist in the propagation of these techniques.

## Preoperative preparation

### Preoperative evaluation

Preoperative evaluation for PN consists of a detailed history and physical examination, baseline laboratory values such as serum creatinine and estimated glomerular filtration rate, which is calculated using the modification of diet in renal disease formula. A three-dimensional renal-dedicated computed tomography (CT) or magnetic resonance imaging (MRI) scan using 0.5–2 mm slice thickness provides details about tumor location, depth, proximity to the collecting system, and renal contact surface area. Arterial and venous phases of the CT scan provide detailed depiction of the extrarenal hilar vascular anatomy.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

During the initial clinical visit, the patient is counseled as to all treatment alternatives, including active surveillance with percutaneous renal mass biopsy [13] and various interventive surgical options. Risks, benefits, potential complications, and the possibility of conversion to open surgery or radical nephrectomy are discussed prior to obtaining surgical consent.

Antiplatelet and anticoagulant medications are discontinued or bridged prior to surgery, as clinically indicated. Medical and anesthesia clearance is obtained. No routine formal bowel preparation is performed prior to surgery. However, per surgeon's preference, a clear liquid diet can begin the prior evening to surgery, with/without bisacodyl suppository or an oral saline cathartic, such as magnesium citrate or sodium phosphates. Antibiotics, such as cefazolin, are administered intravenously preoperatively. To prevent deep venous thrombosis, pneumatic compressive stockings and 5000 U subcutaneous heparin are administered 2 hours prior to the procedure and continued 8–12 hourly postoperatively. Anticoagulation is continued for up to one month after discharge, per surgeon discretion. Upon commencement of the robotic procedure, 1.52 liters of crystalloid intravenous fluids are administered to expand the intravascular volume and initiate a brisk diuresis.

## Operative room setup

We use a four-arm technique for robotic PN; use of the fourth robotic arm provides fixed traction during key maneuvers, enhanced exposure for hilum and tumor dissection, retraction of overlying perirenal fatty tissue for further exposure, less dependence on the assistant, and increased diversity of surgical maneuvers. The bedside assistant is positioned facing the patient's abdomen, and the scrub technician is positioned behind the assistant. Video monitors are placed at the head and foot end of the patient on the side of the robot for easy viewing by the surgical team. A Mayo stand is placed next to the assistant where frequently used instruments are placed. The da Vinci® Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) is docked posterior to the patient with the camera arm coming in to the patient at an angle of 15° in line with the camera trocar site (described in detail below) (Figure 93.1).

## Patient positioning

Under general endotracheal anesthesia, the patient is placed in a modified (60–70°) lateral decubitus position, with the umbilicus over a mid break in the table. An axillary roll is placed, the table is flexed as necessary (usually minimally compared with open flank surgery), and copious padding is used and positioned to support the buttocks and flank. Pillow(s) are placed between the flexed lower and straight upper leg. The upper arm rests on a well-padded arm board (or pillows) without tension on the brachial plexus. Tape is used to secure the patient around the hips, shoulders, and thighs to ensure stability when rolling the table to facilitate bowel retraction (Figure 93.2a). Care is taken to adequately pad all pressure points and place all limbs in neutral position to minimize positioning injuries. The abdominal skin is shaved with clippers and the patient is prepped and draped in standard sterile fashion for a transperitoneal robotic surgery. An 18 Fr urethral catheter is inserted and an orogastric tube is placed. A standard time-out is called prior to incision.

## Instrumentation and equipment list

### Equipment

- Da Vinci® Si or Xi Surgical System (Intuitive Surgical Inc.)
- 0° and 30° robotic scope (Intuitive Surgical Inc.)
- Mono-polar scissors (Intuitive Surgical Inc.)
- ProGrasp™ forceps (Intuitive Surgical Inc.)
- Bipolar Grasper™ forceps (Intuitive Surgical Inc.)
- Needle drivers (Intuitive Surgical Inc.)
- Clip appliers (Intuitive Surgical Inc.).

### Trocars

- 12 mm visual obturator trocar (Visiport, Medtronic Parkway, Minneapolis, MN, USA)
- 5 mm trocar × 2
- 8 mm trocars × 2
- Bariatric 8 mm trocars × 2.

### Assistant instruments

- Suction irrigator device (bariatric length)
- Laparoscopic spoon forceps
- 5 mm locking atraumatic grasper
- Hem-o-lok® applier – bariatric (Teleflex Medical, Research Triangle Park, NC, USA)
- Medium (purple) Hem-o-lok clips (Teleflex Medical)
- Laparoscopic needle driver
- Laparoscopic scissor
- 15 mm specimen entrapment bag
- Laparoscopic Doppler ultrasound probe
- Surgicel® hemostatic gauze (Ethicon, Johnson & Johnson, New Brunswick, NJ, USA)
- FloSeal hemostatic matrix and laparoscopic applier with obturator (bariatric length) (Baxter International, Deerfield, IL, USA)
- Laparoscopic bulldog clamps

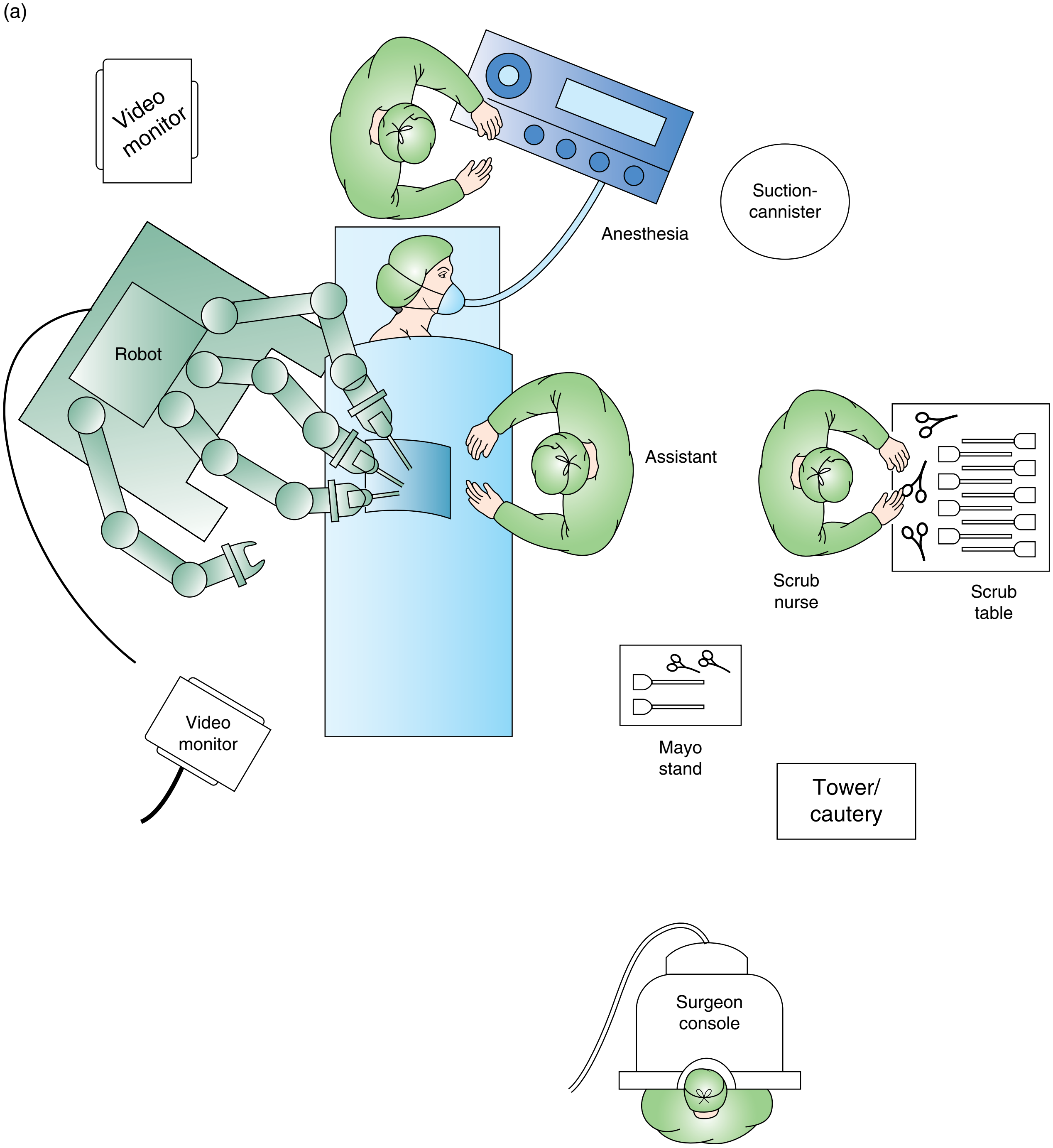
(a)
Video monitor
Anesthesia
Suction-cannister
Robot
Assistant
Scrub nurse
Scrub table
Mayo stand
Video monitor
Tower/ cautery
Surgeon console

**Figure 93.1** Operating room setup. (a) For right partial nephrectomy and (b) left partial nephrectomy.

- Neurosurgical aneurysm micro bulldog clamps (Bear™ disposable vascular clamp, AROSurgical, Newport Beach, CA, USA)
- Mini-vessel loops (Devon Dev-o-loops, Tyco Healthcare, Mansfield, MA, USA)
- Indocyanine dye (Akorn, Lake Forest, IL, USA)
- Hemovac or Jackson–Pratt.

**Recommended sutures**

- 4-0 Polypropylene suture or 3-0 polyglactin suture on an SH needle (Ethicon, Johnson & Johnson)
- 4-0 Poliglecaprone or V-Loc barbed suture (Ethicon, Johnson & Johnson)

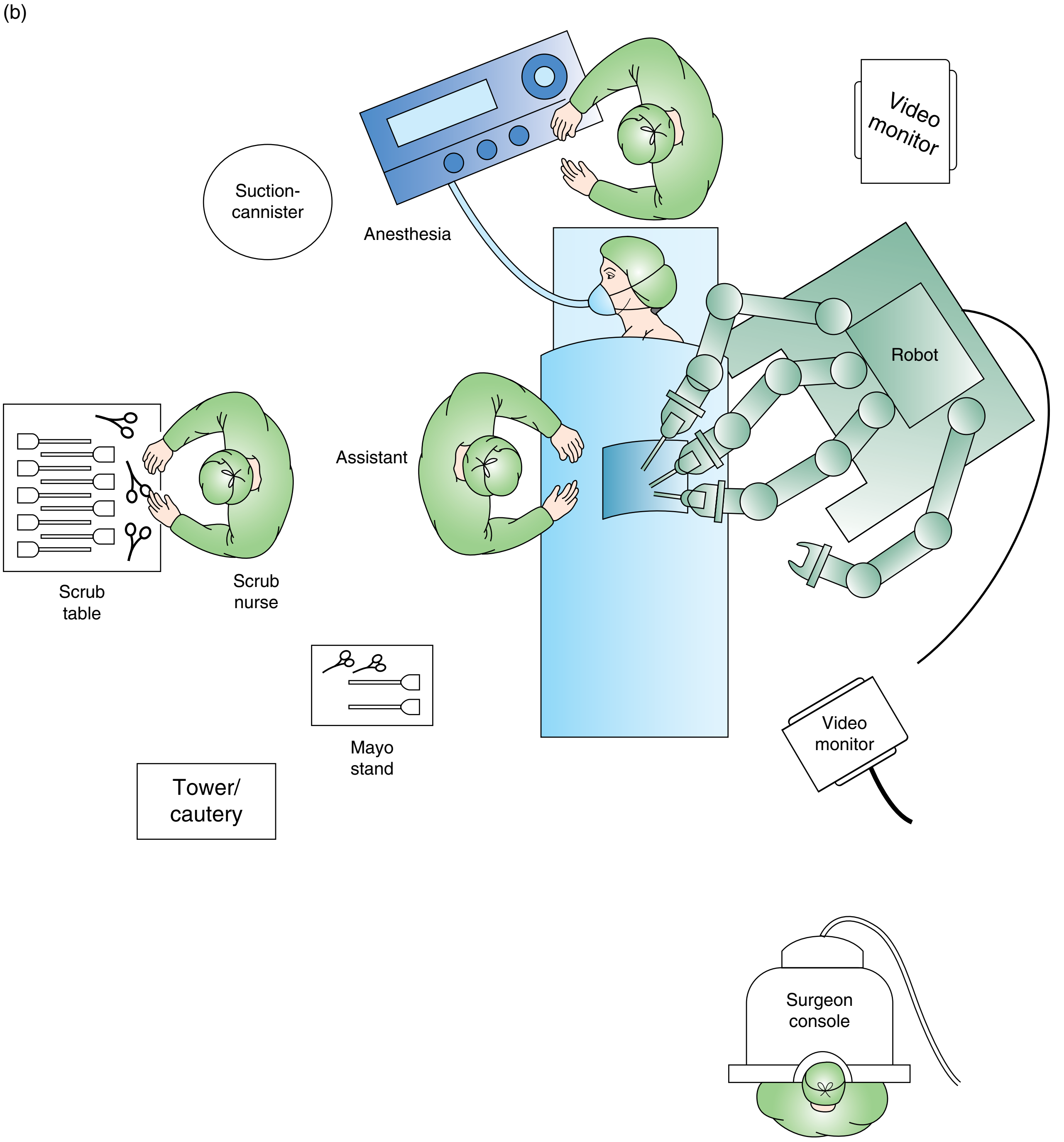
(b)
Video monitor
Suction-cannister
Anesthesia
Robot
Assistant
Scrub table
Scrub nurse
Mayo stand
Video monitor
Tower/ cautery
Surgeon console

Figure 93.1 (Continued)

## Step-by-step technique: robotic partial nephrectomy

### Step 1: Pneumoperitoneum and trocar placement (Figure 93.2b–c)

For the vast majority of tumors, we prefer a transperitoneal approach. Our trocar placement configuration allows for treatment of all renal tumors irrespective of location, whether upper pole, lower pole, or hilar. Four robotic trocars are employed with 1–2 assistant ports. Veress needle pneumoperitoneum is established at 13–15 mmHg and the first trocar (12 mm for the Si robot; 8 mm for the Xi) is inserted on the same level of the 12th rib just lateral to the pararectus line. The robotic camera is then inserted and the peritoneal cavity inspected to

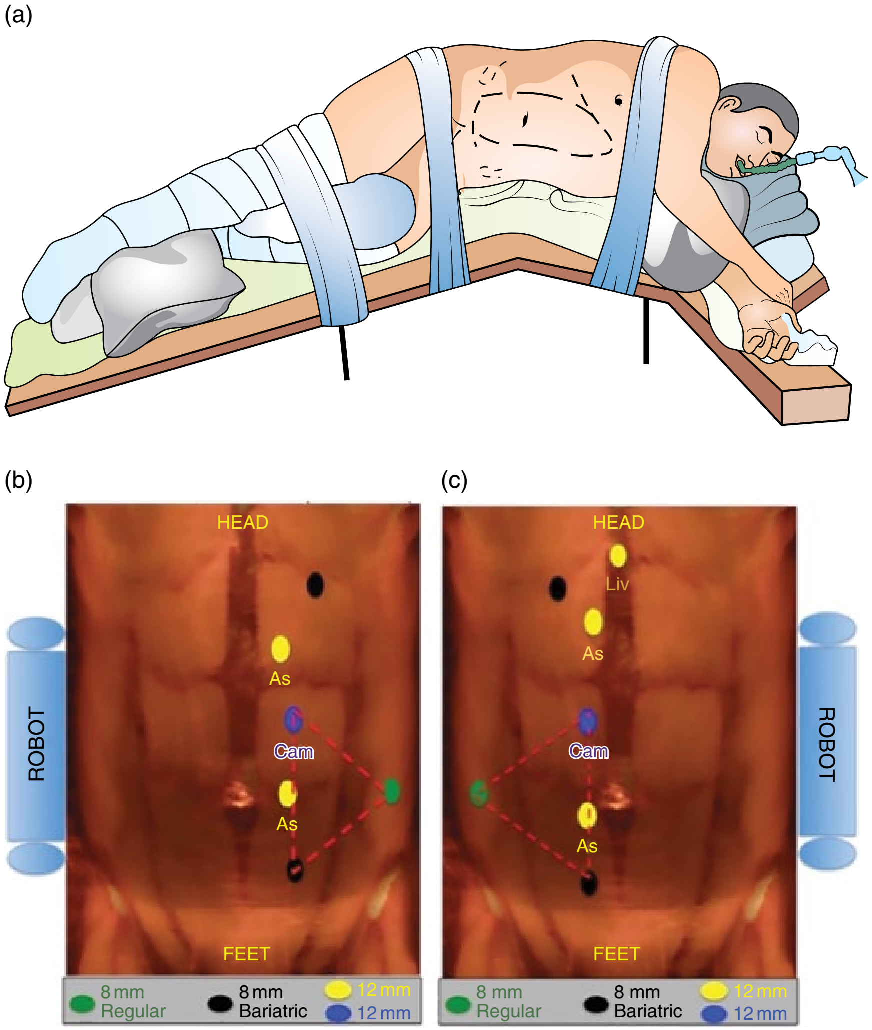

**Figure 93.2** Patient positioning and port placement. (a) Patient positioning. (b) Port placement for a left partial nephrectomy. (c) Port placement for a right partial nephrectomy.

ensure no organ damage occurred during entry. The bariatric 8 mm trocar is located at the costal margin slightly cepahald and lateral to the pubic bone (just lateral to the medial umbilical ligament). A traditional 8 mm trocar is placed two fingerbreadths above the anterior superior iliac spine. Assistant trocars are placed in their traditional locations: one trocar between the camera trocar and uppermost robotic arm, another between the camera and the lower robotic arm. Both assistant trocars are placed slightly more medial than the other trocars.

The trocar configuration should form an equilateral triangle between the camera port, the lower bariatric port, and the lateral traditional robotic port to reduce instrument clashing. For a right robotic PN, an additional incision is made at the xiphisternum for the liver retractor. In this trocar configuration, the lower bariatric trocar is the most "active" arm, regardless of laterality. The use of a bariatric, and thus longer, trocar enhances the reach of the robotic instruments when treating upper pole tumors. Specimen retrieval typically occurs in the more caudal assistant port, though this is patient dependent. The surgical table is tilted, and the da Vinci is docked posterior to the patient with the camera arm coming in to the patient at an angle of 15° in line with the camera port. Robotic instruments are inserted into the peritoneal cavity under direct vision.

## Steps 2–3: Bowel mobilization and hilum dissection

These are standard procedural steps for robotic PN and have been discussed elsewhere. Briefly, the Gerota's fascia-covered kidney and the ureterogonadal packet are visualized and retracted laterally. The main renal artery and vein are circumferentially mobilized and each is encircled with minivessel loops.

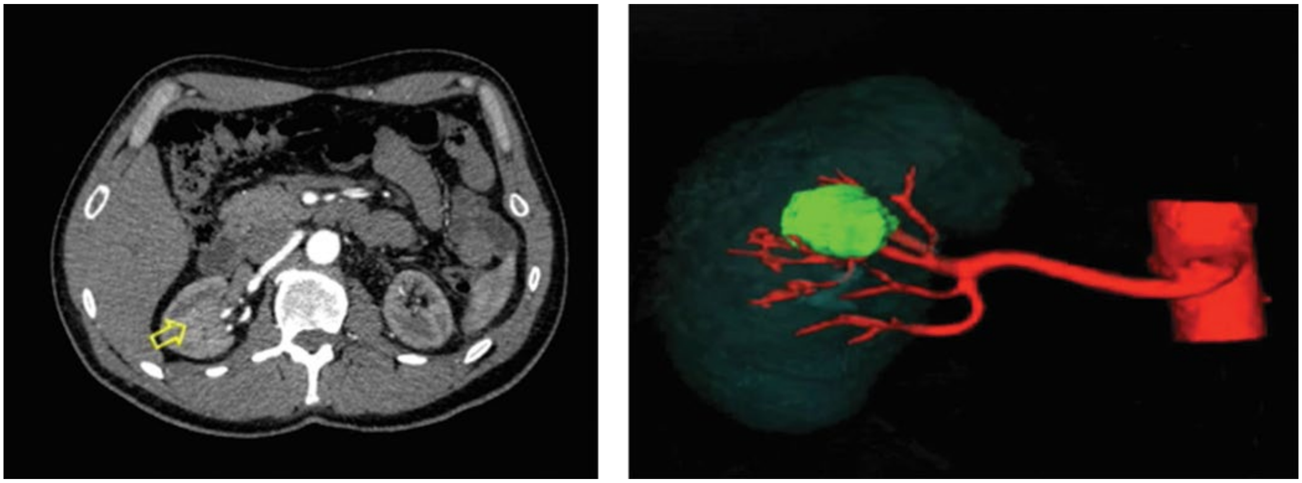

**Figure 93.3** CT and 3D remodeling of kidney with vasculature and tumor reconstruction. This is done to allow the surgeon to gain a complete understanding of the relevant renal arterial branches to help guide and orient the surgeon during arterial microdissection.

## Steps 4–5: Hilar microdissection and superselective arterial clamping

### Medially located tumors and visible confirmation of interrupted perfusion

Radiologic images from the preoperative CT are carefully examined, with or without 3D reconstruction, to gain a complete understanding of the relevant renal arterial branches to help guide and orient the surgeon during arterial microdissection (Figure 93.3). The main renal artery and vein remain unclamped during this procedure. Meticulous and selective vascular microdissection of only the arterial branches (tertiary, quaternary) that supply the tumor is performed toward the tumor and into the renal sinus in a medial-to-lateral direction. Microdissection of the tertiary renal arterial branches is advanced by dissecting into the renal sinus and developing the peripelvic plane of Gil-Vernet [14].

A radial nephrotomy incision is created on the concave, hilar edge of the kidney directly overlying the arterial branch that supplies the tumor (Figure 93.4). Vessel loops are used to isolate and atraumatically retract arterial branches to allow advancement of the microdissection as it approaches the tumor. As the dissection is advanced intrarenally, the radial nephrectomy incision can be extended an additional 2–3 cm if necessary. The radial nephrotomy incision should be made on the hilar edge of the kidney that overlays the anterior surface of that specific arterial branch. Once the terminal, tumor-supplying vessel is identified, a neurosurgical aneurysm microbulldog is placed temporarily (Figure 93.5a). This is done to confirm selective devascularization of the tumor, which is confirmed by visual inspection (normal color and turgor), “fire-fly” indigo-cyanine green fluorescence, and, only if necessary, color Doppler ultrasound (Figure 93.5b). Ongoing perfusion of the surrounding normal kidney is also confirmed. Topical papavarine can be applied onto the renal hilar vessels to counteract any vasospasm.

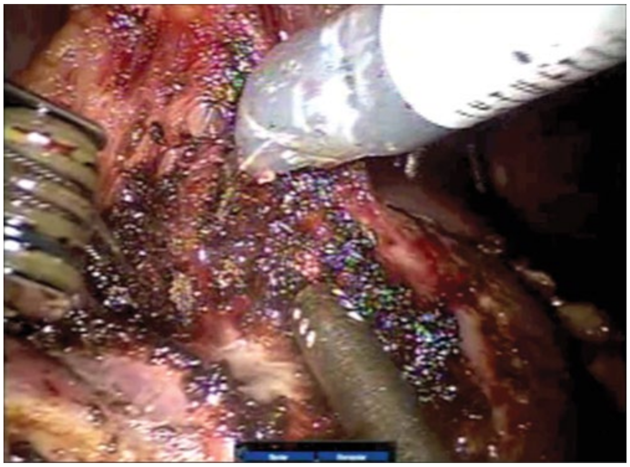

**Figure 93.4** Radial nephrotomy. A radial nephrotomy is made to increase exposure of the tumor and its vasculature, in order to facilitate superselective arterial clamping.

### Laterally located and intrarenal tumors

We recommend clamping of the main renal artery during PN for lateral or intrarenal tumors. This is because the arterial supply of these tumors is multidirectional, which therefore does not lend itself to selective clamping.

## Steps 6–8: Tumor scoring, excision, and renorrhaphy

These steps are detailed elsewhere in this book. Specific steps include circumferential scoring of the tumor and

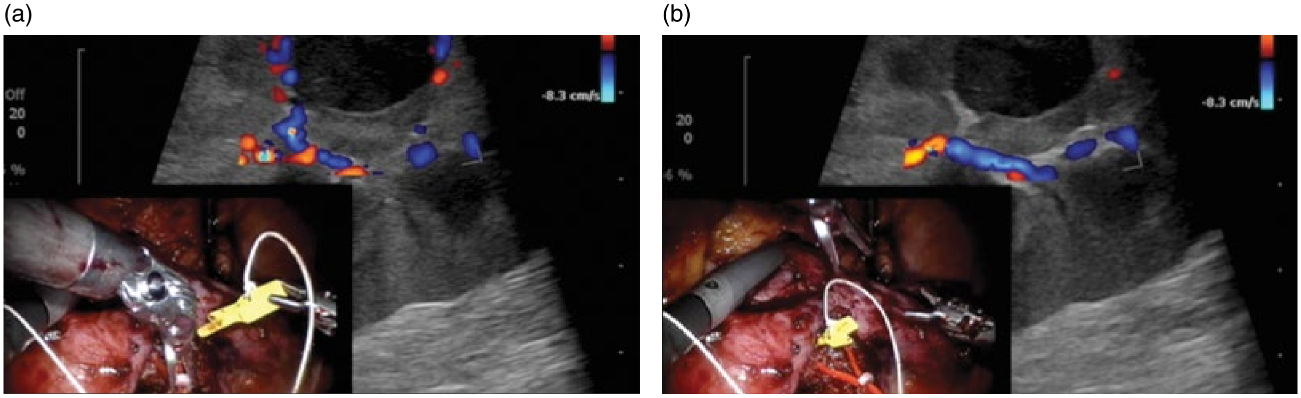

**Figure 93.5** Superselective clamping to facilitate partial nephrectomy. (a) Drop-in color Doppler ultrasound is used to observe the blood supply to the tumor prior to superselective clamping. (b) Following application of the microbulldog, color Doppler ultrasound is again used to demonstrate the observed arterial perfusion to the tumor and all non-tumor-bearing kidney.

tumor excision using both electrocautery and cold scissors. The tumor is bluntly and sharply dissected off the underlying intrarenal vessels, preserving intact the larger intrarenal and hilar vessels. Hemostasis is achieved in the partial nephrectomy bed using a combination of Hem-o-lok clips and point-specific parenchymal suturing. Hem-o-lok clips are applied to the vessels directly supplying the tumor in the deep resection bed; these are then under-sown to prevent clip migration into the calyceal system. The collecting system is suture-repaired with a running 3-0 polyglactin on SH-1 needle. Sutured renorrhaphy of the partial nephrectomy bed is performed, typically without the use of a bolster; however, a bolster can certainly be used to maximize parenchymal hemostasis, per surgeon preference. Water-tightness of the repair is confirmed by repeat retrograde injection of dilute methylene blue through the indwelling ureteral catheter. A biologic hemostatic agent is layered onto the partial nephrectomy bed.

### Step 9: Completely unclamped (zero-ischemia), “minimal-margin” partial nephrectomy

This technique has now evolved into our preferred approach, and is a technical advancement to our prior, superselective segmental arterial clamping technique described above. With this approach, all vascular clamping is completely eliminated; there is no requirement for vascular microdissection or use of microbulldog clamps. In addition, tumor excision is performed with a minimal-margin (1–2 mm) adjacent to the capsular edge. This technique is based on the following anatomic considerations: (i) intrarenal architecture, both parenchymal and vascular, is radially oriented; (ii) the vast majority of small clinical T1 renal tumors possess a distinct intrarenal pseudocapsule; (iii) the tumor–parenchyma interface is histologically altered with sclerotic changes; and (iv) the intrarenal arteries at this junctional interface immediately adjacent to the tumor edge are typically smaller in diameter and fewer in number. These facts form the reasoning for performing a sculpted enucleo-excision in the plane immediately adjacent to the tumor capsule – the “minimal-margin” plane. The purpose of this technique is to maintain a uniform, 1 mm section of benign parenchymal tissue on the tumor capsular surface, without denuding the capsule, which occurs during traditional tumor enucleation.

The renal parenchyma is scored approximately 2 mm from the tumor edge under ultrasound guidance using electrocautery. With the fourth robotic arm, the perirenal fat directly overlying the tumor is retracted, thus elevating the tumor from the kidney. A radial nephrotomy incision is deepened along the cephalad and caudal edges of the tumor, each about 2–3 mm in length. This is done along the scored margin with electrocautery at a setting of 100 W. This bloodless incision is further developed by placing the tip of the robotic bipolar forceps in the left robotic arm into the nephrotomy incision and gently and deliberately opening its jaws (Figure 93.6). This opens the parenchyma along the naturally existing radial plane adjacent to the tumor with cold dissection; point electrocautery is used only sparingly to coagulate any small intrarenal vessels and to guide the enucleative plane. The capsular incision is developed circumferentially around the tumor and then deepened with blunt dissection; the robotic forceps is used to retract the tumor away, off the partial nephrectomy bed. It is important to note that the renal parenchyma is bluntly separated and not incised during the excision. This allows for the dissection to be kept along the natural, relatively avascular intrarenal plane, minimizing injury to the interlobar vessels. If there are any larger intrarenal

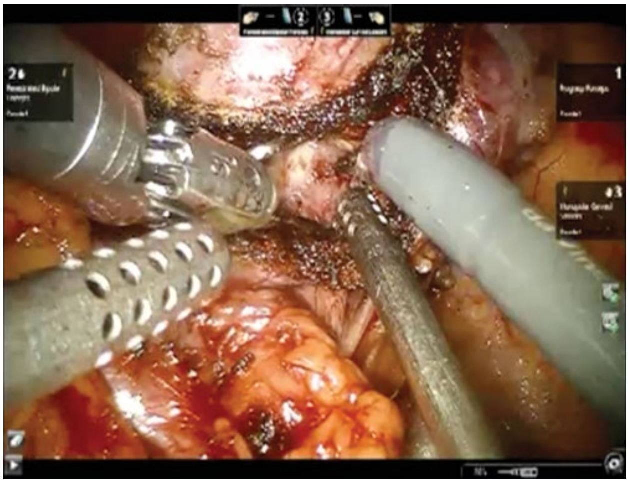

**Figure 93.6** "Minimal-margin" partial nephrectomy. The bloodless incision is further developed by placing the tip of the robotic bipolar forceps in the left robotic arm into the nephrotomy incision and gently opening its jaws. This opens the parenchyma along the naturally existing radial plane adjacent to the tumor with cold dissection; point electrocautery is used only sparingly to coagulate any small intrarenal vessels and to guide the enucleative plane.

vessels feeding the tumor, these can be specifically dissected and controlled with a Hem-o-lok clip before transection. During this procedure, two suction apparatuses are required, one for parenchymal compression and one for suction and irrigation. The assistant at bedside uses the suction cannula to compress any bleeding vessels transiently, while point-specific suturing is performed to secure hemostasis. Once completed, the calyceal system is repaired in a water-tight manner using 3-0 polyglactin on an SH-1 needle.

### Step 10: Near infrared fluorescence using indocyanine green

Similar to the use of Doppler ultrasound to help facilitate superselective PN, intravenous indocyanine green dye is used to confirm tumor devascularization. It can also be used simultaneously to confirm ongoing global perfusion of the remaining normal kidney, providing visual confirmation that the clamping of the terminal artery does not compromise vascularity of the nontumor, normal kidney (Figure 93.7).

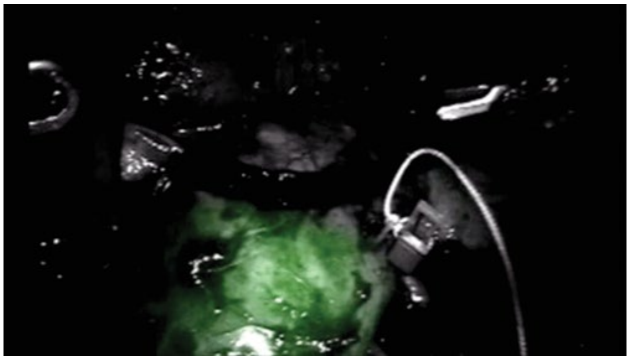

**Figure 93.7** Intravenous indocyanine green dye is used to confirm tumor devascularization and ongoing global perfusion to the remaining normal kidney parenchyma.

## Postoperative management

Following the procedure, the patient is restricted to a clear liquid diet initially and advanced as tolerated. On postoperative day 1, parenteral antibiotics are discontinued and ambulation is encouraged throughout the hospital stay. The Jackson–Pratt (JP) drain is removed once the JP output has decreased to <50 ml per day. Creatinine analysis of the JP fluid drainage determines if there is a urinary leak. Out-of-town patients from longer distances are required to stay in a nearby hotel for 3–4 days to ensure smooth recovery before returning home. Postoperative follow-up depends upon individual patient histology.

## Special considerations

Complications associated with PN surgery include positive cancer margins; compromise of renal function; and urological complications (urine leak, bleed). These and other common complications have been described elsewhere.

## Follow-up

Follow-up comprises the standard procedural steps for robotic PN, which have been discussed elsewhere. See Video 93.1.

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# 94

# Intraoperative Assessment of Tumor Resection Margins

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Every year there are an estimated 338 000 new diagnoses of renal cell carcinoma (RCC) and over 140 000 deaths from it in North America, Europe, and Australia [1]. With this high incidence rate of newly diagnosed RCC and consequent descending stage migration, the use of nephron-sparing surgery (NSS), whenever technically feasible, has significantly increased in comparison to radical nephrectomy during the last decade [2, 3].

A generally suggested indication for NSS is a small renal mass, usually 4 cm or less, located peripherally and easily amenable to resection [4]. However, emerging data suggest that NSS can be performed in patients with anatomically amenable tumors larger than 4 cm, provided that an adequate surgical margin can be safely obtained [5]. As for radical nephrectomy specimens, positive surgical margins (PSMs) are not common, with reported rates of up to 6% [6]. If encountered, the recommendation is to mark with ink the doubtful area of the specimen. If the margins are positive, their anatomic location and whether there is extension into adjacent structures should be described. If there is renal vein invasion, the status of the cut edge of the renal vein or the vena cava should be indicated as well. However, high-powered, prospective, randomized studies to identify the predictors of PSMs after radical nephrectomies are still lacking.

Although oncologic outcomes have been demonstrated to be comparable between procedures (radical nephrectomy vs. NSS), a common concern is the violation of tumor during resection, leaving residual disease in the resection bed [7]. One of the fundamental rules of nephron-sparing oncologic renal surgery is that the largest amount of healthy renal tissue possible should be preserved without compromising the oncological outcomes. Conventionally, concerns about local recurrence due to inadequate tumor excision and the risk of pseudocapsule invasion on the parenchymal side has led most surgeons to remove normal-appearing parenchyma around the tumor. More recently, large series have reported the results of simple enucleation of renal masses versus traditional partial nephrectomies, showing functional and oncological results equivalent to standard partial nephrectomy [8–10].

It has been suggested that a tumor-free margin in the pathologic specimen, regardless of its size, can be sufficient to achieve complete local excision after NSS [11]. However, in some cases, NSS can result in incomplete cancer removal and consequent PSMs. Although NSS has been suggested not to be associated with an increased risk of local recurrence or metastatic disease [12–16], a recent multi-institutional study, which retrospectively evaluated 1240 patients undergoing NSS and analyzed the relationship between positive margins and risk of relapse, concluded that a PSM in NSS increases risk of disease recurrence, primarily in patients with adverse pathologic features (e.g. pT2–pT3a or Fuhrman grade III–IV) [17].

In a recent large prospective multi-institutional study, Schiavina et al. aimed to evaluate predictors of PSM after NSS for renal cell carcinoma. Eight hundred consecutive patients were evaluated and 761 and 39 patients achieved negative and positive margins, respectively. Patients with PSMs were significantly older compared with those with negative margins. A higher incidence of PSMs was observed when NSS was performed for renal masses located in the upper pole. A lower rate of PSMs was found in patients treated with simple enucleation rather than standard partial nephrectomy. A greater incidence of PSMs was found in Fuhrman 3/4 tumors [18].

In another recent study, Khalifeh et al. [19] looked at 943 robotically assisted NSS cases. PSM cases showed statistically significant higher local recurrence and metastasis rates when compared to the negative margin counterparts.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

During NSS, intraoperative frozen section of the nephrectomy bed is commonly performed to confirm the presence of a negative surgical margin [20]. In 2007 a multi-institutional survey in the United States and Europe showed that intraoperative frozen sections in NSS were performed at 15 of 17 (88.2%) of the institutions and random biopsies of the tumor bed were routinely performed at 5 (29.4%). A more recent survey showed that 69% of urologists reported only sometimes obtaining a frozen section during NSS [21].

Despite being highly specific, the sensitivity of tumor bed frozen section in NSS in predicting the presence of a PSM in the resected tumor has been shown to be only 30% [22]. This low sensitivity is secondary to discrepancies between intraoperative frozen section pathology and final pathology and could be explained by numerous factors, including technical reasons, such as missing the remaining tumor during random biopsy, limited availability of special stains, freezing and drying artifacts, and/or pathologist error. Contributing to the controversy is the question whether a positive surgical margin is actually reflective of residual tumor in the patient. Some evidence suggests that even with a positive surgical margin, the remaining tumor burden can be destroyed by use of cautery on the resection bed [23].

Alternatives to intraoperative frozen section have also been developed and studied. Intraoperative imprint cytology examinations have been successfully used in other tumor entities to assess surgical margins. One of the main advantages of imprint cytology is its ability to assess the entire tumor surface rather than a specific area and it has been proven time- and cost-effective [24]. A study by Palermo et al. analyzed 82 patients who underwent either open or minimally invasive NSS with imprint cytology and frozen section evaluation. The results were compared with permanent histology as the gold standard. They found that imprint cytology revealed a PSM in 10 tumors (12%). The sensitivity of the cytologic examination was 87.5%, positive predictive value (PPV) 70%, specificity 95.9%, and negative predictive value (NPV) 98.6% [24]. In another comparative study, imprint cytology showed a specificity of 98%, sensitivity of 100%, a PPV of 90%, and NPV of 100%, while frozen section showed a specificity of 99% and sensitivity of 98% in assessing surgical margins with a PPV of 95% and NPV 98%. They concluded that imprint cytology examinations exhibit equivalent diagnostic value compared with frozen section analysis, while being low-cost and quicker [24, 25].

Intraoperative ultrasound has also been used to guide resection and for margin assessment in NSS. Doerfler et al. performed intraoperative ultrasonography localization before and after tumor removal during laparoscopic NSS, and they found the ultrasound analysis of surgical margins to be negative in all except one patient. The final histologic examination of all specimens confirmed ultrasound results with a 100% correlation [26]. Surgical specimen (*ex vivo*) ultrasound of the surgical specimen's pseudocapsule has been reported to be feasible and efficient at determining the accuracy of margin status. Another work published by Doerfler et al. showed that intraoperative *ex vivo* ultrasound in NSS determined margin status with 100% sensitivity and 97% specificity. Its PPV and NPV were 50% and 100%, respectively [27]. Veeratterapillay et al. showed there is a positive correlation between margin on extracorporeal specimen ultrasound and pathological margins [28].

In an attempt to eliminate frozen section tumor base biopsy and its related time delay, Yilmaz et al. performed "gross intraoperative evaluation (GIE)" in which they evaluated surgical margins of open NSS specimens macroscopically by intraoperative examination of the tumors divided *ex vivo* into two halves. They concluded that GIE of resected NSS specimen has high sensitivity and safety for the evaluation of surgical margins [29].

Indocyanine green (ICG) is the most commonly used contrast agent for intraoperative imaging, as it absorbs and emits light in the near infrared portion of the electromagnetic spectrum (about 800–2500 nm). When injected intravenously, ICG binds to albumin and lipoproteins, remaining predominantly intravascular until excreted by the hepatobiliary system. It is used to enhance intraoperative decision-making in evaluating vasculature, tumor margin identification, and lymph node dissemination of malignancy. Various systems have been developed that can be used in conjunction with open, laparoscopic, and robotic-assisted surgery. Tobis et al. [30] demonstrated the use of intravenous ICG with simultaneous near infrared fluorescence (NIRF) imaging at the time of open partial nephrectomy. Renal tumors were well demarcated by ICG and highly hypofluorescent when compared with the surrounding normal parenchyma. In a study by Manny et al. [31] the degree of hypofluorescence could not be reliably used to differentiate malignant versus benign tumors in 100 consecutive patients undergoing robotic partial nephrectomy with NIRF guidance. In their study, they found NIRF imaging to have a PPV of 87%, NPV of 53%, sensitivity of 84%, and specificity of 57%. This poor differentiation between normal and malignant tissue has been suggested to be related to a nonstandardized dosing of ICG [32].

Optical coherence tomography (OCT) is one of a number of emerging optical biopsy techniques that provide high-resolution, real-time, cross-sectional imaging of tissues. Similar to B mode ultrasound, OCT relies on information gathered by reflected energy. In comparison, however, OCT utilizes near-infrared light rather than acoustic waves and does not require direct contact with tissue as does ultrasound. OCT been investigated for renal imaging in evaluating kidney morphology and renal masses. Preliminary studies have investigated OCT's ability to distinguish benign from malignant renal tumors. Barwari et al. [33] concluded that *ex vivo* OCT attenuation coefficients were different between normal renal parenchyma and RCC tissue, RCC tissue showing a significantly higher attenuation coefficient than normal parenchyma.

Studies are being conducted to assess OCT *in vivo* and, if successful it may be applied to evaluate surgical margins after partial nephrectomy or combined with biopsy needles to provide a functional optical biopsy in which cross-sectional images can be correlated with histopathology [34].

Although there is no clear agreement in the clinical evidence, local recurrence seems to be more likely in patients with PSMs, especially in those with high-grade tumors. Improvement of metastases and cancer-specific survival, as observed in midterm follow-up studies, seems to be comparable to that in patients with negative surgical margins. Considering the worldwide low risk of local recurrence, development of metastasis, or cancer-specific mortality, careful surveillance could be the best management option for most patients with PSMs after NSS. The value of intraoperative tumor resection bed analysis in guiding the patient's intraoperative management remains to be defined. However, it is still recommended to take site-directed biopsies of the partial nephrectomy specimen bed if there is suspicion of an incomplete resection during the procedure or after gross inspection of the specimen (see Video 94.1).

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# Laparoscopic Radical Nephroureterectomy

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## Introduction

Laparoscopic approaches to renal surgery have gained popularity as a result of decreased morbidity for patients and equivalent oncologic outcomes. Since it was first described in 1991, laparoscopic nephroureterectomy (LNU) has also gained popularity [1]. This surgery presents a new set of difficulties over renal procedures, with the surgical field spanning the hemi-abdomen down into the ipsilateral pelvis. Arguably, the approach to resection of the distal ureter is the most difficult part of this case and certainly is highly variable and surgeon dependent. With the laparoscopic approach to nephrectomy described in Chapter 92, this chapter focuses on the means of managing the distal ureter for completion of a nephroureterectomy. There is no approach that has been shown to be clearly superior to another in either oncological or perioperative outcomes and so surgeon preference remains the mainstay of the decision for management of the distal ureter.

## Indications

LNU is used for patients with upper tract urothelial tumors, which accounts for about 5% of all urothelial tumors [2]. The surgery involves the removal of the kidney and the entirety of the ureter, including the ureteral orifice with a cuff of bladder urothelium. This remains the gold standard approach for management of renal pelvis and ureteral tumors. With many tumors being lower grade and stage and with increasing goals to maintain renal function, less invasive means can be used, including endoscopic management (ureteroscopic and percutaneous) and segmental ureterectomy [3–5]. Nephroureterectomy with *en bloc* excision of the ureteral orifice with bladder cuff, however, remains the optimal choice for bulky, high-grade, and/or invasive tumors.

Open nephroureterectomy (ONU) uses two incisions and with this comes significant morbidity. LNU decreases this morbidity at a minimum for the nephrectomy portion of the procedure. The indications for laparoscopic approach remain the same as those for open. The principles of oncologic control should apply regardless of approach – open versus laparoscopic. There are copious data comparing laparoscopic and open approaches.

### Oncological outcomes

A large multicentered retrospective study out of France found no difference in 5-year cancer-specific survival between laparoscopic and open nephroureterectomy [6]. In addition to their main outcome, there was also no difference in 5-year recurrence-free survival, metastasis-free survival, or complications between surgical techniques, including when stratified by pathological stage. Despite suffering from inherent flaws with retrospective study design, this study offered a highly powered comparison between surgical approaches.

Similar findings were obtained by Fairey et al. in their multi-institutional study [7]. They had a total of 849 patients, approximately half in the laparoscopic cohort, who had a median follow-up of 2.2 years without significant differences in disease-specific survival between laparoscopic and open groups. Multivariate analysis did not find that surgical approach influenced survival, but the authors did express some concern as there was a slight trend towards worse recurrence-free survival in the laparoscopic group (hazard ratio = 1.01, $P = 0.08$). Again, limitations exist because the study is retrospective.

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Companion website: www.wiley.com/go/smith/textbookofendourology

A prospective study by Simone examined 80 patients randomized to LNU or ONU [8]. Subjects who underwent a laparoscopic approach had lower average blood loss and length of stay but 5-year cancer-specific survival and metastasis-free survival were also lower; however, this difference was not statistically significant. When stratified by tumor stage, subjects with stage pT3 had statistically significant lower cancer-specific survival and metastasis-free survival, suggesting laparoscopic may be inferior to open approach in patients with locally advanced disease. Despite having a small sample size owing to the relative rarity of upper tract urothelial carcinoma, the data provided are supportive of LNU as being an oncologically sound operation at least of low-stage disease.

### Perioperative outcomes

Given the size of the surgical field spanning the hemiabdomen, there is significant morbidity associated with an open approach, predominantly with two sizeable incisions. Hospital length of stay may serve as a surrogate marker of patient convalescence after surgery. A retrospective analysis of a major British national registry found minimally invasive (pure or robot-assisted laparoscopic) nephroureterectomy afforded a significantly decreased hospital stay compared to open (5 vs. 8 days) [9]. The superiority of minimally invasive nephroureterectomy in reducing length of stay is echoed in several other studies [6, 8, 10].

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) is a multi-institutional database providing perioperative outcomes of various operations. Hanske et al. queried this database and compared outcomes between patients who underwent open or minimally invasive nephroureterectomy [11]. They found no statistically significant difference in 30-day postoperative complications, readmission rate, and perioperative mortality. Minimally invasive approach was superior to open with regard to transfusion rate (9.2% vs. 21.5%, $P < 0.05$) and need for repeat surgical intervention (odds ratio = 0.24 95% confidence interval (CI) 0.07–0.83, $P < 0.05$).

Although all these series seem to indicate comparable oncologic and perioperative outcomes, there remain multiple approaches for excision of the distal ureter during a laparoscopic approach.

## Operative technique

### Patient positioning

Patient positioning is similar to that for laparoscopic nephrectomy as described in Chapter 92 with modified lateral decubitus positioning. The hips should be more externally rotated to open the pelvis and expose the lower quadrant. It is often advantageous to mark the midline prior to positioning to aid in appropriate trocar and incision alignment before the skin shifts when the patient is positioned on their side. This positioning allows for access for nephrectomy as well as the distal ureterectomy portion for purely laparoscopic and for open excision approaches. This also prevents patient repositioning.

There are various ways to manage the distal ureter. The entire ureter, including the intramural portion, ureteral orifice, and bladder cuff, should be removed. Approach used is generally based on surgeon preference. There are minor variations among techniques for distal ureteral management but most fall into four main categories: purely laparoscopic, open, endoscopic “pluck,” and endoscopic “intussusception.” The endoscopic approaches require patient repositioning into the dorsal lithotomy position for that portion of the case. The modified lateral decubitus positioning is still used for the nephrectomy portion.

### Procedure

#### Pure laparoscopy

For a purely laparoscopic approach, trocars should be placed to allow for dissection in the hemi-abdomen as well as the pelvis (Figure 95.1). Just as in renal surgery, trocars are shifted laterally in obese patients. Upper abdominal trocars are placed and used just as that described for a nephrectomy (umbilical camera port and upper midline and lateral ports for right and left hands). A laparoscopic nephrectomy takes place (as described in Chapter 92) without transection of the ureter. Clips should be placed across the ureter as early as possible below the level of the primary tumor to prevent tumor spillage. Once the kidney is freed, the ureter is traced down into the pelvis. It is about at the level of the iliac

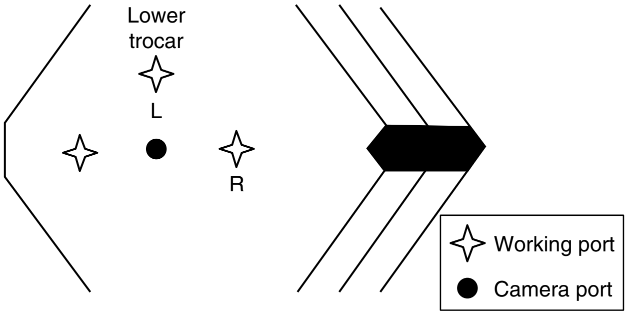

**Figure 95.1** Trocar layout for purely laparoscopic right nephroureterectomy. Initial trocars used for nephrectomy portion of the case are designated. L and R represents which hand is used for each port. Orientation of picture: left – caudad; right – cranial; top – right flank; bottom – left flank.

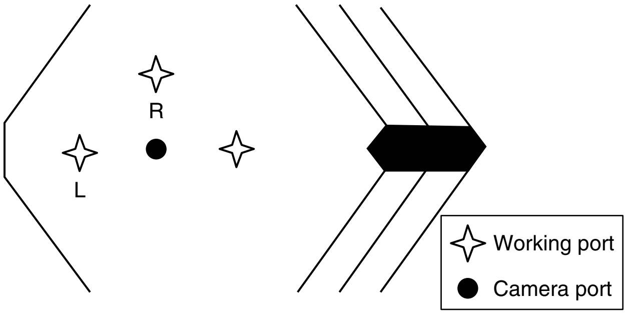

**Figure 95.2** Trocar layout for purely laparoscopic right nephroureterectomy. Trocars used for distal ureterectomy portion of the case are designated. L and R represents which hand is used for each port. Orientation of picture: left – caudad; right – cranial; top – right flank; bottom – left flank.

vessels where a lower abdominal approach must be taken. It is at this point that the trocar configuration is transitioned into the pelvis (Figure 95.2). The camera port remains at the umbilicus and right and left hands are shifted to the trocars within the pelvis (lateral and lower midline trocars). The surgical bed can be adjusted into a Trendelenburg position to help in visualization by shifting the colon cephalad.

Dissection takes place along the ureter distally. The peritoneum should be incised medial to the obliterated (medial umbilical ligament) to enter the perivesical space lateral to the bladder. Great care should be taken to identify and transect the ipsilateral superior vesical vasculature to prevent bleeding. The round ligament/vas deferens can be clipped and divided. Traction can be placed on the ureter to aid in dissection down to and through the intramural portion. There are two primary means of managing the ureter at this point – laparoscopic stapling or laparoscopic excision with bladder cuff.

Use of a laparoscopic stapling device for distal ureteral transection risks incomplete resection of the ureteral orifice if dissection is not taken distally enough. Additionally, if staples are exposed within the bladder urothelium, this can be a nidus for stones.

For laparoscopic excision of the ureter, an extravesical or transvesical approach can be used. In an extravesical approach, the intramural ureter is dissected circumferentially until the bladder is entered. It is often advantageous to place a stay suture lateral to the ureteral orifice to prevent tumor spillage and aid in visualization of the cystotomy and prevention of bladder retraction prior to closure. Extravesical closure then takes place. Care should also be taken to prevent deep suture placement that could compromise the contralateral orifice. For a transvesical approach, the anterior bladder is incised and the ureteral orifice is visualized directly. The ureteral orifice and bladder cuff can be visualized directly and incised circumferentially. A combination of extra- and transvesical dissection can then be used to free the ureter completely. The site of ureterectomy should be closed followed by the cystotomy.

The specimen can then be delivered through a low midline incision (incorporating the lower midline abdominal trocar site and possibly umbilical site).

### Open excision

As extraction of the specimen is needed *en bloc*, many surgeons argue for use of open excision of the distal ureter and bladder cuff. This approach most mimics the open approach. The patient is positioned as previously described in the purely laparoscopic approach section. The nephrectomy portion is performed and ureteral dissection is taken down as distally as possible. With this modified positioning, the bed can be externally rotated slightly to more closely mirror supine positioning (and thus prevent repositioning of the patient). A Gibson incision is performed in the ipsilateral pelvis. Pfannenstiel and low midline incisions may also be used (Figure 95.3). The same ureteral dissection takes place with incision of the peritoneum medial to the medial umbilical ligament and the ureter can be traced down to the bladder. Options for distal excision again include extravescial or transvesical approaches. A transvesical approach with an anterior cystotomy is most common as again it most closely mimics the *en bloc* resection that takes place via an open approach. It also ensures complete excision of the ureteral orifice with a bladder cuff. The final *en bloc* specimen can be removed via this incision. Complete extravesical excision can also be used, requiring closure of only that single bladder cystotomy.

### Endoscopic "pluck"

Endoscopic techniques were created to try to obviate the need for an open excision and ease distal dissection of the ureter. The endoscopic portion of this case takes

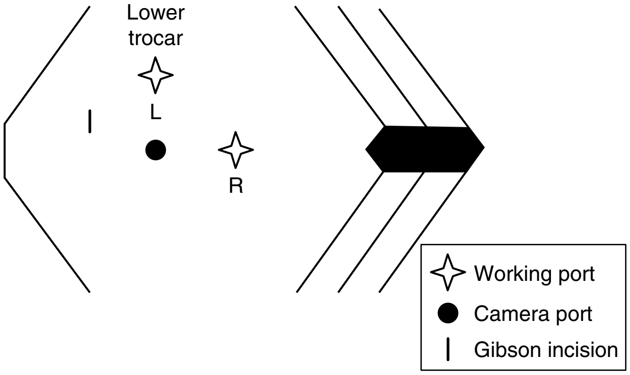

**Figure 95.3** Surgical incisions/trocars for right nephroureterectomy with open distal ureterectomy. Gibson incision is designated. L and R represents which hand is used for each trocar port. Orientation of picture: left – caudad; right – cranial; top – right flank; bottom – left flank.

place first and with the patient in a dorsal lithotomy position. A resectoscope can be used to resect the ureteral orifice along the path of the intramural ureter down into the perivesical fat. Another option is use of a Collins knife to circumscribe the ureteral orifice with a bladder cuff and then dissect the intramural ureter down into the perivesical fat [12]. Once complete, the patient is positioned in the modified lateral decubitus position and a "pure laparoscopic" approach is undertaken (see above). With the endoscopic dissection having previously taken place, it is easier to place tension on the ureter intra-abdominally and thus free the ureter from the bladder muscle. An extravesical closure then takes place and the entire specimen can be extracted via a midline incision.

With this technique it is important to try to place clips on the ureter as early as possible once the intra-abdominal portion of the case begins. There have been many procedures proposed to accomplish ureteral occlusion prior to the intra-abdominal portion. The pluck technique has higher risk of tumor spillage and hence is most appropriate for patients with proximal/renal pelvis tumors that are low grade [13]. This technique is not appropriate for patients with very distal ureteral tumors or concomitant bladder tumor due to risk of tumor spillage and seeding.

#### Endoscopic "intussusception"

An alternative method involves transurethral removal of the distal ureter by removing the kidney and ureter piecemeal with the distal portion removed by intussuscepting the ureter into the bladder. This is also known as the "stripping" technique. An endoscopic approach is used initially with the patient in the dorsal lithotomy position. A bulb-tipped ureteral catheter is placed into the ipsilateral ureter first with the bulb occluding the ureter. This potentially can be done in the lateral decubitus position with the pelvis and perineum prepped into the surgical field. A laparoscopic nephrectomy is then performed after the patient is repositioned into the modified lateral decubitus position. The ureter is dissected free and the bulb is identified within the ureteral lumen. The ureter is tied off above and below the bulb to secure the ureter to the catheter. The ureter is clipped proximal to this and then the ureter is transected. The renal unit and proximal ureter are extracted via a midline incision. The patient is then repositioned into the lithotomy position. Traction is placed onto the ureteral catheter to intussuscept the ureter into the bladder and a bladder cuff is made transurethrally using a Collins knife until the ureter is freed (similar to the pluck technique). The specimen is removed per urethra [14].

## Results

The superiority of a technique should be judged by its ability to remain oncologically sound while minimizing operative morbidity. Distal ureterectomy during nephroureterectomy is a critical step to prevent tumor recurrence. The goal is to excise the diseased urothelial tissue down to and including the ureteral orifice. The intramural ureter should be removed with negative margins. In addition, caution should be taken when removing the ureter from the bladder to prevent spillage into the retroperitoneum.

Distal ureterectomy via laparoscopic stapling (or using a sealing device) efficiently ligates the diseased collecting system to prevent tumor spillage and avoids creating a cystotomy. A retrospective single-center experience by Hattori et al. examined distal ureteral management via open, pure laparoscopic (with distal ureteral stapling or sealing) approach and combined approach (LNU with open distal ureteral excision) [15]. When examining the laparoscopic groups, 53 patients underwent pure laparoscopy compared to 36 who had a combined approach. They found the pure laparoscopy group required less time to dissect the distal ureter ($0.8 \pm 0.5$ hours vs. $1.8 \pm 1.1$ hours) but no difference in time to convalescence, blood loss, or overall operative time. The ureteral orifice was not excised in 15% of patients in the pure group versus 11% of patients in the combined group (authors did not indicate if this difference was statistically significant). Recurrence rates were 25% in each group and all of these were treated successfully by transurethral resection. With regard to oncologic outcomes, there was no statistically significant difference in cause-specific survival, extravescial recurrence, and intravesical recurrence between open, pure laparoscopy, and combined cohorts.

In a small (36 patients) retrospective study by Ritch et al., open excision of the distal ureter and bladder cuff was compared to the laparoscopic techniques of pure laparoscopic dissection and closure and laparoscopy with extravesical stapling [16]. With respect to perioperative outcomes, the laparoscopic approaches had significantly shorter operative time and the laparoscopic dissection and closure had significantly shorter (two days) length of stay than the other two groups (perhaps because of smaller sample size). With respect to oncologic outcomes, there was no statistically significant difference in 2-year recurrence-free survival between the groups. It is important, however, to note that in the laparoscopic stapling group, 50% of patients had cystoscopic evidence of an ipsilateral ureteral orifice remnant.

Kapoor and colleagues retrospectively compared three techniques and their effects on tumor recurrence following radical nephroureterectomy. Their series included 820 patients who underwent ONU or LNU and had their distal ureter excised either via an open intravesical, open extravesical, or an endoscopic pluck technique with either resection down to the perivesical fat or circumferential excision with occlusion of the distal ureteral orifice with an EndoLoop® (Ethicon, Inc., Somerville, NJ, USA) [17]. More than half of all patients (53.4%) underwent laparoscopic nephroureterectomy and among these, the distal ureter was approached via open extravesical (46%), intravesical (34%), and endoscopic pluck (22%) techniques. Their group found the intravesical technique to have the best recurrence-free survival rate for both overall tumor recurrence and intravesical recurrence at 2 and 5 years. With a median follow-up of 24.6 months, their long-term results should be interpreted cautiously.

A larger series of both open and laparoscopic cases by Xylinas et al. was presented by combining data from 24 institutions comprising 2681 patients. They retrospectively reviewed patients who underwent open intravesical, open extravesical, or endoscopic pluck approaches to the distal ureter (for both laparoscopic and open nephroureterectomy). For the endoscopic pluck approach, the ipsilateral ureteral orifice was fulgurated with a resectoscope and a 1 cm margin was incised around the intramural ureter. The dissection was carried down to the perivesical fat [18]. In this series, the vast majority of patients underwent ONU (80.9%) with open intravesical excision being the most common method of managing the distal ureter (67.5%). Endoscopic approach was the least common method (3.2%), but the endoscopic technique was most utilized in patients who had undergone a laparoscopic approach (84.7%). Recurrence-free survival was 71%, 73%, and 77% for intravesical, extravesical, and endoscopic approaches to distal ureterectomy at 2 years, respectively. At 5 years, the rates were 66%, 66%, and 69% for intravesical, extravesical, and endoscopic methods, respectively. There were no statistically significant differences between the three groups when compared pairwise. With regard to intravesical tumor recurrence, the highest recurrence rate was seen in the endoscopic management group, with recurrence-free survival of 42% at 5 years versus 58% for open intravesical excision and 51% for open extravesical excision. Endoscopic management and concomitant carcinoma-in-situ were independent predictors of tumor recurrence in a matched-pair analysis with patients matched for TNM stage and nodal status. Cancer-specific survival and overall survival were similar across all management groups however.

There is copious literature that speaks to the efficacy of the laparoscopic approach to nephroureterectomy. The management of the distal ureter within this literature is highly variable, however. Most LNU data comprise of open resection technique for management of the distal ureter which obviously most closely resembles a pure open approach. As such, it is not surprising that the oncological outcomes for open and laparoscopic approaches are not significantly different. The data on endoscopic techniques are more limited and generally altered by inherent selection bias, with patients having lower grade and lower stage tumors. Both endoscopic techniques (pluck and intussusception) risk tumor spillage and require repositioning of the patient intraoperatively. There are far fewer data on a pure laparoscopic approach. What does seem clear is that laparoscopic extravesical stapling techniques have a high rate of incomplete resection of the ureteral orifice, which violates one of the primary oncologic principles. More data are needed to ensure that a pure laparoscopic approach with distal ureteral excision and bladder closure is oncologically comparable to its open counterpart.

See accompanying Video 95.1.

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# Laparoscopic and Robotic Radical Cystectomy in Males and Females

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## Introduction

Bladder cancer is largely a disease of the elderly, presenting with a median age of 73 years in men and 74 years in women [1]. It is the fourth most common cancer in the United States; in 2016, an estimated 76 960 new diagnoses and 16 390 deaths were predicted [2]. Bladder cancer is also the fourth leading cause of cancer death in men aged 80 and older [2]. In managing patients with bladder cancer, the primary therapy relies on initial staging from transurethral resection of bladder tumor (TURBT) [1]. For patients with muscle-invasive bladder cancer and for those with high-risk recurrent non-muscle-invasive disease, open radical cystectomy (ORC) remains the gold standard of treatment [1]. Attempts at a minimally invasive approach were first made in the early 1990s with the introduction of laparoscopic cystectomy [3, 4], followed by the introduction of robot-assisted radical cystectomy in 2003 [5]. When compared to ORC, recent studies have shown laparoscopic radical cystectomy (LRC) to be a safe, feasible, and reliable alternative with lower morbidity and perioperative complications [6–10]. Furthermore, robot-assisted radical cystectomy (RARC) has also been shown to be a safe alternative, presenting with reduced perioperative complications, less estimated blood loss with lower need for perioperative blood transfusion, hastened gastrointestinal recovery, lower narcotic requirement, and shorter length of stay [11–19]. Given the technical similarities between LRC and RARC, both approaches will be addressed collectively; however, given its growth in popularity, a greater focus will be placed on robotic cystectomy.

## Indications and patient selection

LRC and RARC are usually indicated for patients with organ-confined, nonbulky bladder cancer [20] with the goal of surgical cure of disease. On rare occasions, palliative cystectomy is performed in patients with severe symptoms from disease as an adjunct to chemotherapy. Contraindications to robot-assisted cystectomy generally vary from patient to patient and should be assessed on a case-by-case basis with decisions to proceed based on the surgeon's experience. For example, patients with prior abdominal surgery can present with extensive intra-abdominal adhesions [21] requiring careful lysis of adhesions. Yet, while patients with previous abdominal surgery have a higher risk of postoperative complications, the likelihood of a safe completion of robot-assisted cystectomy is not affected [21]. Similarly, although previous pelvic radiation is a relative contraindication to a robotic approach, in experienced hands complications rates after RARC do not show significant differences between patients with or without a history of pelvic irradiation [22]. Other relative contraindications include evidence of locally advanced disease and obesity [20].

## Operative technique

### Patient preparation

Prior to surgery, bowel preparation includes 48 hours clear liquid diet, 300 ml of magnesium citrate, and one tablespoon of mineral oil the day before surgery. If the patient is undergoing continent cutaneous diversion

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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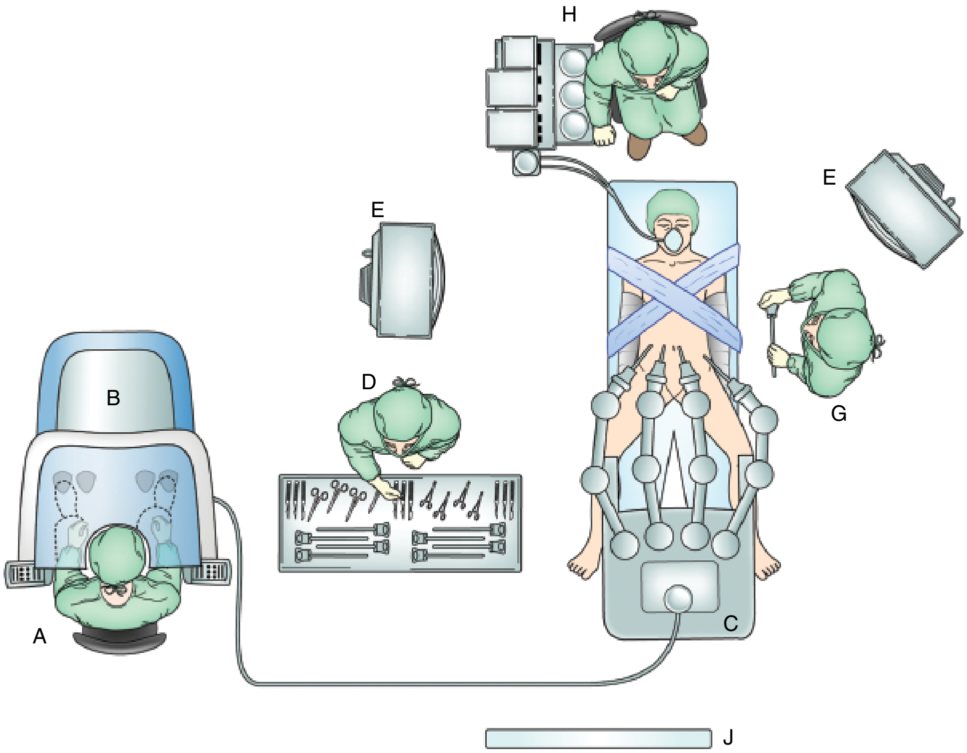

**Figure 96.1** Schematic overhead of operative set up for robotic-assisted radical cystectomy. (A) Surgeon; (B) robotic console; (C) da Vinci®; (D) scrub nurse; (E, J) high-definition monitors; (G) bedside assistant; (H) anesthesiologist. *Source:* Golombos DM. *Robot-Assisted and Partial Cystectomy*. Berlin: Springer-Verlag, 2017. Reproduced with permission of Springer.

with the right colon, 4 liters of polyethylene glycol is used for bowel prep the day before surgery, and antibiotics (1 g of oral neomycin and 1 g of erythromycin), with one tablespoon of mineral oil are given the day before surgery. Rectal enema is also done the evening before and morning of surgery.

## Operative setup

Specifics of the operative setup for RARC will be dictated by the characteristics of the individual surgeon's operating room. At our institution, we employ a single assistant on the patient's right side, and feel that at least three monitors are needed to allow for each team member to have optimum viewing. Figure 96.1 provides a schematic overhead view of our preferred operative setup.

## Patient positioning and preparation

As illustrated in Figure 96.2, the patient is placed in a dorsal lithotomy position using standard operative stirrups. The arms are tucked and protected using egg-crate foam padding, legs placed in sequential compression stocking devices, and a cross-shoulder harness is used to secure the patient to the operating table. The table is tilted to a steep 30–40° Trendelenburg position. A urethral catheter is placed sterilely on the operative field. Along with perioperative antibiotics, we routinely administer 5000 units of subcutaneous heparin prior to the start of the operation.

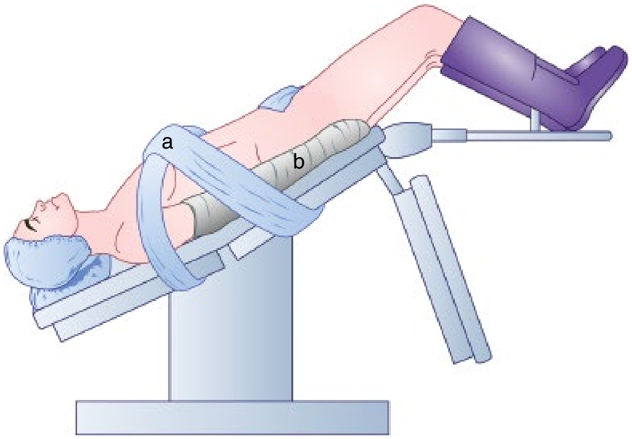

**Figure 96.2** Preferred patient positioning for robot-assisted radical cystectomy displaying (a) cross-shoulder harness and (b) arms passed and tucked at the patient sides. *Source:* Golombos DM. *Robot-Assisted and Partial Cystectomy*. Berlin: Springer-Verlag, 2017. Reproduced with permission of Springer.

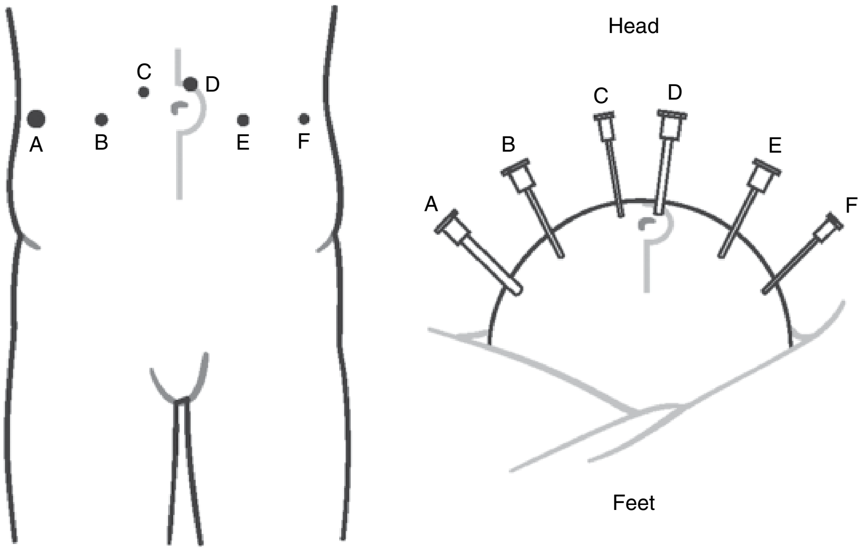

**Figure 96.3** Preferred trocar placement for robotic-assisted radical cystectomy including (B, E, F) 8 mm robotic trocars, (D) 10–12 mm camera trocar, (A) 5–15 mm Versaport™ Plus 5–15 mm trocar and (C) 5 mm AirSeal® Access port. *Source:* Golombos DM. *Robot-Assisted and Partial Cystectomy*. Berlin: Springer-Verlag, 2017. Reproduced with permission of Springer.

## Trocar configuration

Initial insufflation of the abdomen is done via the Veress needle technique to 15 mmHg. Figure 96.3 outlines our standard trocar configuration for RARC. A camera trocar is placed in the periumbilical location using a 10–12 mm, blunt, disposable trocar. At 10 cm lateral and 4 cm inferior to the camera trocar, a left 8 mm robotic trocar is placed. Three centimeters superior to the anterior superior iliac spine (ASIS), a second 8 mm robotic trocar is placed along the midaxillary line. At 4 cm inferior and 10 cm lateral to the camera trocar, a right 8 mm is placed. The main right assistant trocar is placed at 3 cm superior to the ASIS in the midaxillary line using a Versaport™ Plus 5–15 mm trocar (Covidien/Medtronic, Minneapolis, MN, USA). Midway between the right robotic trocar and the camera trocar, a 5 mm AirSeal® Access Port (Conmed, Utica, NY, USA) is placed, which is used primarily for suction–irrigation.

## Steps of the procedure

The techniques described below apply directly to robotic cystectomy; laparoscopic cystectomy, however, follows a similar procedural flow with noted differences in the instruments used. We begin the procedure with identifying and dissecting the right ureter by incising the posterior peritoneum along the white line of Toldt and sweeping the bowel medially to expose the psoas muscle. The ureter can usually be readily identified medially along the psoas at its crossing of the external iliac artery. Proximal dissection is performed first to approximately the level of the gonadal vessels, with care taken to preserve blood supply and to avoid direct grasping. Distal dissection is then performed to the level of the ureteral hiatus, with the final distal dissection performed after the division of the anterior pedicle.

Development of the avascular plane between the left bladder and pelvic sidewall reveals the anterior bladder pedicle, which contains the superior vesicle artery. The pedicle can be isolated and transected by various techniques, including the robotic vessel sealer. Once the pedicle is divided, the dissection of the remainder of distal ureter is performed. Prior to transection of the ureter, a large clip is applied distally and a second large clip with a long suture attached is applied proximally, which will facilitate identification duration the later steps of the procedure. Once the clips are secured, the ureter is transected sharply. A similar dissection is carried out on the right side, exposing the right anterior bladder pedicle, ureter, and pelvic sidewall.

After both the anterior pedicle and ureter are divided, a posterior plane is developed by separating the bladder from the rectum. The surgeon lifts the bladder anterior while the bedside assistant retracts the posterior peritoneal edge. Using a combination of blunt and sharp dissection, the posterior plane between the bladder and rectum beneath the posterior leaflet of Denonvilliers' fascia is carried as distally as possible to the level of the prostatic apex, allowing for identification of the posterior pedicles of the bladder. The posterior bladder pedicles are divided using the vessel sealer device for non-nerve-sparing operation, and large Hem-o-lok® (Teleflex Medical, Research Triangle Park, NC, USA) clips in a nerve-sparing procedure. The division is complete once the endopelvic fascia is encountered.

The endopelvic fascia is then divided sharply as caudally as possible, because once the bladder is released from the anterior abdominal wall, the posterior prostatic apex becomes difficult to visualize. The prostatic pedicles are then divided using either the vessel sealer device or Hem-o-lok and titanium clips depending on desired nerve-sparing. During this dissection, to avoid injury to the rectum, the bladder and prostate are retracted superomedially while the rectum is retracted posteriorly using the robotic third arm and prograsp, respectively.

The bladder is released from its anterior abdominal attachment by removing the urachus with the bladder en bloc and taking wide peritoneal wings. The puboprostatic ligaments, which are seen after entering the space of Retzius, are preserved for orthotopic urinary diversion. In nonorthotopic diversion, the urethra is not preserved and the puboprostatic ligaments are divided. The dorsal vein complex (DVC) is secured using a 0-polyglactin suture. Once secured, the DVC is divided, exposing the underlying urethra. In nerve-sparing procedures and in patients undergoing orthotopic neobladder, we avoid the use of electrocautery during this dissection and during the division of the uretha. The anterior portion of the uretha is then divided to expose the urethal catheter. The catheter tip is then pulled through the urethral opening, and after the lumen is secured using a large clip to prevent possible tumor spillage, the catheter is divided using scissors. The remainder of the urethra and the remaining apical attachments are divided, and a 15 mm Endo Catch™ bag (Covidien/Medtronic, Minneapolis, MN, USA) is used to immediately collect and remove the bladder, prostate, and seminal vesicles.

Regardless of surgical approach, pelvic lymphadenectomy (PLND) is a central component of radical cystectomy, and the extent of lymphadenectomy has been correlated with improved oncologic outcomes [23–27]. Although various factors can influence lymph node yields, including method of lymph node submission and variability in pathologic practices and reporting, several studies have demonstrated that experienced surgeons can perform a PLND using robot-assisted surgery comparable to that performed using an open technique [28–30]. Timing of the lymph node dissection is generally dependent on surgeon preference. We begin our PLND after the entire extirpative portion of the procedure is finished by completely skeletonizing the external iliac iliac vessels and removing its surrounding lymphatic tissue. Liberal application of clips are used during lymphadenectomy to minimize the risk of postoperative lymphocele. The borders of our PLND are Cooper's ligament inferiorly, the genitofemoral nerve laterally, and the sacral promontory medially, up to the level of the aortic bifurcation. All presacral, hypogastric, external iliac, obturator, and common iliac lymph node packets are removed en bloc. After ipsilateral dissection, packets are immediately placed in a 10 mm Endo Catch retrieval device, and contralateral dissection is then performed. Nodal packets are placed in separate bags and can be distinguished by placing a knot or clip on one of the retrieval bags.

Prior to the urinary diversion, the left ureter is transposed to the right side of the pelvis through a window created posterior to the sigmoid mesentery and superior to the aortic bifurcation just anterior to the great vessels. The assistant places a grasper underneath the sigmoid colon and the tie on the left ureter is placed in the grasper and delivered to the right side of the patient.

Before the robot is undocked, we place a 15 Fr round Jackson–Pratt drain through the left 8 mm robotic trocar. For orthotopic neobladders, the drain is placed after the vesicourethral anastamosis has been completed robotically.

After the robot has been undocked, the periumbilical cameral incision is extended inferiorly in a curvilinear fashion around the umbilicus. Depending on the body habitus of the patient, the incision used for specimen extraction and extracorporeal urinary diversion typically ranges from 5 to 7 cm. The three separate Endo Catch retrieval bags are removed through this incision, although in female patients the specimens can be removed through the vagina. Urinary diversions including ileal conduit, continent cutaneous diversion, and orthotopic ileal neobladder and the bilateral ureteral anastomoses are performed in the standard open fashion [31, 32].

For patients undergoing orthotopic neobladder, the newly created neobladder is brought down into the pelvis. We then place a urethral catheter per urethra and into the opening created in the neobladder and the catheter balloon is inflated with 15 ml of sterile water and the catheter placed on mild traction to bring the neobladder in closer proximity to the urethra. Prior to redocking of the robot for the urethral–neobladder anastomosis, a suprapubic tube and ureteral stents, brought through a single stab wound in the right lower quadrant, are used to stabilize the neobladder and facilitate the urethral–neobladder anastomosis. The robot is then redocked, pneumoperitoneum is re-established, and the urethral–neobladder anastomosis is performed as shown in Figure 96.4. All wounds are copiously irrigated with sterile water and subsequently closed in a running subcuticular fashion.

## Special considerations for female cystectomy

In female patients, radical cystectomy typically involves concomitant hysterectomy, bilateral salpingo-oophorectomy, and resection of the anterior vaginal wall. However, in select patients (i.e. anterior bladder tumors) preservation of the internal genital organs may be considered, which can provide good functional outcomes, improve sexual function, and preserve potential for fertility [33].

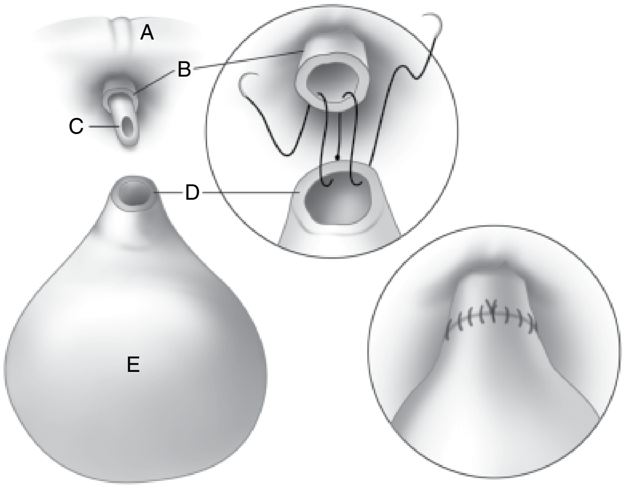

**Figure 96.4** Running urethral–neobladder anastomosis displaying (A) pubic bone, (B) urethra, (C) urethral catheter, (D) everted mucosa of neobladder neck, (E) neobladder. *Source:* Golombos DM. *Robot-Assisted and Partial Cystectomy*, 2017. Berlin: Springer-Verlag. Reproduced with permission of Springer.

When performing a radical cystectomy in a female patient, a sponge stick is placed in the vagina at the beginning of the case. The labia majora can be sutured together to prevent loss of pneumoperitoneum through the vagina, although this is rarely necessary. After ureteral mobilization as previously described, the uterine and ovarian vessels are identified and divided using either Hem-o-lok clips or the vessel sealer device, followed by identification and transection of the round and cardinal ligaments. The uterus, fallopian tubes, and ovaries may be sutured to the bilateral umbilical ligaments to facilitate the posterior dissection. The peritoneum is incised in the rectouterine pouch, and with the aid of the sponge stick, the fundus is opened at the posterior fornix below the level of the insertion of the cervix. The dissection proceeds distally to the level of the bladder neck. The specimen is then transected just distal to the bladder neck, and the vaginal wall is closed longitudinally or transversely using a continuous interlocking stitch with absorbable suture.

## Postoperative care

Patients are managed postoperatively in accordance with the interventions outlined in the enhanced recovery after surgery (ERAS) protocols [34] with the hopes of reducing surgical stress response and optimizing management [35]. Important principles for optimizing ERAS for RARC include early mobilization and sparing use of opiates for analgesia. Nasogastric tubes are not routinely used postoperatively and can be removed in the recovery unit. Oral diet should be started as soon as possible after surgery, as tolerated by the patient. Early ambulation is enforced and patients are followed by both physical and occupational therapy. Prevention of postoperative ileus and promotion of bowel recovery requires a multimodal approach including prokinetic agents (e.g. metoclopramide) and peripherally acting μ-opioid receptor antagonists (e.g. alvimopan) [36].

## Results

Although ORC remains the gold standard for treatment of muscle-invasive bladder cancer and for high-risk recurrent non-muscle-invasive disease [1], the use of RARC has steadily grown following the successful implementation of minimally invasive techniques in management of bladder cancer. Between 2004 and 2010, the percentage of robot-assisted cystectomies increased from 0.6% to 12.8% [37].

Perioperative and postoperative outcomes following LRC and RARC have been well documented and compared with ORC. Current data reveal that LRC and RARC are both associated with reduced estimated blood loss and need for blood transfusion, lower narcotic requirements, and shorter length of stay. A systematic review and meta-analysis done by Tang et al., comparing LRC to ORC, showed that LRC had less blood loss, shorter length of hospital stay, less need of blood transfusion, less narcotic analgesic requirement, shorter time to ambulation, and shorter time to regular diet [6]. Parekh et al. also proposed similar findings in its randomized clinical trial of ORC versus RARC, where it was shown that RARC presented with decreased estimated blood loss (400 ml compared to 800 ml of ORC) and trended toward a decreased rate of excessive length of stay (greater than 5 days) [38]. When compared to ORC, RARC has been shown to have longer surgical time (454.9 vs. 349.1 minutes) [39]. Lastly, a comparison of health-related qualify of life (HRQoL) outcomes for RARC patients versus ORC patients was recently addressed by Messer et al. in their prospective randomized clinical trial of 40 patients from 2009 to 2011 [40]. The study found no significant differences in the HRQoL outcomes using a Functional Assessment of Cancer Therapy–Vanderbilt Cystectomy Index (FACT–VCI) questionnaire preoperatively and then at 3, 6, 9, and 12 months postoperatively [40].

Concerns of oncologic efficacy regarding the use of RARC have been assessed by several studies, with main focus being placed on positive surgical margins (PSMs), lymph node yields, and survival outcomes. PSM after radical cystectomy has been shown to be an independent predictor of metastatic progression as well as decreased

**Table 96.1** Oncologic outcomes literature review.

| Study | Dotan et al. [41] | Cathelineau et al. [47] | Pruthi et al. [48] | Kauffman et al. [49] | Snow-Lisy et al. [50] |
|---|---|---|---|---|---|
| Year of study | 2007 | 2005 | 2010 | 2011 | 2014 |
| Number of patients | 1589 | 84 | 100 | 85 | 121 |
| Type of surgery | ORC | LRC | RARC | RARC | RARC, LRC |
| RFS | 67% (5 years); 57% (10 years) | 83% | – | 74% (2 years) | 71% (3 years); 65% (5 years) |
| CSS | 71% (5 years); 66% (10 years) | – | 94% | 85% | 73% (3 years); 71% (5 years) |
| OS | – | 100% | 91% | 79% | 55% (3 years); 48% (5 years) |
| Follow-up (months) | 120 | 18 | 21 | 18 | 66 |

ORC, open radical cystectomy; LRC, laparoscopic radical cystectomy; RARC, robot-assisted radical cystectomy; RFS, recurrence-free survival; CSS, cancer-specific survival; OS, overall survival.

disease-specific survival [41]. The 5-year cancer-specific survival rate after cystectomy for negative surgical margin was 72%, while that of a positive surgical margin was 32% [41]. Nix et al. carried out a prospective RCT in 2010 comparing the oncologic and pathologic outcomes of ORC to RARC in 41 patients and found no significant differences in PSM rates or lymph node yield [13]. Another study by Raza et al. revealed a PSM rate of 8% after RARC [42], which is similar to the PSM rates after ORC (0–10%) reported in several other studies [15, 38, 41, 43–45]. In a retrospective study addressing the recurrence patterns for 383 consecutive patients who either underwent ORC ($n = 120$) or RARC ($n = 263$), Nguyen et al. revealed that no statistical differences existed in terms of local and distant recurrence [46]. Several other studies have further assessed the oncologic outcomes of RARC and LRC in comparison to ORC with regards to their recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS). A selected few of such studies are outlined in Table 96.1.

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# Robot-assisted Laparoscopic Partial Cystectomy

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## Introduction

Partial cystectomy has emerged as an effective treatment strategy for select patients with muscle-invasive bladder cancer (MIBC). Although early studies assigned a poor oncologic outlook to this management strategy, rigorous patient selection, improvements in surgical technique, and the utilization of multimodal treatment strategies have contributed to substantial improvement in outcomes for MIBC [1–4]. It is currently estimated that between 5 and 10% of patients with MIBC are eligible for partial cystectomy. Enhanced quality-of-life metrics compared with radical cystectomy, specifically preservation of sexual function and voiding patterns, encourage utilization of partial cystectomy in these subgroups. A minimally invasive approach to partial cystectomy offers potential to further enhance perioperative outcomes, including diminished operative blood loss, improved postoperative pain, and shorter hospital stay [5].

## Outcomes

The earliest of series evaluating outcomes after partial cystectomy for MIBC date back to the 1970s. Novick and Stewart described a cohort of 50 patients with muscle-invasive disease in which 5-year cancer-specific survival was less than 50% among patients with MIBC, with the survival rate being less than 20% for those with T3 disease [1]. A similar retrospective review of 45 patients by Schoborg et al. cited recurrence rates as high as 100% and 5-year disease-specific survival of less than 40% among patients with high-grade lesions irrespective of stage [2]. The historically dismal prognosis associated with partial cystectomy, particularly in relation to total extirpative therapy, obscured its utility in the management of muscle-invasive disease until only recently.

A critical review of these reports reveals that the indiscriminate use of partial cystectomy for patients with MIBC is in large part responsible for inferior treatment outcomes. The importance of disease selection has been borne out in several contemporary studies that demonstrate cancer control to have been highly comparable to radical cystectomy [3, 4]. Among patients with a solitary focus of muscle-invasive disease who lack concomitant carcinoma *in situ* (CIS), a matched cohort comparison of both procedures performed by the Mayo Clinic found no significant differences between partial cystectomy and radical cystectomy with respect to 10-year metastasis-free survival (61% vs. 66%, $P = 0.63$) and cancer-specific survival (58% vs. 63%, $P = 0.67$). Overall survival was also found to be similar between treatment groups [3]. These results echo that of a population-based treatment comparison utilizing the SEER database, which demonstrates similar cancer-specific and overall survival for unifocal muscle-invasive disease amenable to complete resection with partial cystectomy [4].

## Indications and contraindications

Success of partial cystectomy for management of MIBC is highly contingent on patient selection and nature of disease. As such, critical review of patient pathology and disease history is of paramount importance when determining eligibility. Among patients without lymph node metastasis or extravesical extension, pathologic features predictive of inferior recurrence-free and cancer-specific survival outcomes include tumor size

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>5 cm, need for ureteral reimplantation, and histologic evidence of lymphovascular invasion [6, 7].

Tumor multifocality on initial stages has also been deemed a relative contraindication to partial cystectomy [7, 8]. A review of 86 patients undergoing partial cystectomy for localized MIBC revealed a 3.4-fold higher risk of 5-year cancer-specific mortality in the setting of synchronous lesions compared with unifocal disease [7]. Similarly, the presence of metachronous disease confers a poor oncologic outlook as cancer-specific and recurrence-free survival are reduced approximately threefold in patients with prior history of urothelial cancer [6]. Pathologic evidence of CIS during initial staging generally precludes partial cystectomy due to significant risk for development of intravesicular as well as advanced disease relapse [8]. Prior to planned partial cystectomy, random biopsies of the remaining bladder should be performed to confirm the absence of tumor multifocality or concomitant CIS.

Tumor location is not inherently predictive of oncologic outcomes [8]. Rather, the oncologic efficacy of partial cystectomy is highly dependent on the ability to achieve an adequate negative surgical margin. In this context, solitary tumors on the bladder dome or anterior wall are most amenable to partial cystectomy, whereas lesions situated at the trigone or bladder neck pose a technical challenge of achieving an acceptable disease-free perimeter. No study formally evaluates the optimal extent of a negative surgical margin with partial cystectomy. However, consensus is that resection be performed to achieve a 2 cm margin devoid of malignancy. Tissue from the edge of the resection bed should be sampled by intraoperative frozen section to ensure the absence of residual disease. Positive surgical margins may insinuate a more infiltrative process for which radical cystectomy may be better suited. Lesions in the posterior or lateral wall are technically amenable to partial cystectomy, however, ipsilateral ureteral reimplant may be necessary to enable adequate resection, which invites increased risk for postsurgical relapse [6–8].

A reduction in bladder capacity can be expected after partial cystectomy and may result in urinary frequency or urgency. Eligibility is questionable in patients with severe baseline lower urinary tract symptoms or bladder dysfunction due to risk of exacerbation and perturbed quality of life.

## Bladder-preservation therapy

Data regarding the utility of neoadjuvant chemotherapy prior to partial cystectomy remains scant. Nevertheless, oncologic benefit is inferred based on prospective studies demonstrating a 5% reduction in cancer-specific mortality after radical cystectomy [9]. Preoperative chemotherapy should therefore be considered in all patients eligible for partial cystectomy.

In comparison, chemotherapy has a more established role in alternative forms of bladder-preservation treatment. Trimodality therapy (TMT), which also encompasses maximal transurethral resection and concurrent radiation, is similar to partial cystectomy in that patient selection is of paramount importance to achieve acceptable outcomes. Among medically operable patients, the presence of CIS, tumor multifocality, and hydronephrosis are considered high-risk features and represent relative contraindications to TMT [10, 11]. In addition, large-volume disease that does not lend itself to maximal resection would also preclude TMT [12]. Pooled analyses of trials evaluating the oncologic efficacy of TMT estimated cancer-specific survival and overall survival to be 71% and 65%, respectively, at 5 years and 57% and 36%, respectively, at 10 years [13]. No prospective comparison to radical cystectomy exists. However, several long-term retrospective studies evaluating radical cystectomy and TMT as well as recent studies utilizing national cancer registries demonstrate that radical cystectomy may offer superior cancer-specific survival and overall survival on both multivariable and propensity-matched analysis [12, 14, 15]. However, the differences may be marginal if stringent selection criteria for TMT are applied [16].

Patients being considered for bladder-preservation therapy should be counseled on TMT and partial cystectomy in the appropriate setting. Currently, there are no comparative studies in the literature to evaluate the oncologic efficacy of each treatment. Given the significant overlap in eligibility criteria, advantages and disadvantages of both procedures should be emphasized to facilitate an informed decision. A clear benefit of partial cystectomy is the capacity to perform simultaneous pelvic lymph node dissection, which serves both prognostic and therapeutic value [17]. More accurate pathologic staging of the primary tumor is also possible due to full-thickness resection, again enabling better prognostic stratification as well as the delivery of more tailored adjuvant and salvage therapies. Indeed, a report by Tritschler et al. demonstrated significant risk for pathologic understaging based on imaging alone due to limitations in the capacity of radiologic metrics to gauge local and systemic disease extent [18].

Surveillance is an integral component of both treatment strategies, given early detection of recurrence can optimize cancer control. The incidence of recurrence (both non-muscle-invasive and muscle-invasive) after partial cystectomy is estimated to be 38%, whereas relapse among complete responders ranges between 24 and 43% after TMT [4, 13, 19]. Muscle-invasive recurrence accounts for a relatively small proportion in both groups. The rate of salvage cystectomy is almost 20% after partial cystectomy and as high as 30% with TMT if taking into account the nonresponder cohort [3, 13, 19, 20].

## Minimally invasive partial cystectomy

The advent of the robotic platform has encouraged a paradigm shift in the management of MIBC. Although robotic radical cystectomy is an increasingly utilized treatment option, a recent prospective study demonstrated no difference in pathologic outcomes and clinical metrics, including 90-day complications rate, hospital length of stay, and six-month quality of life [21]. Nevertheless, its non-inferiority may justify constituency in the treatment armamentarium for this disease.

A formal comparison of robotic and open approaches to partial cystectomy remains to be performed. However, several retrospective studies have demonstrated favorable oncologic and perioperative outcomes associated with the robotic technique. The largest of these reviews revealed a 90-day complication rate of 17%, with all having been minor in nature. In addition, median hospital stay in this cohort was only 1 day and median blood loss was only 50 ml [5]. In this context, a robotic approach to partial cystectomy is feasible in patients who meet eligibility criteria for bladder-sparing treatment.

## Patient preoperative evaluation and preparation

A diagnosis of bladder cancer is often prompted by microscopic or gross hematuria. Hematuria workup should ensue and encompasses cross-sectional imaging of the abdomen and pelvis. Cytology should be considered in high-risk patients as the presence of atypical or malignant cells warrants a thorough evaluation for high-grade disease, particularly CIS [22, 23].

Contrast-enhanced computed tomography (CT) remains the ideal imaging study, with emphasis placed on the excretory phase [22, 23]. Regions in the upper urinary that do not demonstrate intraluminal opacification are concerning for a neoplastic process and may be investigated further with ureteroscopy. Filling defects within the bladder may also herald presence of a bladder tumor, however, a more infiltrative process lacking protuberant architecture can present primarily as asymmetrical thickening of the bladder wall. Retrograde pyelography and ureteroscopy for evaluation of the upper urinary tracts should be considered if contrast-enhanced imaging is contraindicated [23].

Cystoscopy is integral to the hematuria workup as it enables direct inspection of the bladder mucosa for tumors and other abnormalities [22, 23]. In the event a tumor is identified, initial mapping of the bladder should be performed to establish focality, size, and location. Tumors should be resected completely, including deep resection into the muscularis to enable accurate clinical staging. Random bladder biopsies can be performed during the initial transurethral resection or second-stage cystoscopy to evaluate for multifocal disease, particularly CIS. Debate exists regarding the utility of prostatic urethral biopsies given that the presence of disease precludes partial cystectomy. Sampling of the prostatic urethra should be considered in the setting of a positive cytology without an identifiable bladder tumor, confirmed CIS within the bladder, or tumor situated at the bladder neck.

If muscle-invasive disease is identified during initial transurethral resection, restaging resection is not necessary unless there exists concern over incomplete resection or the presence of synchronous lesions. Prior to treatment planning, CT of the chest, abdomen, and pelvis should follow to evaluate for systemic disease. Imaging of other organ sites, specifically the brain and bone, is indicated in the presence of symptoms or aberrant serum studies [22, 23].

Patients being considered for partial cystectomy should undergo a comprehensive medical workup which involves obtaining relevant laboratory studies such as basic metabolic profile, complete blood count, liver function tests, and urine culture. Serum creatinine should be optimized as cisplatin-based neoadjuvant chemotherapy should be considered in patients prior to surgical intervention [9]/ A negative urology culture should be documented pre-procedurally to minimize risk of infection.

In addition to discussion of the risks inherent in performing partial cystectomy, patients should be counseled on the possible need for a completion radical cystectomy if more extensive disease is suspected intraoperatively. In this respect, there should be appropriate bowel preparation prior to surgery.

## Operating room configuration and patient positioning

After anesthetic preparations are complete, the patient is secured to the operating table in the dorsal lithotomy position with the hips abducted and arms tucked to the side. The patient should be placed in steep

Trendelenburg to ensure there is no cardiopulmonary compromise. Such position enhances visualization during the transperitoneal approach by shifting intestinal contents cephalad out of the pelvis. The abdomen, pelvis, groin, and perineum are sterilely prepped after which an 18 Fr Foley catheter is placed and included in the sterile field.

Depending on the specific model of da Vinci (Intuitive Surgical Inc., Sunnyvale, CA, USA) system utilized, the robotic tower is positioned between the patient's legs for the da Vinci Si® system or at the side of the operating table for the da Vinci Xi® system. The patient is placed in a steep Trendelenburg position prior to docking the robotic arms to their respective ports.

## Trocar placement

Pneumoperitoneum of 15 mmHg is first established using a Veress needle placed through the umbilicus. For patients with a history of prior abdominal surgery in whom there is concern for adhesions, the Veress needle can be placed in the subcostal location. Low pressures encountered on initial insufflation indicate proper placement of the Veress needle within the intraperitoneal cavity. Six robotic ports are subsequently placed, beginning with the midline camera port approximately 2 cm above the umbilicus or 20–25 cm above the pubic symphysis. A 12 mm port is utilized for the Si system whereas the smaller caliber endoscope of the Xi unit enables use of an 8 mm port. Two 8 mm robotic ports are placed on either side of the midline approximately 8 cm away from the robotic port at the level of the umbilicus. A third 8 mm robotic port is placed on the patient's right side approximately 8 cm lateral to the paramedian robotic port at the level of the umbilicus. Similarly, a 12 mm assistant port is placed 8 cm lateral to left-sided paramedian robotic port. A 5 mm assistant port may be placed in the left upper quadrant at a triangulated distance of 8 cm from the camera port and second robotic port (Figure 97.1).

## Procedure

The bladder is first mobilized by incising the anterior peritoneum lateral to the medial umbilical ligaments (Figure 97.2). The extent of the incision is the vas deferens inferiorly and umbilicus superiorly. The medial umbilical ligaments are subsequently divided, enabling transection of the urachus. The space of Retzius is then developed using a combination of blunt and sharp dissection from cephalad to caudad, allowing the bladder to be mobilized off the anterior abdominal wall (Figure 97.3). Posterior wall tumors may not require full mobilization of the bladder. Instead, the peritoneum can be dissected over its surface, after which the cystotomy can be made.

Flexible cystoscopy is performed by the bedside assistant to identify the tumor site. Transillumination through the bladder helps delineate the initial site of incision so as to avoid violation of the tumor. A longitudinal cystotomy is made and as the bladder is entered, fluid and urine

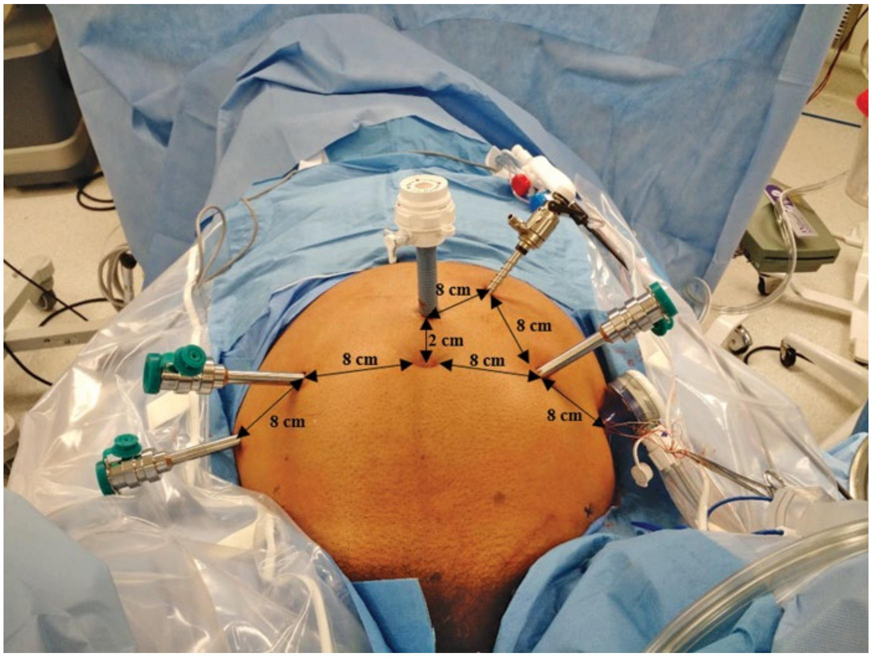

**Figure 97.1** Robotic port placement.

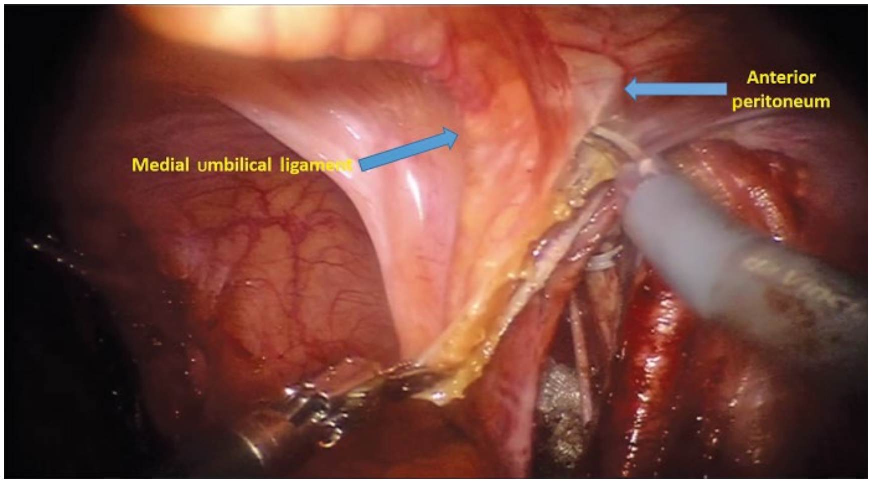
Anterior peritoneum
Medial umbilical ligament

**Figure 97.2** Incision lateral to medial umbilical ligament to access space of Retzius.

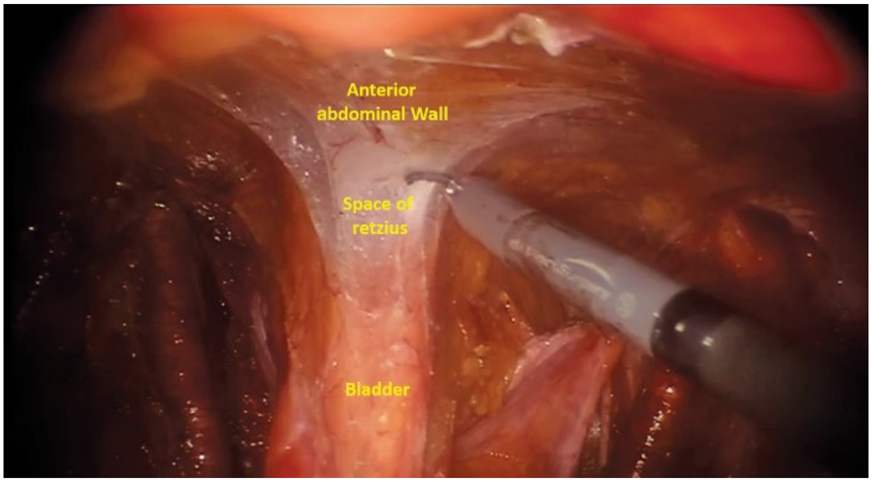
Anterior abdominal Wall
Space of retzius
Bladder

**Figure 97.3** Development of the space of Retzius by dropping the bladder.

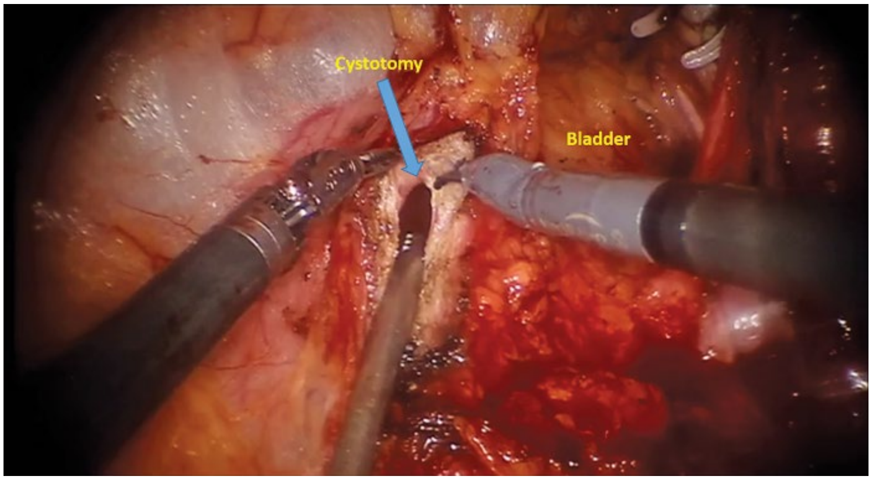
Cystotomy
Bladder

**Figure 97.4** Creation of cystotomy.

should be aspirated using a suction device to minimize risk of tumor spillage (Figure 97.4). The Foley catheter and flexible cystoscope are withdrawn and the bladder mucosa is carefully inspected (Figure 97.5). The tumor site should be inspected to ensure the feasibility of obtaining a 2 cm margin grossly devoid of tumor without disrupting the integrity of the ureteral orifices. The presence of satellite lesions should also be excluded (Figure 97.6).

Full-thickness resection of the bladder wall and perivesicular tissue is performed around the tumor site

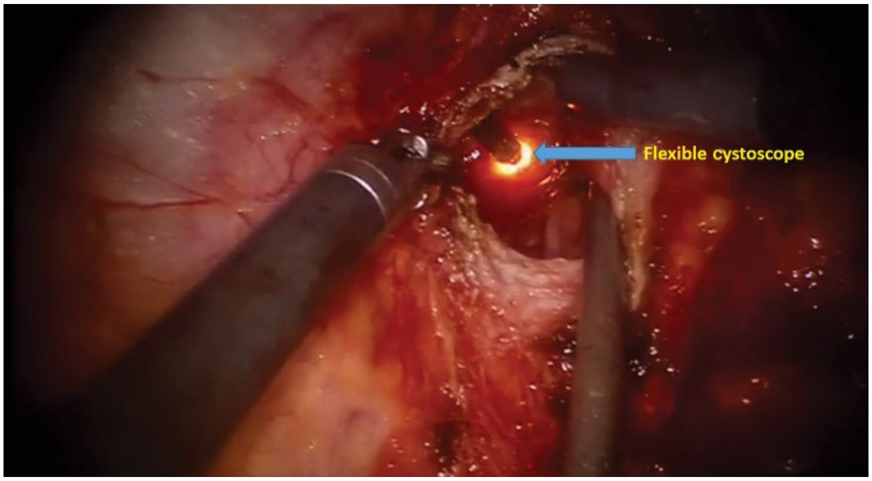

**Figure 97.5** Flexible cystoscopy to facilitation localization of tumor site.

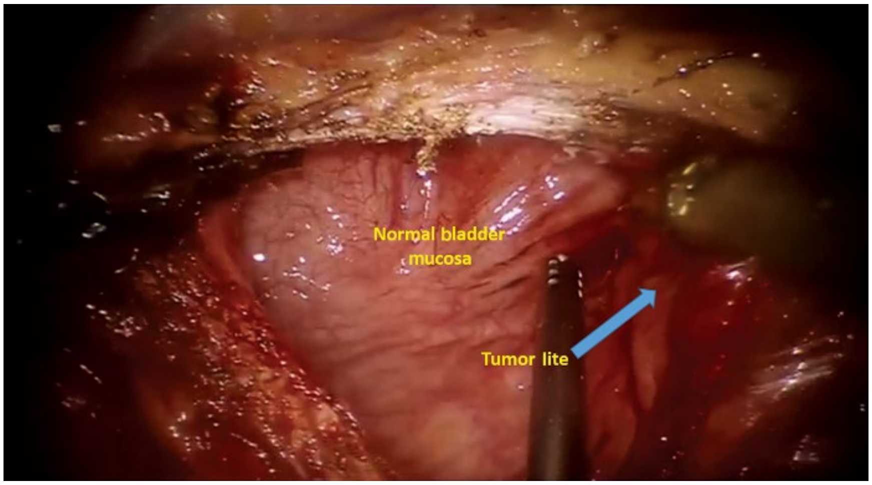

**Figure 97.6** Intraoperative inspection of bladder mucosa to rule out presence of satellite pathology.

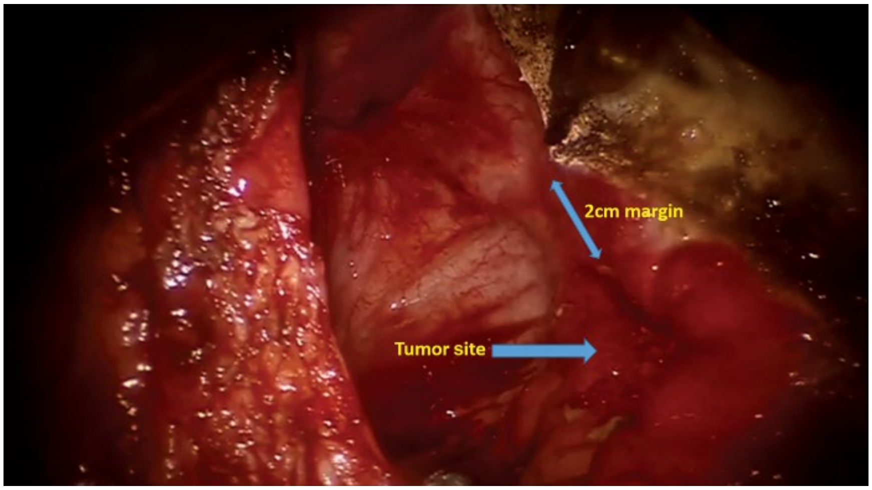

**Figure 97.7** Full-thickness circumferential resection of tumor site with normal parenchymal margin.

with care taken to obtain a 2 cm margin grossly devoid of tumor (Figure 97.7). The specimen is placed in a 10 mm Endo Catch™ (Covidien/Medtronic, Minneapolis, MN, USA) bag (Figure 97.8). Mucosal and detrusor tissue from the edge of the resection bed are sampled circumferentially by frozen section to evaluate for residual disease (Figure 97.9). Cystorrhaphy is performed only after frozen section analysis confirms the absence of disease. The bladder is closed in a two-layer running fashion using 2-0 polyglactin or 2-0 V-Lok™ (Covidien/

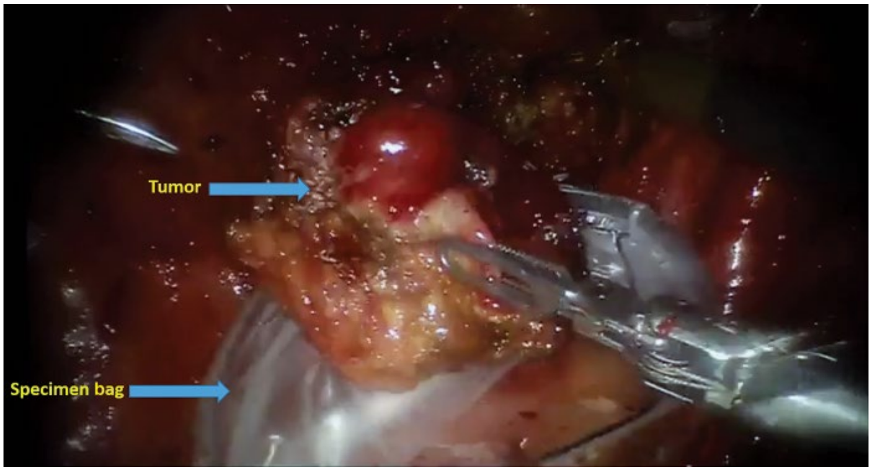
Tumor
Specimen bag

**Figure 97.8** Placement of specimen in Endo Catch specimen bag.

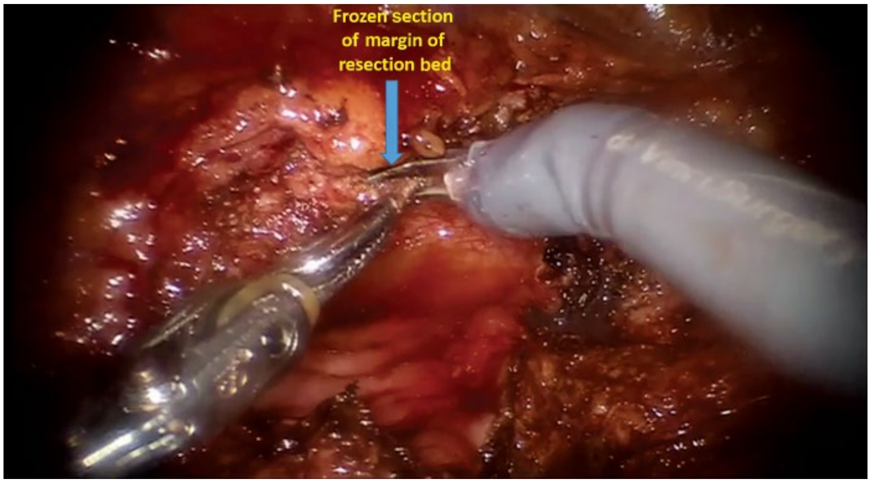
Frozen section of margin of resection bed

**Figure 97.9** Frozen sections obtained from tissue margins from resection bed.

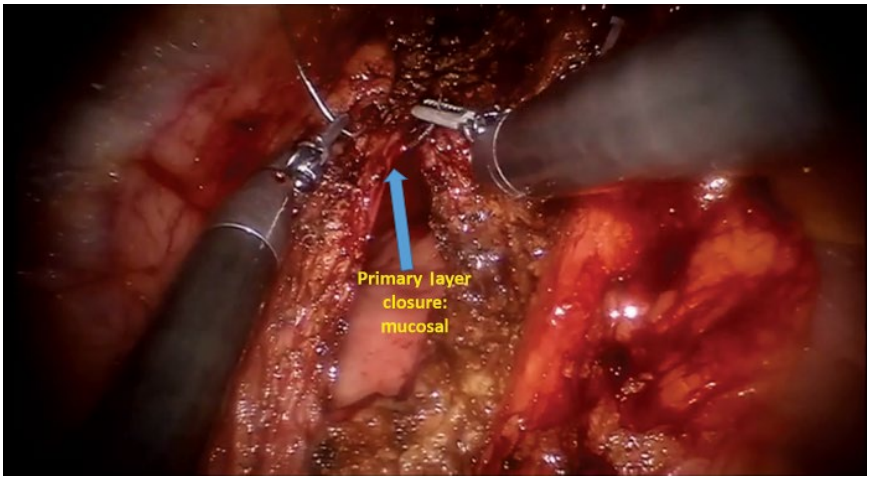
Primary layer closure: mucosal

**Figure 97.10** Cystotomy closed in two-layer manner, with initial primary closure of bladder mucosa.

Medtronic) suture. Care should be taken to ensure the primary layer incorporates the bladder mucosa (Figures 97.10 and 97.11). The bladder is irrigated with sterile water to assess integrity of the closure. Defects in the suture line should be buttressed with full-thickness figure-of-eight suture. Extended bilateral pelvic lymph node dissection is performed as described elsewhere.

A new 20 Fr Foley catheter is inserted into the bladder and placed to gravity drainage. A 19 Fr Blake drain is positioned in the vicinity of the cystorrhaphy and

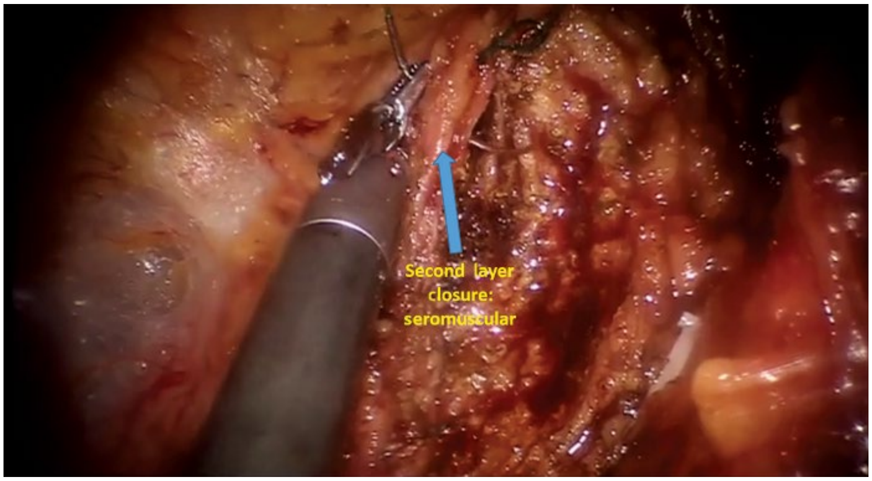

**Figure 97.11** Reapproximation of seromuscular lining of bladder.

brought out to the skin through the right lateral-most robotic port site. The drain is secured to the skin with nonabsorbable suture. Gas insufflation is stopped and the robot is undocked, after which the ports are removed. Specimens are extracted by extension of the midline camera port site. Fascia of the specimen extraction site and the left lateral 12 mm assistant port is closed with figure-of-eight 0-polyglactin suture in an interrupted fashion. Skin incisions are closed with 4-0 monofilament suture.

## Postoperative management

The patient is placed on a clear liquid diet postoperatively until return of flatus, at which point diet can be advanced to regular. Patient-controlled epidural anesthesia may be offered prior to the procedure to facilitate pain control. Early ambulation is critical in enhancing hospital recovery and the prevention of venous thromboembolic events. The Foley catheter is kept to gravity drainage to facilitate healing of cystorrhaphy. Output as well as fluid creatinine from the the pelvic drain helps monitor integrity of the cystotomy suture line. Fluid creatinine may be a more reliable metric to evaluate for urine leak as outputs can be confounded by fluid-shifts due to third-spacing.

Adequate drainage from the Foley catheter and decreasing outputs from the pelvic drain should prompt measurement of fluid creatinine from the pelvic drain. Equivalence between serum and fluid creatinine indicates adequate healing of the cystotomy closure. The pelvic drain may be discontinued the day prior to discharge unless fluid creatinine is found to exceed serum creatinine, in which case the drain should be continued. An outpatient cystogram should demonstrate the absence of contrast extravasation prior to removal of the Foley catheter.

## Surveillance

Postoperative surveillance is critical to optimizing oncologic outcomes after partial cystectomy for muscle-invasive disease. Local disease relapse remains a critical concern after partial cystectomy. Implicit in outcomes being on par with radical cystectomy for select patient groups is the feasibility of controlling intravesical recurrence with salvage therapy. Local recurrence is estimated to occur in 38% of patients, with the majority being non-muscle-invasive in nature. Because of this, transurethral resection and intravesicular instillation of bacillus Calmette–Guérin maintain an important role in preserving the oncologic integrity of partial cystectomy [4].

Although muscle-invasive disease accounts for a relatively small fraction of recurrences, salvage radical cystectomy is necessary in 20% of patients after partial cystectomy [4]. Early recognition is critical as salvage radical cystectomy for organ-confined lesions, which are present in approximately 60% of patients, offers highly favorable disease-free and cancer-specific survival, essentially equivalent to that of primary radical cystectomy. The presence of extravesical extension or lymph node involvement, disease features present in 20% of patients from each group at time of salvage surgery, were poor prognosticators and associated with inferior cancer control when compared with primary radical cystectomy [20]. In this context, the role of close follow-up and early intervention cannot be overemphasized, particularly during the initial 2-year postoperative window when muscle-invasive recurrence is most frequently encountered [4, 20].

Urine cytology and cystoscopy should be performed every three months during the initial 2 years, after which follow-up may be more spaced out. Periodic CT urography is also encouraged to evaluate for upper tract recurrence [22].

## Complications

A key advantage of partial cystectomy is the significant reduction in morbidity and mortality risk relative to radical cystectomy. The incidence of complications after radical cystectomy is estimated to be as high as 70%, with a substantial number being major complications [24]. Comparatively, a review of the National Inpatient Sample observed complications in 16% of patients undergoing partial cystectomy, with complication rates being lowest at high-volume centers. In-hospital mortality after surgery was also significant lower after partial cystectomy [25]. Aside from the risks inherent in any surgical procedure, there are several unique complications inherent to partial cystectomy that require a high index of clinical suspicion.

Urinary leakage across the cystotomy closure may result in the development of a urinoma. High output from the pelvic drain or a drain fluid creatinine that exceeds serum creatinine is concerning for urinary extravasation across the cystorrhaphy. Mild–moderate urine leaks are managed by continuing the Foley catheter for longer duration to facilitate healing of the suture line. Cystogram should be performed prior to Foley removal. The development of a more sizeable urinoma, however, may result in fever, leukocytosis, or abdominal pain. Imaging is necessary if there is suspicion for infected urinoma or pelvic abscess which may require percutaneous drainage. Urinary diversion with bilateral percutaneous nephrostomy tubes should be considered for urinary leaks that are refractory to conservative measures.

Ureteral injury is another recognized complication of partial cystectomy. Care should be taken to avoid the ureteral orifices during tumor resection, particularly given efforts to obtain a wide margin free of tumor. If intraoperative injury is suspected, an attempt should be made to place a ureteral stent in a retrograde manner. Inability to place a stent in this setting warrants ureteral reimplantation at the time of surgery. For lateral wall tumors, preoperative placement of ureteral catheters can be considered. Iatrogenic injury that goes unrecognized may present itself as flank pain, fever, acute kidney injury, or the development of urinoma in the early postoperative period. Cross-sectional imaging, preferably CT urography, should be performed to evaluate for new-onset hydronephrosis or contrast extravasation from the ureter. Disruption in the integrity of the ureter would necessitate an ipsilateral percutaneous nephrostomy tube. Attempt should be made at antegrade stent placement; however, if unsuccessful, a delayed distal ureteral reimplant may be required.

See accompanying Video 97.1.

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# 98

# Laparoscopic Cystoprostatectomy with Intracorporeal Ileal Conduit

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## Introduction

The use of laparoscopic and robotic techniques in the performance of urological procedures has been expanding since the early 1990s. Laparoscopic radical prostatectomy opened the doors for laparoscopic cystectomy, retroperitoneal lymph node dissection, and other complex operations. Radical cystectomy and prostatectomy have been subjected to intense scrutiny and criticism as being inferior to the more traditional open techniques. Robotic prostatectomy, however, has stood the test of time and now over 80% of prostatectomies are performed robotically. Laparoscopic and robotic cystoprostatectomies are on the same path. Early criticism of inadequate lymphadenectomies and poor-quality cancer techniques have been answered and rectified. Each hurdle presented has been well-received and viewed as an opportunity to grow and refine the operation. The very real initial and substantive hurdle was to complete the cystoprostatectomy with a laparoscopic or robotic urinary diversion, completely intracorporeally. Great strides have been made and soon completing the entire operation intracorporeally will be the norm. In this chapter we discuss the history and current state of intracorporeal laparoscopic and robotic ileal loop.

The first intracorporeal ileal loop was accomplished laparoscopically by Kozminski, as reported in the *Journal of Endourology* in 1992. Multiple reports of intracorporeal ileal loops have followed. Since this first effort the early outcomes of improved blood loss, reduced hospital stay, and increased patient satisfaction has encouraged the undertaking of these complex procedures, albeit primarily at large, high-volume academic centers as reported by Gupta et al. [1]. Although extracorporeal ileal conduit has been the traditional mainstay despite the advent of robotic cystectomy, Goh and other have reported on new techniques for intracorporeal urinary diversion described in the literature, such as intracorporeal ileal conduit and intracorporeal continent diversion [2]. Because of such advances, the choice of urinary diversion should no longer be limited by the decision for a robotic-assisted laparoscopic approach.

Many factors are critical to the decision behind intracorporeal ileal conduit creation. These include institutional culture, access to equipment, and knowledgeable support staff. Regardless of approach, radical cystectomy is associated with significant morbidity, mortality, and a complication rate up to 40–70%. Surgeon experience and access to appropriate resources to complete this technical procedure is important. Similarly, patient selection is critical in determining optimal urinary diversion choice. In general, patients with motor or cognitive impairment, chronic renal impairment, or occult malignancy at bladder neck are likely to be better candidates for ileal conduit diversion [3].

Robotic cystectomy with intracorporeal ileal conduit was first described in 2000 by Gill et al., and has since demonstrated excellent long-term outcomes [4]. Since then many small series from single centers have been reported. A retrospective review by Guru et al. of 13 patients, each undergoing intracorporeal or extracorporeal cystoprostatectomy with ileal conduit at Roswell Park Cancer Institute, demonstrated similar mean operative times, blood loss, positive surgical margin rate, and lymph node yields [5]. Other initial reports comparing extracorporeal and intracorporeal ileal conduits suggested higher complication rates and prolonged operative times. However, this was felt to be due to the steep learning curve and ongoing technique mastery. Rahman et al. reported their experience in nine patients [6]. They used the Wallace technique for the uretero-ileal anastomosis

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and reported excellent outcomes. The operative times, although somewhat variable, were felt to be acceptable (compared to open norms). None of the patients needed to be converted to open surgery. Patients were discharged within 7 days, although the authors point out they could have left the hospital sooner but needed to stay longer for ostomy nurse education etc. All patients returned to full normal activities within two weeks.

Bishop et al. reported their experience with eight intracorporeal ileal loop diversions in 2013 [7]. Again, patients recovered quickly with significantly lower postoperative pain levels and rapid return of normal bowel function. All patients were able to be discharged in less than a week. An analysis of the International Robotic Cystectomy Consortium retrospective data between 18 institutions and 935 patients revealed 787 extracorporeal urinary diversions (75% of which were ileal conduits) and 148 intracorporeal diversions (of which 59% were ileal conduits). Their results found no difference in operative times between extracorporeal urinary diversion and intracorporeal diversion, but did note lower blood transfusion rates and 90-day readmission rates in favor of intracorporeal diversion. In addition, intracorporeal diversion was associated with significantly lower gastrointestinal complications [8]. However, no subset analysis was completed for extracorporeal versus intracorporeal ileal conduits only. Other small series have also shown the ability and usefulness of this procedure and the learning challenges experienced [9–11].

The largest series by a single institution was reported by Azzouni et al. in 2013 [12]. They reported on 100 patients with intracorporeal ileal loop using the “marionette” technique. In this technique, after the ileal loop is created it is suspended at the distal end to the abdominal wall by a suture passed through the abdomen on a Keith needle and then through the loop. By moving the suture up and down (much like a puppeteer or marionette) the loop can be controlled or moved to facilitate an easier uretero-ileal anastomosis. Others use this technique and find it very helpful. The authors report total operative time for the cystoprostatectomy, node dissections, and loop creation of just under 6 hours, which is very reasonable. The ileal loop creation was generally 2 hours, although in our experience we have found that as the surgeon moves up the experience curve the time to create the loop can be reduced to 90 minutes or less. Azzouni et al. also report an 81% overall complication rate at 90 days. About 60% or so were infections (urinary tract infections etc.) and gastrointestinal disorders (small bowel obstruction, *Clostridium difficile* enteritis, etc.). At 90 days 85% of the complications were Clavien $\leq$ II level and 15% $\geq$ Clavien III. The mortality rate was 1% in a patient who expired secondary to myocardial infarction. The 30-day readmission rate was 16%.

This important series has shown that complete intracorporeal ileal loop creation is reasonable, rational, safe, and can be completed in an acceptable time (as compared to the standard open techniques). Its use will continue to grow as urologists gain more experience and through young urologist graduates with the necessary skills gained in residency.

The perceived advantage of intracorporeal ileal conduit is thought to be secondary to avoidance of mini-laparotomy incision and, as a result, reduced bowel handling and exposure. In addition, the intracorporeal approach enables the surgeon to make uretero-ileal anastomoses at the physiologic location in the ileal loop where they will lie post procedurally, likely resulting in less tension and mobilization required. Less handling and mobilization of the ureter are felt to create fewer issues with ureteroenteric stricture. Regardless of intracorporeal or extracorporeal diversion type, robot-assisted radical cystectomy has been shown to be associated with similar oncologic outcomes. This is likely secondary to the fact that the oncologic portion of procedure is completed first, prior to diversion, and has been corroborated in the literature, demonstrating no significant differences in positive surgical margin rates, lymph nodes or cancer-specific or overall survival rates [12].

As surgeon experience improves, the volume of robot-assisted cystectomies with intracorporeal diversions will likely increase. Early results from the literature support decreased complication rates and reduced length of stay, and risk of conversion to open surgery decreases as surgical volume and experience improve [13]. Techniques such as colored stay sutures and bowel detubularization tools are already being published in the literature as techniques to improve operative efficiency [14, 15].

## Technique for robotic intracorporeal ileal conduit

All patients undergoing robotic cystectomy and intracorporeal diversion follow an enhanced recovery pathway that is initiated 24 hours prior to surgery. Patients are instructed to consume clear liquids and a high-calorie carbohydrate load the day before surgery. In the pre-op area, patients receive a μ-opioid antagonist to optimize bowel function. A site for the ileal conduit is selected with the assistance of an ostomy care nurse prior to induction of anesthesia.

The authors employ a standard six-port robotic cystectomy configuration for performance of the cystectomy as well as intracorporeal ileal conduit. The assistant stands on the left side of the patient. Placement of the assistant ports on the left abdomen facilitates bowel stapling directed toward the right lower quadrant.

After completion of robotic cystectomy and extended lymph node dissection, the ileal conduit is developed. Atraumatic double-fenestrated graspers are used for bowel manipulation. The ileocecal valve is identified and at least 15 cm of terminal ileum is spared. The distal segment of the ileal conduit is divided using a 60 mm bowel load stapler (staple height 3.5 mm thickness). The bowel segment for the conduit is then measured from the sacral promontory to the previously marked stoma site at the abdominal wall generally measuring 15–17 cm in length. The proximal division of bowel is then performed.

After segmentation, a standard side-to-side bowel anastomosis is performed using a 60 mm bowel load stapler. The antimesenteric sides of small bowel are joined, and then the anastomosis is completed with a perpendicular fire of the bowel stapler.

The uretero-ileal anastomoses are performed using a Bricker anastomosis with minimal handling of the ureter. Other approaches have described a Wallace technique for ureteral anastomosis. The left ureter is transposed under the sigmoid mesentery. The uretero-ileal anastomoses are performed at the proximal end of the conduit in a dependent manner. The anastomosis is performed using 4-0 Vicryl in a running fashion. Single-J stents are placed percutaneously through a small 2 mm port placed over the loop only for that purpose. We gently slide the double-fenestrated grasper down the open end of the loop to pull the free ends of the stents to the distal loop. The free ends emanate from the stoma of the conduit. The distal end of the conduit is then delivered through the previously marked stoma site and matured to the skin in the standard fashion.

See accompanying Video 98.1.

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# 99

# Laparoscopic/Robotic Continent Diversion

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## Introduction

For patients undergoing robot-assisted radical cystectomy (RARC), continent urinary diversion is a surgical option that may provide for better cosmesis and quality of life. As the utilization of RARC for the treatment of muscle-invasive bladder cancer has increased over the last decade, minimally invasive continent urinary diversion has become a feasible and safe alternative to the open procedure. The general advantages of laparoscopic surgery and robot-assisted laparoscopic surgery, including reduced morbidity, quicker recovery time, improved visibility, and reduced blood loss, have driven interest and advancement in minimally invasive surgery. Potential benefits specific to minimally invasive continent urinary diversion include less manipulation of bowel with quicker return of bowel function, reduced pain, and less morbidity from incisions.

Advances in minimally invasive radical cystectomy and urinary diversion occurred stepwise in the preceding decades. The first laparoscopic radical cystectomy with extracorporeal ileal conduit was reported in 1995 [1]. This was followed by the first described laparoscopic radical cystectomy with intracorporeal ileal conduit in 2000 [2]. Laparoscopic radical cystectomy with intracorporeal ileal neobladder was first reported in 2002 [3]. Initial obstacles to minimally invasive radical cystectomy and urinary diversion included the limited maneuverability of laparoscopic tools, a steep learning curve, and long operative times.

Since the US Food and Drug Administration (FDA) approval of the da Vinci Surgery System in 2000, wristed laparoscopic instruments and other advancements have allowed urologists to overcome many of the limitations of conventional laparoscopic surgery. The first case report of RARC with completely intracorporeal urinary diversion was described in 2003 [4]. In a seminal report in the same year, RARC with extended pelvic lymph node dissection and urinary diversion was described in 17 patients [5]. Three patients received ileal conduit urinary diversion and 14 received orthotopic neobladders in a hybrid approach. The orthotopic neobladder (ONB) was constructed extracorporeally through the specimen extraction site, and the urethral-neobladder anastomosis was performed robotically after placing the neobladder back in the abdomen and closing the incision. RARC and urinary diversion was described in three female patients in 2004 [6]. Review of initial RARC and urinary diversion cases showed that the procedure could be performed with relatively short operative time, low blood loss, and safely without intraoperative complications [7]. Multiple case series have since demonstrated the safety of RARC and completely intracorporeal ONB [8–16]. RARC and urinary diversion has also been shown to have oncologic outcomes equivalent to open radical cystectomy [17]. Robotic continent cutaneous urinary diversion has only recently entered the repertoire of the robotic surgeon after its first description in 2015 [18].

Probably owing to the numerous perceived disadvantages of a minimally invasive approach, including the technical difficulty, longer operative time, and increased cost, urologists have been slower to adopt minimally invasive urinary diversion than other robot-assisted urologic procedures. Despite perceived disadvantages, RARC with intracorporeal urinary diversion is being performed with increasing frequency. Based on data published by the International Robotic Cystectomy Consortium (IRCC), 7% and 11% of 935 patients undergoing RARC between 2003 and 2011 had a completely intracorporeal neobladder or ileal conduit, respectively [19].

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## Indications and contraindications

All patients who are candidates for radical cystectomy should at least be considered for laparoscopic or robotic continent diversion. Prior abdominal surgery, radiotherapy, obese body habitus, advanced age, poor functional status, and certain medical conditions such as poor pulmonary compliance may preclude a minimally invasive technique. Candidates for continent urinary diversion also need to be physically and intellectually able to perform scheduled voiding and urethral catheterization if necessary.

For ONB, patients should have a patent urethra, an absence of stress urinary incontinence, and an absence of tumor in the urethra distal to the prostate in men and in the bladder neck in women. Preoperative biopsy and/or intraoperative frozen section should be performed if indicated. ONB is contraindicated in patients with chronic kidney disease with serum creatinine of greater than 2 mg/dl or GFR <40 ml/min/1.73 $m^2$. However, if significant recovery of renal function is anticipated with alleviation of renal obstruction by urinary diversion, an exception can be made. Cirrhosis is a contraindication to ONB as reabsorption of ammonia can lead to hyperammonemia. Inflammatory bowel disease, short bowel disease, and extensive abdominal/pelvic radiotherapy are also contraindications to ONB.

## Preoperative evaluation and preparation

The preoperative evaluation of patients undergoing robotic/laparoscopic continent diversion begins with a thorough history and physical examination. Patients should have medical clearance, especially if the American Society of Anesthesiology (ASA) class is III or greater. Assessment of renal function, and metabolic and hematologic abnormalities are carried out with laboratory studies. A preoperative urine culture is obtained, and preoperative antibiotic prophylaxis is administered as indicated. If radical cystectomy is being performed for malignancy, staging studies including chest X-ray or thoracic computed tomography (CT) scan and abdominal and pelvic CT scan are conducted. Bone scan is performed only if metastasis to the skeleton is suspected, such as with elevated alkaline phosphatase or bone pain. All patients being considered for radical cystectomy for malignancy should have referral to an oncologist for possible neoadjuvant chemotherapy.

In all cases, patients need marking for the potential of a conduit or catheterizable stoma. Mechanical bowel prep is not recommended as there has not been any clearly demonstrated benefit, and mechanical bowel prep can cause electrolyte abnormalities [20]. The day prior to surgery, patients are prescribed a clear liquid diet and are to be nil per os from the midnight before surgery. Also in the preoperative period, patients can be given instruction in clean intermittent catheterization.

### Operating room configuration and patient positioning

The patient is placed in the supine position. Prophylactic heparin or low molecular weight heparin is given before surgery. General endotracheal tube anesthesia is administered, and a broad-spectrum antibiotic is given to cover enteric organisms. An oro- or nasogastric tube is inserted to decompress the stomach. A urethral catheter is inserted and left to gravity drainage. The patient is then placed in the dorsal lithotomy position with arms tucked. The extremities are padded carefully to avoid neuropraxia and compartment syndrome. If RARC is being performed, the patient is moved into a steep Trendelenburg position (30–45°), which facilitates movement of the bowels out of the pelvis. With ONB construction, Trendelenburg position is reduced to 10–15°, or the patient can be placed in the supine position, and the robot can be side-docked to avoid potential complications from a prolonged lithotomy position. After patient positioning, the skin is shaved with a clipper, and a sterile field is created by prepping the perineum, genitals, proximal thighs and the infraxiphoid abdomen and pelvis.

Instrumentation required for RARC with ONB is listed in Box 99.1.

### Trocar placement

#### The da Vinci S and Si robotic systems

The abdomen is insufflated to 15 mmHg utilizing a Veress needle. A 12 mm bladeless trocar is inserted about 5 cm above the umbilicus. The camera is inserted, and the abdomen is inspected for iatrogenic injury, adhesions, and metastatic disease. Three 8 mm robotic ports are then placed under direct visualization (Figure 99.1a). Two robotic ports are placed 7–10 cm lateral and cephalad to the umbilicus. A additional robotic port is placed in the right lower quadrant of the abdomen 7–10 cm lateral to the right-sided robotic port and 5–7 cm superior to the iliac crest. A 12 mm AirSeal trocar (ConMed, Utica, NY, USA) is placed in the left abdomen 5–7 cm superior to the iliac crest. Positioning of the assistant port in the left abdomen and fourth robotic arm on the right side aids with bowel manipulation and the avoidance of acute-angle stapling.

**Box 99.1 Instrumentation for robot-assisted radical cystectomy with intracorporeal ileal neobladder [21].**

**Nondisposable instrumentation**

- Four-arm da Vinci Si system (Intuitive Surgical Inc., Sunnyvale, CA, USA)
- Plasmakinetic bipolar generator (Gyrus ACMI PK, Gyrus ACMI, Norwalk, OH, USA)
- Laparoscopic grasper
- Laparoscopic scissors
- Laparoscopic KOH Macro Needle Holder (Karl Storz, Tuttlingen, Germany)
- Hot Shears (monopolar curved scissors) (Intuitive Surgical Inc.)
- Maryland (bipolar forceps) (Intuitive Surgical Inc.)
- Atraumatic Cadiere forceps (Intuitive Surgical Inc.)
- Large SutureCut needle driver (Intuitive Surgical Inc.)
- Ligasure (Valleylab, Boulder, CO, USA)
- 16 mm stapler (Endo GIA, Covidien, Dublin, Ireland)
- Lapra-Ty absorbable clips (Ethicon Endo-Surgery, Cincinnati, OH, USA)
- Laparoscopic Kelly
- Ligaloop Strings (Braun-Dexon, Spangenberg, Germany)
- 10 mm Stryker suction tip (Stryker, Kalamazoo, MI, USA)
- 5 mm long Stryker suction tip (Stryker)
- Small, large, and extra-large laparoscopic Hem-o-lok appliers (Weck Closure Systems, Research Triangle Park, NC, USA)
- Three 8 mm cannulas with obturator and seals (Intuitive Surgical Inc.)

**Disposable instrumentation**

- Basic accessory kit and drapes (Intuitive Surgical Inc.)
- Camera head (Intuitive Surgical Inc.)
- 0° and 30° endoscopes (Intuitive Surgical Inc.)
- StrykeFlow 2 suction/irrigation system (Stryker)
- Echelon Flex Powered Endopath Stapler (Ethicon Endo-Surgery)
- Large and extra-large Hem-o-lok clips (Weck Closure Systems)
- Veress needle (Ethicon Endo-Surgery)
- One Endopath Xcel 12 mm bladeless bariatric trocar for camera port (Ethicon Endo-Surgery)
- One Endopath Xcel 12 mm bladeless trocar (Ethicon Endo-Surgery)
- One Endopath Xcel 15 mm bladeless trocars (Ethicon Endo-Surgery)
- Endo Catch II 15 mm Specimen Pouch (Covidien, Norwalk, CT, USA)
- Two extra-large Hem-o-lok clips prepared with suture attached (Weck Closure Systems) for clipping and tagging of the ureters

**Optional instrumentation**

- ProGrasp forceps (Intuitive Surgical Inc.)
- 0 Vicryl on CT-1 needle (Ethicon, West Somerville, NJ, USA)
- Echelon Endopath 45 mm Stapler (Ethicon Endo-Surgery)
- 1-0 V-Loc 90 (glycolic acid–trimethylene carbonate, Covidien) for vaginal reconstruction
- Harmonic ACE curved shears 8 mm (Ultrasonic Energy Instrument, Intuitive Surgical Inc.)
- Large robotic clip applier (Intuitive Surgical Inc.)
- EndoWrist One suction/irrigator (Intuitive Surgical Inc.)
- EndoWrist vessel sealer (Intuitive Surgical Inc.)
- EndoWrist stapler (Intuitive Surgical Inc.)
- LigaSure Atlas (Covidien)
- Enseal tissue sealing device (Ethicon Endo-Surgery)
- Silicone vessel loops (Aspen Surgical Products, Caledonia, MI, USA)
- Endo GIA Ultra universal stapler (Covidien)
- Lapro-Clip (Covidien)
- Firefly near-infrared fluorescence visualization system (Novadaq Technologies, Mississauga, Ontario, Canada)

*Source:* Bishoff JT, Kavoussi LR. *Atlas of Laparoscopic and Robotic Urologic Surgery*. London: Elsevier, 2016. Reproduced with permission of Elsevier.

If conversion to an ileal conduit is likely, a second assistant port can be inserted in the prospective stomal site between two robotic ports. Stapling of the pedicles in RARC is facilitated by placement of a 12 mm robotic port near the midline. A robotic stapler may be utilized through this port.

For RARC, Hot Shears (Intuitive Surgical Inc., Sunnyvale, CA, USA) are used in the right robotic arm, PK dissecting forceps (Gyrus ACMI PK, Gyrus ACMI, Norwalk, OH, USA) in the left robotic arm, and Prograsp or Cadiere forceps (Intuitive Surgical Inc.) in the third robotic arm. For intracorporeal ONB, two needle drivers are needed. A 30° down lens aids with dissecting deep in the pelvis and for extended pelvic lymph node dissection. A 30° up lens is helpful for dropping the bladder, dissecting behind the prostate, and for facilitating increased urethral length in the retro-apical dissection. A 0° camera lens is used for the apical dissection and the urethral-neobladder anastomosis.

### The da Vinci Xi robotic system

As with the Si and S robotic systems, six ports are utilized (Figure 99.1b). With the Xi system, an 8 mm universal camera–robotic port is used instead of a 12 mm camera

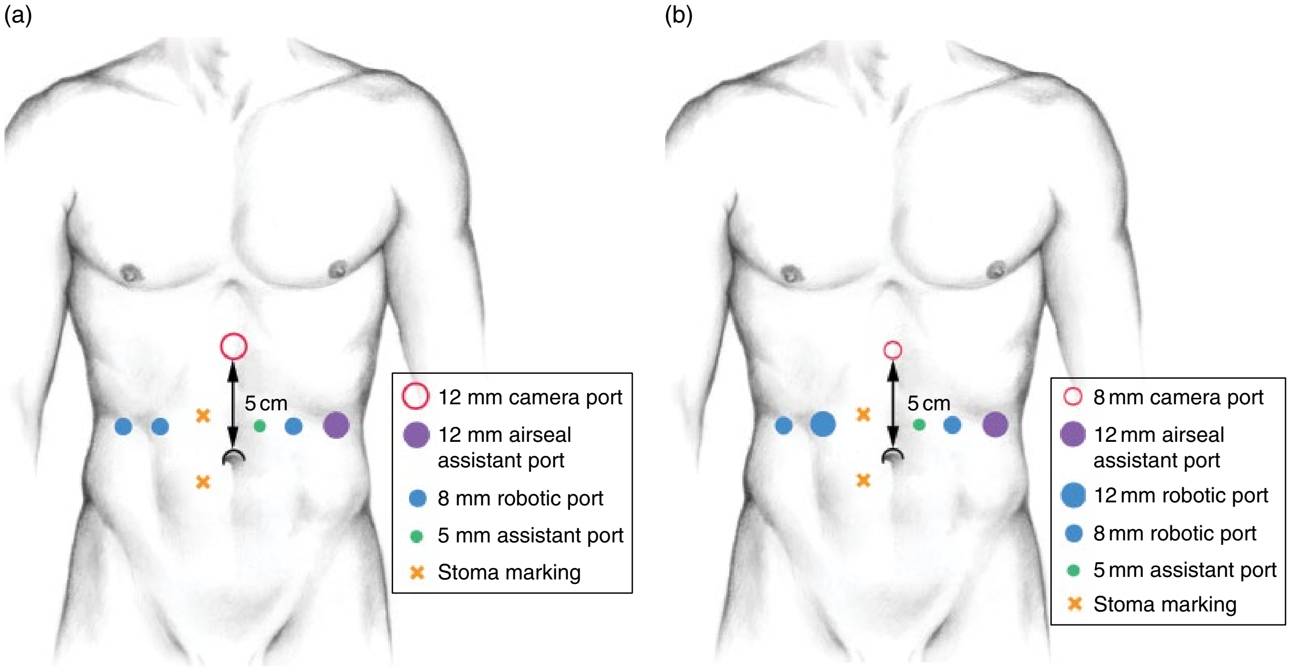
(a)
5 cm
○ 12 mm camera port
● 12 mm airseal assistant port
● 8 mm robotic port
● 5 mm assistant port
✕ Stoma marking
(b)
5 cm
○ 8 mm camera port
● 12 mm airseal assistant port
● 12 mm robotic port
● 8 mm robotic port
● 5 mm assistant port
✕ Stoma marking

**Figure 99.1** (a) da Vinci S/Si system port placement for ileal neobladder; (b) da Vinci Xi system port placement for ileal neobladder.

port. A notable advantage to the Xi system is that it facilitates ONB creation with greater ease in the supine position, which decreases the risk of positioning-related complications. A 12 mm robotic port can be placed instead of an 8 mm robotic port for the medial right robotic arm. A robotic or laparoscopic stapler can then be utilized from this site. This site can be converted to 8 mm when not in use for stapling.

Accessories that may be utilized for Si and Xi robotic systems during RARC with urinary diversion include the EndoWrist One Vessel Sealer and the EndoWrist Stapler (Intuitive Surgical Inc.). The EndoWrist One Vessel Sealer may be used for ligating small vessels and mesentery while the EndoWrist Stapler may be employed instead of a laparoscopic stapler.

### Laparoscopic

Six ports are utilized for laparoscopic radical cystectomy with intracorporeal ONB creation (Figure 99.2). A 10–11 mm camera port is placed above the umbilicus. Two 12 mm ports are placed on the left and right lateral edges of each rectus muscle just inferior to umbilicus. A 10 mm port is placed in the left iliac fossa. A 5 mm port is placed on the right at the level of the anterior superior iliac spine. A 5 mm port is placed between the umbilicus and pubic symphysis.

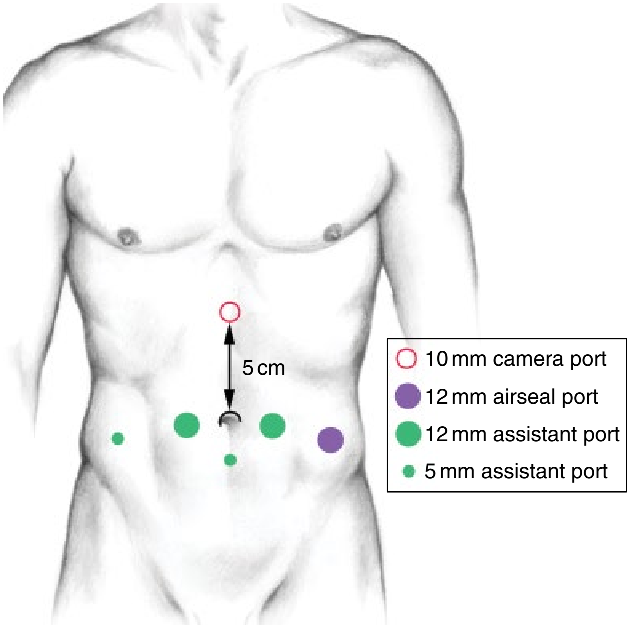
5 cm
○ 10 mm camera port
● 12 mm airseal port
● 12 mm assistant port
● 5 mm assistant port

**Figure 99.2** Laparoscopic port placement for ileal neobladder.

## Procedure

Different options are available for minimally invasive continent urinary diversion, including ONB, continent cutaneous urinary diversion, and, if no other option is available, a cutaneous ureterostomy. Various techniques for robot-assisted ONB have been described and may be performed based on surgeon preference. Different types of ONB have been reported. Initial neobladder types constructed in a hybrid procedure included the W-pouch and T-pouch [5]. Neobladder types that have been routinely constructed completely intracorporeally include the Studer pouch [9, 10], W-pouch [15], U-pouch [8], and pyramid neobladder [14]. The most popular type constructed intracorporeally is the Studer neobladder.

### Hybrid technique of neobladder construction

In this technique, the neobladder is constructed outside the abdomen, placed back in the abdomen, the incision is closed, and anastomoses between the neobladder and ureters and urethra are performed robotically. Before undocking the robot for extracorporeal neobladder construction, certain steps are conducted to aid with robotic intracorporeal anastomoses. Vicryl or barbed suture is placed at the 3, 6, and 9 o'clock positions of the urethra. The ureters are clipped and tagged with dyed and undyed suture to help distinguish each. A silk suture or vessels loop is used to mark the distal end of the segment of ileum to be selected for neobladder formation at a point 15 cm from the ileocecal junction. The left ureter is then transposed to the right side under the sigmoid mesentery. A 20 Fr Foley catheter is inserted in the urethra. Specimens and anchoring sutures are secured to the abdominal wall with Hem-o-lok® (Weck Closure Systems, Research Triangle Park, NC, USA) clips or to a grasper at the medial-most port site to facilitate easy retrieval and identification after the midline incision is made. The robot is then undocked, and a 5–6 cm incision is extended from the inferior aspect of the midline camera port. The surgical specimen is removed and the ureters are oriented appropriately using the suture markings. The terminal ileum is identified and the neobladder is constructed.

For the uretero-neobladder anastomosis, ureteral positioning is confirmed within the pelvis prior to anastomosis. The anastomosis can be completed with the Bricker technique with 5-0 Monocryl suture or 4-0 Vicryl suture if braided suture is preferred.

Several options are available for the urethral-neobladder anastomosis. In one technique, the posterior anastomosis is carried out using the 3, 6, and 9 o'clock urethral sutures. The anastomosis is then continued to the anterior midline in a running fashion. Another technique for intracorporeal robot-assisted anastomosis involves a hemi-circumferential anastomosis. In the clockwise direction, the suture needle is passed outside-in at the 5 o'clock position on the neck of the neobladder, then inside-out on the urethra up to 11 o'clock position. A second suture is started outside-in on the urethra and then inside-out on the neobladder at the 7 o'clock position. The anastomosis continues until complete in the counterclockwise direction.

The uretero-neobladder anastomosis can also be performed extracorporeally.

### Pure intracorporeal ileal studer neobladder (see Video 99.1)

Ileum is generally preferred for construction of the neobladder, though sigmoid colon may also be utilized if use of ileum is contraindicated.

### Bowel isolation

A 60 cm segment of distal ileum is selected, starting 15 cm proximal to the ileocecal junction. The segment is identified and then marked. Two red vessel loops are placed through the mesentery to mark the distal end of the selected bowel segment, and two blue vessel loops are placed in the mesentery to mark the proximal end of the segment. Use of vessel loops in the mesentery assists with bowel manipulation. Bowel is measured using a sterile flexible tape measure, premeasured silk suture, or a premeasured open-ended ureteral catheter. Cadiere forceps are used on the right and fenestrated bipolar forceps on the left for manipulation of the bowel.

Mesenteric angiography can be obtained by using the Firefly visualization system (Novadaq Technologies, Mississauga, Ontario, Canada) with the robot after administration of 2–5 ml of 2.5 mg/ml unconjugated indanocyanine green [22]. This step helps to preserve the blood supply to the neobladder and precludes the need for intracorporeal backlighting of the mesentery, which can be awkward. The distal end of the selected ileal segment is transected with a 60 mm laparoscopic stapler via the 12 mm left assistant port and a blue stapler load (3.5 mm thickness). The distal mesenteric window is opened further using white vascular stapler loads. This step is important, as it facilitates mobilization of the reservoir into the pelvis. Vessel loops help with manipulation of the bowel. The transected distal bowel segment is marked with a red vessel loop in the mesentery and a purple-dyed 3-0 Vicryl suture. The ileal segment is marked at the 25 cm point with undyed suture to mark the apex of the posterior apical plate of the neobladder. The 50 cm point is marked with undyed suture to designate the beginning of the afferent limb. The proximal end of the ileum is transected, and another purple-dyed 3-0 Vicryl suture is placed to mark the proximal end of the isolated ileal segment.

### Ileoileal anastomosis

Importantly, the anastomosis needs to be carried out cephalad to the isolated ileal segment to allow for mobilization of the neobladder into the pelvis. Bowel segments are brought in apposition, and a side-to-side ileoileal anastomosis is carried out using a 60 mm laparoscopic stapler. The stapler load is applied on adjacent antimesenteric bowel walls. Vessel loops are used in this step to place the bowel on traction. The open end of the anastomosed bowel is then closed with the 60 mm laparoscopic stapler by applying a transverse stapler load. Alternatively, an end-to-end ileoileal anastomosis can be made with interrupted 3-0 Vicryl suture.

#### Detubularizing the bowel

The previously placed undyed suture at the 25 cm mark of the isolated bowel segment is grasped by the fourth arm and brought down into the pelvis. The two 25 cm ileal segments are brought adjacent to each other symmetrically. The additional 10 cm of ileum is used as an afferent limb. The distal 50 cm of the excluded ileal segment is then detubularized by making an incision on the antimesenteric side over a 24 Fr red rubber catheter, chest tube, or without an intraluminal tube.

#### Posterior plate of the neobladder

Apposing edges of the posterior wall of the neobladder are approximated with 2-0 absorbable interrupted sutures at 6–8 cm intervals; 6 cm tags are left for bowel manipulation. The posterior wall is then closed with a running suture in a watertight fashion with 2-0 barbed suture. After the posterior plate is completed, a 3-0 barbed suture is placed at midpoint of the right side of posterior plate at the point of the future urethral-neobladder anastomosis.

#### Urethral-neboladder anastomosis

The posterior plate is rotated 90° counterclockwise with caudal traction. The anastomosis is made with the previously placed barbed suture in a running fashion. The posterior section of the anastomosis is carried out over a 24 Fr hematuria catheter. The anterior portion of the anastomosis is completed with interrupted sutures or continuing to run the posterior sutures.

Maneuvering the ileum into the pelvis for the urethral-neobladder anastomosis can be challenging. Tricks that may help include using a Penrose drain inserted in the ileal mesentery as a handle to provide traction via the fourth robotic arm in the direction of the urethral stump. The seromuscular layer of the neobladder may be sutured to the rectourethralis muscle with a barbed suture to keep the urethra in close proximity to the neobladder neck. Releasing the peritoneum over the mesentery of the neobladder, stapling the proximal region of the mesentery of the neobladder without compromising the blood supply, and dissecting around the ileum around the ileocecal junction may also help.

#### Uretero-neobladder anastomosis

The distal ends of the ureters are spatulated. Each ureter is anastomosed to the afferent limb of the neobladder using the Bricker technique with 5-0 Monocryl suture in an interrupted or running fashion. A Vicryl stitch may be used to bolster the anastomosis and maintain orientation.

Prior to completing the uretero-neobladder anastomosis, each ureter is intubated with a 6 Fr 30 cm double-J (JJ) ureteral stent which can be inserted through one of the previously placed assistant ports or through a 2 mm port in the right iliac fossa. The stents are to be completely internalized. The additional length of the stents helps with cystoscopic retrieval.

Alternatively, a Wallace technique can be used for the uretero-neobladder anastomosis. The medial wall of the spatulated ureters are sewn together before this is anastomosed to the afferent limb of the neobladder in an end-to-side manner.

#### Closing the neobladder

The posterior plate of the neobladder is cross-folded on itself and the midpoint is fixed with a horizontal mattress stitch. The anterior wall of neobladder is closed with a running 2-0 barbed suture. A suprapubic tube, which is optional, can be placed through a small opening along this suture line. Suprapubic tube placement through the anterior neobladder wall helps with fixing the neobladder to the anterior abdominal wall, which can facilitate future percutaneous procedures if indicated. The neobladder is then irrigated by transurethral Foley catheter to ensure there is a watertight closure. Leaks are closed with 2-0 Vicryl suture. The surgical specimen is extracted through an opening in the vagina in women or through an extended incision at the midline camera port site in men. A closed-system suction drain is then placed in the abdomen via a lateral port site.

#### Abdominal wall closure

Any port site 10 mm or greater is closed with 1-0 Vicryl suture at the fascia. Fascia at the specimen extraction site is closed with figure-of-eight polydioxanone (PDS), and Scarpa's fascia is closed with running Vicryl suture. The skin is closed with subcuticular 4-0 Monocryl suture, and Dermabond (Ethicon, Cincinatti, OH, USA) or a sterile surgical dressing is applied.

There are different variations to intracorporeal neobladder construction. Wiklund et al. complete the urethral-neobladder anastomosis at the beginning of the procedure after isolation of an ileal bowel segment [9]. The proximal anterior portion of the neobladder is left open after closing the anterior portion of the neobladder, and the ureteral-neobladder anastomosis is performed with a Wallace technique.

Gill and colleagues have improved operative times in intracorporeal neobladder creation and have detailed modifications to the University of Southern California (USC) protocol [23]. In this update, 60 cm of ileum is used for construction of the neobladder, 44 cm is utilized for the reservoir, and the remaining 16 cm is used for the afferent limb. A 5 cm segment of bowel proximal to the afferent limb is discarded. This step may help prevent neobladder–enteric fistula by providing more separation between the neobladder and bowel anastomosis. Bowel measurement starts with identification of the most dependent loop of terminal ileum. This region, which is to become the site of the future urethral-neobladder anastomosis, is marked with a suture. A premeasured 11 cm suture is utilized to measure out the ileum from this marking. All markings on the urinary diversion are performed with undyed suture, and all markings of the bowel ends of the future ileoileal anastomosis are made with blue suture. Color coordination of sutures markings helps avoid any confusion and errors in the bowel anastomosis resulting from a limited field of vision. Prior to performing the urethral-neobladder anastomosis, the previously placed suture on the ileal side of the future urethral-neobladder anastomosis is sutured posterior to the urethra at the cut edge of Denonvilliers' fascia to reduce tension at the urethral-neobladder anastomosis. The urethral-neobladder anastomosis is carried out in a running fashion with a double-armed 3-0 Monocryl suture on an RB-1 needle starting at the 6 o'clock position. Alternatively, a 3-0 barbed suture can be used if there is minimal tension on the anastomosis.

## Robot-assisted continent cutaneous urinary diversion

Continent cutaneous urinary diversion is another option for patients who may not be candidates for ONB and was recently described [18].

### Patient positioning and port placement

The robot is undocked after RARC, and the patient is placed in a modified lateral position. Three additional ports are placed in addition to those previously described for RARC (Figure 99.3).

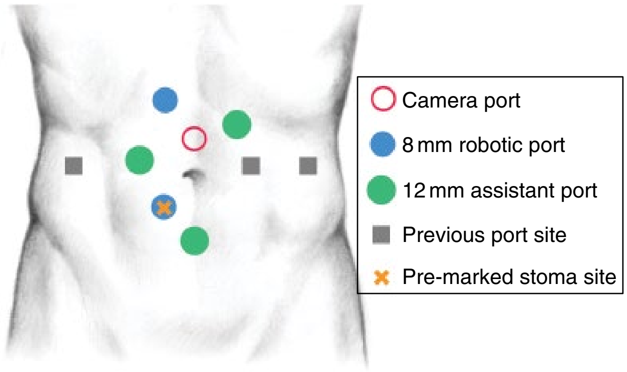

Figure 99.3 Port placement for side-docking for continent cutaneous urinary diversion.

### Bowel isolation

The robot is then brought over the patient's right side. Cecum and ascending colon are mobilized. The colon is mobilized beyond the hepatic flexure to the midtransverse colon, and a 30 cm segment of ascending colon is measured. Bowel is manipulated using double-fenestrated bowel graspers. A laparoscopic stapler is introduced via the midline 12 mm assistant port and is used to transect the large bowel. A 10 cm section of small bowel is measured from the ileocecal valve, and small bowel is divided using the left upper quadrant assistant port.

### Ileocolonic anastomosis

A side-to-side ileocolonic anastomosis is performed with two stapler loads. The anastomosis is made by first inserting the stapler through the right lateral assistant port and applying the stapler load to connect the small bowel to the colon. The open end is then closed with a stapler load applied transverse to the first staple line after reinsertion of the stapler through the midline assistant port. Vicryl suture is used to reinforce the anastomosis.

### Detubularizing the bowel

The stapled end of the isolated bowel segment is removed. Colon is detubularized along the entire antimesenteric side of the colon, starting from the previously stapled end.

### Ureterocolonic anastomosis

The left ureter is transposed under the sigmoid mesentery to the right side. A 1 cm hiatus is made for each ureter on the posterior side of the pouch. Ureters are passed from outside the pouch to in, and a Bricker anastomosis is carried out with two 4-0 Vicryl sutures.

A 2 mm port is used for percutaneous stent placement. Two 7 Fr single-J ureteral stents are utilized.

### Closing the pouch

The open end of the pouch is folded over and approximated at the midline with 2-0 Vicryl suture. Appendectomy is performed, creating a cecostomy. Stents are externalized through the cecostomy. The pouch is then closed in a running fashion with barbed absorbable suture. A suprapubic tube is then passed through the cecostomy alongside the stents, and suprapubic tube and ureteral stents are secured within using a purse-string suture. The pouch is irrigated through the suprapubic tube to ensure a watertight closure.

### Tapering of the efferent limb

The robot is undocked and surgical specimen extracted through an extended incision at the camera port site. Through the extraction site, the ileal efferent limb is tapered over a 14 Fr catheter using a surgical stapler. Interrupted 2-0 silk sutures are used to reinforce the ileocecal valve over the catheter. The efferent limb is brought out through stoma site, and the end is matured and sutured to the skin. Stents and suprapubic tube are externalized via the right-sided assistant port. A surgical drain is placed through the right robotic assistant port

### Robot-assisted ureterosigmoidostomy

Robot-assisted ureterosigmoidostomy may be considered if other forms of diversion are contraindicated. Ureterosigmoidostomy should be a last resort, as severe electrolyte disorders, urinary tract infections, and significantly increased risk of colon cancer are common postoperative issues.

### Laparoscopic continent urinary diversion

Gill and colleagues were the first to report on the laparoscopic technique [3]. Similar steps are used in performing the laparoscopic procedure. However, modifications in steps are required due to different equipment and port placement and the ergonomic limitations encountered with laparoscopic tools. Several steps can be adapted from robot-assisted surgery to make the procedure more versatile.

## Postoperative management

The postoperative management of patients undergoing minimally invasive continent urinary diversion is similar to that for open surgery. Early mobilization is vital to prevent deep venous thrombosis, pneumonia, and patient debility. Patients are encouraged to ambulate the day of surgery, and are at least to stand at bedside in the first 24 hours. Heparin or Lovenox and sequential compression devices are continued postoperatively for deep venous thrombosis prophylaxis. A modified enhanced recovery after surgery (ERAS) protocol is used for advancing the diet. Alvimopan may be utilized. The nasogastric tube is discontinued immediately after surgery. A Cochrane meta-analysis showed no benefit to leaving a nasogastric tube in place after abdominal surgery [24]. For pain control, reduced use of narcotic medication is encouraged. Xu and colleagues showed significantly reduced occurrence of postoperative ileus and length of hospital stay with use of an ERAS pain management protocol [25]. The protocol calls for nonopioid analgesics including IV acetaminophen being given intraoperatively. Oral acetaminophen, ketorolac, and continuous subfacial infusion of local anesthetic are used postoperatively with narcotic medication for breakthrough pain only. Ileal neobladders are irrigated gently every 8 hours to prevent mucus build-up clogging catheters. The surgical drain is removed on the second postoperative day or when output is low.

Patients are instructed on catheter irrigation prior to discharge. A pouchogram is performed at the time of stent removal four weeks after surgery. If no leak is present, ureteral stents are removed via cystoscopy and the suprapubic tube is removed. The urethral catheter is removed 2–3 days later.

Fluid and electrolyte problems are common after neobladder construction. Hypochloremic metabolic acidosis and hypovolemia are frequently encountered. Goal fluid intake is 2–3 liters of fluid a day. A high-salt diet is needed to replenish sodium losses. Sodium bicarbonate may be prescribed if significant metabolic acidosis occurs. Acid–base and electrolyte disturbances are usually more pronounced with colon reconstruction.

Regimented voiding is important following neobladder formation. Patients are instructed to void every 2–3 hours. Voiding frequency is gradually increased to every 4–5 hours to facilitate an increase in neobladder capacity. Goal neobladder volume is 500 ml. If the patient does not void as frequently as instructed, the neobladder may become overdistended, and a poorly emptying bladder may result. If patients are not able to void or if high post-void residuals are present, clear intermittent catheterization needs to be conducted.

## Outcomes

Multiple series have been published on single and multi-institution experience with RARC with ONB (Table 99.1). Desai and colleagues reported on 132 patients with RARC and ONB at two institutions in the largest series [13]. They found that 47% of patients had a 30-day complication and that 27% of patients had a 30- to 90-day complication; 15.2% of 30-day complications were Clavien-Dindo grade III and higher, and 12.9% of 30- to 90-day complications were grade III and higher. Infectious complications were most common, with sepsis being the most common early complication and urinary tract infection being the most common late complication. Four patients had conversion to an open procedure and were not included in the study. Urine leak was reported in 4.5% of patients, and 7% of patients had a gastrointestinal complication, which included four patients with ileus, two with bowel leak, and two with a neobladder–enteric fistula. The long-term complication rate was low: 2% had reservoir stones, 3.8% of patients had an ureteroileal anastomotic stricture, and less than 1% of patients had a neobladder–vaginal fistula. Mean operative time was 456 minutes. Operative time, hospital

**Table 99.1** Series of robot-assisted radical cystectomy with intracorporeal orthotopic neobladder.

| Series | Type of ONB | Patients (*n*) | Operative time (min) | EBL (ml) | LOS (days) | Clavien I–II complications | Clavien III–V complications | PSM rate (%) | Continence |
|---|---|---|---|---|---|---|---|---|---|
| Pruthi et al. 2010 [8] | U-pouch | 3 | 330 | 221 | 5 | – | – | – | – |
| *Jonsson et al. 2011 [9] | Studer | 36 | 480 | 625 | 9 | 36% | 36% | – | 96% daytime continence |
| *Goh et al. 2012 [10] | Studer | 8 | 450 | 225 | 8 | 63% | 38% | 0% | 75% daytime continence |
| Canda et al. 2012 [11] | Studer | 27 | 594 | 429 | 10.5 | 48% | 26% | 3.7% | 65% daytime continence; 17.6% nighttime continence |
| *Collins et al. 2014 [12] | Studer | 80 | 420 | 475 | 9 | 48% | 46% | 1% | 87% Daytime continence; 80% night time continence |
| *Desai et al. 2014 [13] | Studer | 132 | 456 | 430 | 11 | 46% | 29% | 0.8% | 84% complete daytime and nighttime continence |
| Tan et al. 2015 [14] | Pyramid | 20 | 330 | 250 | 10 | 14 complications | 19 complications | – | 95% daytime continence; 70% nighttime continence |
| Butt et al. 2015 [15] | W-pouch | 4 | 522 | 237 | 12.8 | 3 complications | 1 complication | 0% | 75% nighttime continence |
| Schwentner et al. 2015 [16] | Studer | 62 | 477 | 385 | 16.7 | 24% | 26% | 6.4% | 88% overall |

*Study may include overlapping data.

ONB, orthotopic neobladder; EBL, estimated blood loss; LOS, length of stay; PSM, positive surgical margins.

*Source:* Modified from a contemporary review of RARC with intracorporeal ONB [26].

stay, and estimated blood loss improved with surgeon experience.

Complications associated with robot-assisted ONB are similar in nature and frequency to those experienced with the open procedure. Hautmann and colleagues published on 1013 patients undergoing open neobladder creation after radical cystectomy and pelvic lymph node dissection [27]. They reported that 58% of patients experienced at least one complication within 90 days of surgery. Infectious complications were the most common, and 24% of the complications were classified as infectious and 15% were gastrointestinal; 22% of patients experienced a Clavien III–V complication. Notably, 57% of complications were specific to urinary diversion.

The benefits of RARC over open radical cystectomy are not completely defined. In a retrospective review of 100 patients undergoing RARC versus 100 patients undergoing open radical cystectomy from 2006 to 2010, patients in the RARC group had comparable oncologic outcomes with significantly fewer overall and major complications, less estimated blood loss and transfusions, and shorter hospital stay [28]. Mean operative time was approximately 1 hour longer with RARC. Other studies have shown less favorable results for RARC. RARC with extracorporeal urinary diversion was compared to open radical cystectomy in a randomized controlled trial [29]. The RARC group had significantly less intraoperative blood loss but longer operative times. Length of hospital stay and rate of complications were similar. A cost-analysis showed that RARC was more expensive.

The full benefits of minimally invasive surgery may not be realized with an extracorporeal diversion. Potential advantages to a completely intracorporeal procedure were elucidated by the comparison of outcomes of intracorporeal diversion to extracorporeal diversion in patients undergoing RARC in a database by the IRCC [19]. Operative times were similar. Gastrointestinal complications, blood loss, and readmission rate were significantly lower in the intracorporeal group.

There are limited data on health-related quality of life pertaining to intracorporeal urinary diversion. Poch et al. used the Bladder Cancer Index for assessment of bowel, urinary, and sexual domains and the European Organisation for Research and Treatment of Cancer Body Image Scale to measure health-related quality of life outcomes after RARC in 43 patients [30]. In this study, 53% of patients underwent intracorporeal urinary diversion. Five neobladders were created. Patients undergoing intracorporeal diversion had quicker recovery of urinary function than those undergoing extracorporeal diversion. Patients undergoing intracorporeal urinary diversion had lower Body Image Scale (BIS) scores for most postoperative time points, indicating higher patient satisfaction.

Multiple groups have published on functional outcomes after RARC and ONB (see Table 99.1). Daytime continence is excellent while nighttime continence is variable. The majority of patients have good daytime continence. Nighttime continence may be more related to a patient's nighttime voiding habits.

Regarding sexual function, Tyritzis et al. reported on the outcomes of 70 patients who underwent RARC with intracorporeal ONB creation [31]. They reported that 81% of men who underwent a nerve-sparing procedure were potent with or without a phosphodiesterase type 5 (PDE5) inhibitor medication at 12 months following surgery. In the same series, 4 of 6 women evaluated remained sexually active after surgery.

## Keys to success

### Patient positioning

- It is helpful to place the patient in steep Trendelenburg position for performing the RARC and pelvic lymph node dissection.
- Positioning-related injuries can be potentially avoided by placing the patient in a more shallow Tredelenberg position or a supine position and side-docking the robot for creation of the neobladder. The Xi robotic system allows for greater ease with side-docking in the supine position.

### Trocar placement

- All ports are placed at least 2 cm cephalad to the level of the umbilicus.
- The camera port is placed 5 cm cephalad to the umbilicus.
- The robotic fourth arm is placed on the right side.
- Assistant ports are placed on the left side to facilitate stapling bowel and paramedian to aid with suctioning and stapling across the pedicles.

### Bowel isolation

- A premeasured suture can help with measuring out segments of bowel.
- Color-code markings of the bowel (*b*lue for *b*owel segments for future enteric anastomosis and *u*ndyed for *u*rinary conduit) to minimize confusion.
- Vessel loops can be used as markers and handles on the mesentery to reduce direct manipulation of the bowel.
- An indocyanine green arteriogram can be used to delineate bowel vasculature.

### Detubularizing the bowel

- It is helpful to incise bowel over a 24 Fr lubricated chest tube to prevent injury to the posterior bowel wall.

### Posterior plate of the neobladder

- The fourth arm is used to hold traction on the apical stay suture.
- The bowel should be sutured every 15–20 cm with stay sutures for bowel alignment.
- Barbed suture is used for the posterior plate of the neobladder.

### Urethral-neobladder anastomosis

- A Penrose drain can be inserted into the ileal mesentery, and is used as a handle by the fourth robotic arm to provide traction in the direction of the urethral stump.
- The seromuscular layer of the neobladder may be sutured to the rectourethralis muscle with a barbed suture to keep the urethra in close proximity to the neobladder neck for the urethral-neobladder anastomosis.
- A 0° lens is used for the urethral-neobladder anastomosis.

### Uretero-neobladder anastomosis

- A 7.5 cm long suture on a cutting needle is used in a continuous manner.
- Use of 30 cm long ureteral stents aids with their cystoscopic stent removal.

### Closing the neobladder

- Fifty milliliters of sterile saline is injected into the neobladder under direct vision to check for leaks.

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# 100

# Laparoscopic Radical Prostatectomy

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## Introduction

In the United States more than 70% of radical prostatectomies are robot assisted using the da Vinci device. In Europe, there is skepticism concerning the spread of robotic systems, based on unfavorable experiences in orthopedics and cost pressures [1]. In Germany and Italy, 25% of radical prostatectomies are performed by laparoscopy. The advantages of this approach include reduced access trauma, less pain and bleeding, and lower transfusion rates [2, 3]. Furthermore, all robot-assisted techniques are based on laparoscopy.

## Historical background

In 1992, Schuessler et al. attempted the first laparoscopic radical prostatectomy (LRP) [4]. However, his technique did not provide any advantages over retropubic radical prostatectomy (RRP) [5]. In 1995, Raboy et al. published a case of extraperitoneal LRP [6]. Richard Gaston (personal communication, 1998) pioneered LRP in 1997, followed by Guillonneau, Vallancien, and Abbou, who popularized the transabdominal access to seminal vesicles [7–10]. In 1999, Rassweiler et al. developed a retrograde technique similar to RRP [11, 12]. In the following years, several groups revisited the French technique [13–16], and in 2000, Bollens et al. revisited the extraperitoneal approach [17].

In 2002, a survey in Germany and Switzerland revealed that 15% of departments performed LRP, but that only 5% did more than 15 cases per year [18]. In 2004, 19.2% of German departments were offering LRP [19]. In 2005, a multicenter study including 5800 patients treated by 50 surgeons was published [20]. In the United States, Gill and colleagues was one of the few groups establishing a program of laparoscopic pelvic surgery [21]. Menon et al. initiated the change when hiring Vallancien and Guillonneau to establish LRP at his institution [22]. Perhaps more importantly, he invested in the da Vinci system and managed to perfect robot-assisted laparoscopic prostatectomy (RALP).

Although RALP has led to a significant decrease in the use of classical LRP within the last decade, particularly in the United States, in Europe, about 25% of all prostatectomies are performed laparoscopically, 35% robot assisted, and 40% still by open technique [23, 24]. Moreover, recent technical improvements including 3D high-definition (HD) or even ultra-HD video-technology, the use of an ergonomic chair, and instruments providing six degrees of freedom have significantly reduced the ergonomic difficulties of the procedure [25–27]. Accordingly, LRP has yielded excellent oncologic outcomes, even in advanced stages [28, 29]. There is still a continuous role for LRP [24, 30] since no study has yet proven any substantial inferiority in oncologic and functional results.

## Indications and contraindications

Indications include men with localized prostate carcinoma and a life expectancy greater than 10 years [30]. All patients with stage less than T3, Gleason score less than 8, and prostate specific antigen (PSA) less than 10 ng/ml are candidates for nerve preservation. Those with suspected extracapsular invasion (T3) or perineural invasion in core biopsies should not undergo nerve-sparing surgery (Table 100.1).

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 100.1** Criteria for nerve sparing.

| Clinical stage | |
|---|---|
| T1 | When PSA is relatively low and the number of positive biopsies or the extent of biopsy involvement is limited |
| T2a | A contralateral nerve-sparing procedure can be proposed |
| T2b | A nerve-sparing attempt can result in positive surgical margins and give rise to local failure |

PSA, prostate specific antigen.

Previous transurethral resection of the prostate, abdominal or pelvic surgery, laparoscopic hernia repair, pelvic irradiation, and gross obesity can add to surgery complexity, and such patients should be approached only after considerable experience [28, 31, 32]. Absolute contraindications are abdominal wall infection, generalized peritonitis, bowel obstruction, and uncorrected coagulopathy.

## Anatomy of the prostate

Despite early descriptions by Walsh et al. and a recent consensus paper by Walz et al. [33–35], there is still no consensus on the nomenclature of all described anatomical structures. Therefore recently, the European Association of Urology (EAU) Section of Uro-Technology (ESUT) proposed a uniform nomenclature [36].

### Different types of nomenclature and terminology

In general terms, descriptions/nomenclatures are either surgical, anatomical, or eponymical, but some authors use different terminologies (Table 100.2). The anatomical description is defined according to the Federative Committee on Anatomical Terminology's *Terminologia Anatomia, International Anatomical Terminology* published in 1998 [37]. Usually, surgeons describe their technique based on the "surgical terminology," using

**Table 100.2** Summary of existing anatomical descriptions of relevant anatomy during radical prostatectomy.

| Anatomical structure (surgical nomenclature) | Anatomical description (anatomical nomenclature) | Eponymical description | Other description(s) |
|---|---|---|---|
| Pelvic fascia | Fascia pelvis parietalis | Endopelvic fascia | – |
| Levator fascia | Fascia levatoris | Outer layer of Walsh's lateral pelvic fascia | Periprostatic fascia<br>Parapelvic fascia |
| Prostatic fascia | Fascia prostatica | Inner layer of Walsh's lateral pelvic fascia | |
| Posterior prostate visceral fascia | Septum rectovesicale | Denonvillers' fascia | Prostato-seminal vesicular fascia<br>Posterior prostatic and seminal vesicle fascia |
| Vesico-prostatic muscle | Musculus vesico-prostaticus | | Anterior layer of Denonvillers' fascia<br>Posterior longitudinal fascia |
| Rectal fascia | Fascia propria rectalis | Outer leaf/posterior layer of Denonvillers' fascia | |
| Dorsal vein plexus | Plexus venosus dorsalis penis | Santorini's plexus | Dorsal vascular complex |
| Puboprostatic ligaments | Ligamenta puboprostatica | | Pubovesical ligaments |
| Anterior prostate visceral fascia | Visceral endopelvic fascia | | Anterior periprostatic fascia (covering detrusor apron and McNeal's anterior fibromuscular stroma) |
| Fascial tendinous arch of plevis | Arcus tendineus fasciae pelvis | | Puboprostatic collar (plus puboprostatic ligaments) |
| Puboperineal portion of levator ani | Musculus levator urethrae (hiatus urogenitalis) | Quick stop muscle of Gosling | Puboperinealis muscle |
| Rhabdo-sphincter of urethra | Sphincter urethrae externus | | Striated urethral sphincter |
| Lisso-sphincter of urethra | Sphincter urethra internus | | Intrinsic sphincter |
| Ischioprostatic ligaments | | Walsh's pillars | |
| Posterior raphe | Musculus anoperinealis | | Rectourethralis muscle |

Modified from Rassweiler et al. [36].

terms translated from Latin. One example would be the term “endopelvic fascia” instead of “fascia pelvis parietalis.” Eponymical descriptions are based on the name of the first surgeon or anatomist publishing an article on the relevant anatomical structure, such as the “plexus Santorini” or “Denonvilliers’ fascia” [38, 39]. In addition to this, some authors use different terms to describe important structures, such as the “paraprostatic or periprostatic fascia” instead of “levator fascia” or “fascia levatoris ani” [40].

## Periprostatic fascial anatomy

Walsh et al. described three layers covering the anterolateral surface of the prostate [33, 34]: the prostatic fascia overlaying the prostatic capsule and levator fascia (fascia diaphragmatica pelvis superior). Both fasciae fuse laterally to form the lateral pelvic fascia covered by the endopelvic fascia (fascia pelvis parietalis) reflecting off the transversalis fascia (Figure 100.1). This area is also described as the tendinous arch of the pelvis. Posteriorly, there are two layers: Denonvilliers’ fascia (prostatoseminal-vesicular fascia; septum retrovesicale) and the prostatic capsule. The neurovascular bundles run along the posterolateral part of the prostate between levator and prostatic fascia and contain branches from the inferior vesical arteries running medial to cavernosal nerve branches originating from the pelvic plexus. These vessels enter the capsule through the prostatic fascia. Some authors describe the levator fascia also as the periprostatic or parapelvic fascia [40].

## Course and branches of pudendal nerve

For preservation of continence, the course of intrapelvic branches of the pudendal nerve is more relevant than the course of neurovascular bundless [41]. N. pudendus has three branches: (i) nervi rectales inferiors, (ii) nervi perinealis, and (iii) nervus dorsalis penis. The perineal rami support the penile muscles (m. bulbospongiosus, m. ischiorectalis, m. ischiocavernosus) and the striated urethral sphincter. Lesions of perineal branches lead to incontinence. A., V. and N. pudendus enter the small pelvis through the foramen ischiadicus minus, then follow the canalis pudendalis (Alcock’s canal). Finally the nerve divides medially into its three branches. The perineal rami supporting the striated urethral sphincter run underneath the levator fascia (fascia diaphragmatica pelvis superior).

## Anatomy of urethral sphincter apparatus and the bladder neck

The urethral sphincter apparatus consists of the horseshoe-shaped rhabdosphincter and smooth-muscle longitudinal and circumferential lissosphincters [35]. In addition, the prostate is connected laterally to the urethra by thickened

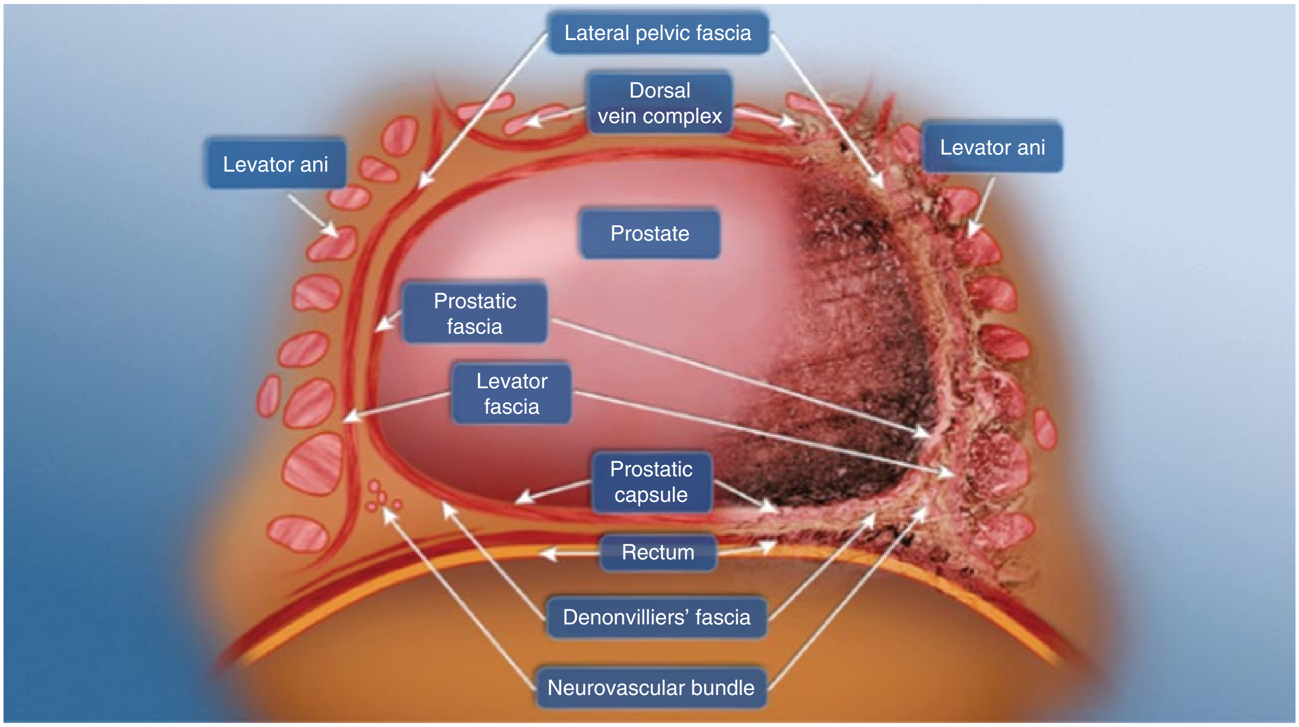


**Figure 100.1** Anatomical basis of the prostate: fascial anatomy of the prostate according to Walsh et al. [33].

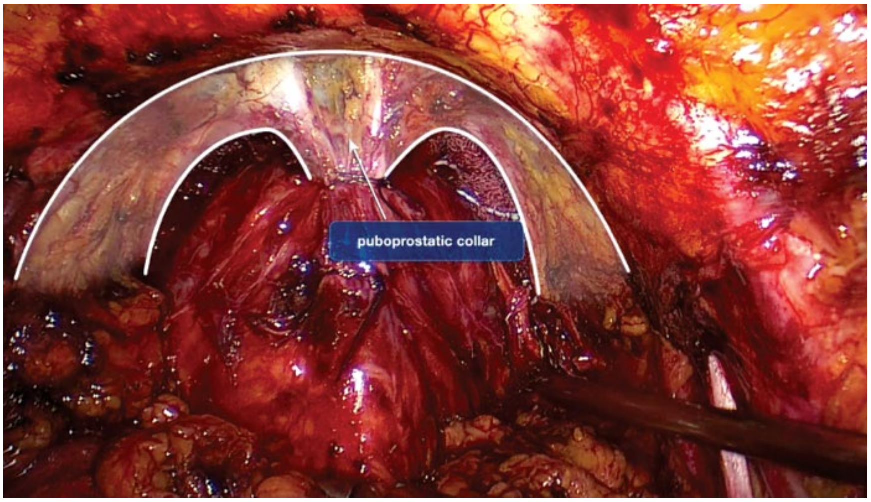


**Figure 100.2** Concept of preservation of puboprostatic collar according to Takaneda et al. [58].

fascial band components (Walsh's pillars, Müller's ischioprostatic ligaments). Anteriorly, puboprostatic (pubovesical) ligaments suspend the urethra. For preservation of the puboprostatic collar it is important to keep this part completely intact (Figure 100.2). Posteriorly, the sphincter apparatus is supported by the median fibrous raphe and rectourethralis muscle. In addition, the striated sphincter is flanked by thickened anteriomedial edges of the anterior levator ani muscle (i.e. urogenital hiatus), forming an incomplete sling behind the urethra. On contraction they forcefully propel the prostate and prostatourethral junction upward and forward, enabling quick cessation of urination.

The precise anatomy of the bladder neck and its effect on continence is still unclear. In the transverse plane, the bladder neck is composed of two different muscles, the ventrolateral and dorsal longitudinal muscles, which are positioned in an oblique direction. When the bladder neck is examined in a truly transverse direction, there is a distinct circular muscle called the musculus sphincter vesicae, possibly representing the rationale for bladder neck preservation [36].

### Neurologic aspects of urinary continence mechanism

Both somatic pudendal nerve and autonomic branches of the pelvic plexus are involved in the urinary continence mechanism. Somatic motor innervation passes from the anterior horn of S2–4 segments and travels to the external sphincter via an intra- and an extrapelvic branch of the pudendal nerve. Additional intrapelvic extrapudendal nerve fibers from S2–3 pass lateral to the pelvic plexus and then continue along the dorsolateral surface of the rectum, until they disappear into the levator ani muscle and terminate in the urethral sphincter [40]. In addition to the efferent autonomic and somatic nerve fibers innervating the sphincteric musculature, intrapelvic afferents from the membranous urethra contribute to urinary continence. Intact afferents lead to a conscious sensation of urine entering the membranous urethra, inducing either a spinal reflex or voluntary contraction of the rhabdosphincter. These afferent fibers run in branches of the pelvic plexus and the intrapelvic branch of the pudendal nerve.

## Operative techniques

Four approaches have been described: (i) transperitoneal descending with initial dissection of the seminal vesicles [8]; (ii) transperitoneal ascending [12]; (iii) extraperitoneal descending [42, 43]; and (iv) extraperitoneal ascending [44].

### Patient positioning and trocar arrangement

The patient lies in lithotomy position. A rectal balloon catheter is inflated with 40–60 ml of air. The operating table is placed in a 15–20° Trendelenburg (Figure 100.3a). A 16 Fr Foley catheter is inserted. Some authors prefer an incline of up to 30–40° [7]. A semi-lunar or W-shaped arrangement of 5 and 10 mm trocars is recommended (Figure 100.3b,c).

### Access to the prostate

Transperitoneal access is accomplished with a Veress needle (maximum pressure 15 mmHg). The peritoneum is incised over both seminal vesicles and the vas deferens are exposed and divided. Thereafter, the space of Retzius is developed by transection of the urachus after filling the bladder with 200 ml of saline.

Extraperitoneal access uses a periumbilical incision followed by extraperitoneal blunt dissection of the space of Retzius (balloon trocar; Figure 100.4). The other

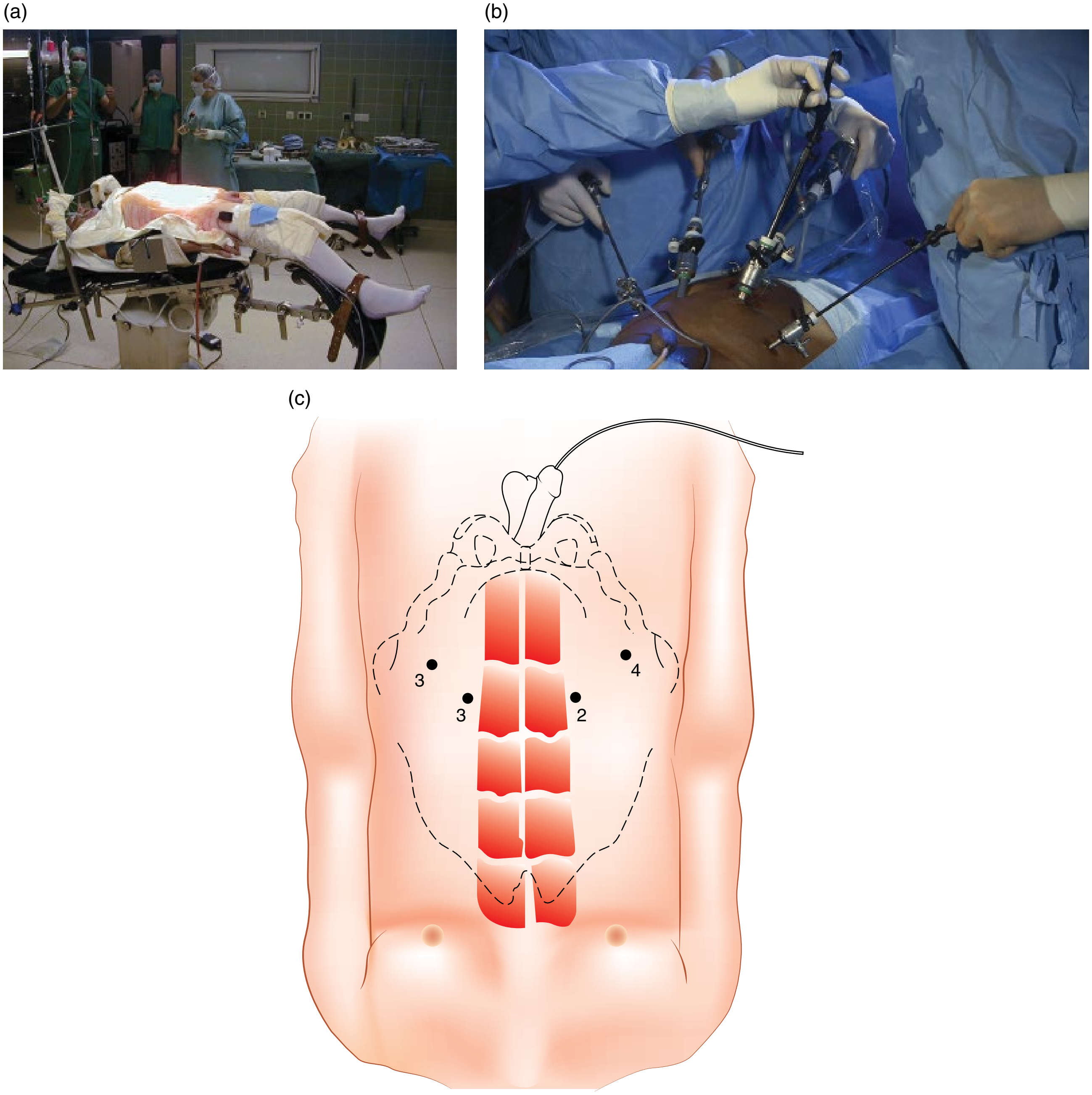


**Figure 100.3** Positioning of the patient and trocar arrangement for laparoscopic radical prostatectomy. (a) Lithotomy position. (b) Classic supine with adducted legs and 15–20° Trendelenburg and W-shape arrangement (Heilbronn technique). (c) Semilunar arrangement according to Ukimura et al. [21].

ports are placed after establishing the pneumo-extraperitoneum (maximum 12 mmHg).

### Extraperitoneal versus transperitoneal approach (Table 100.3)

Transferability of the transperitoneal access was demonstrated [10–14, 45–48]; however, the extraperitoneal descending technique is easier to learn, as reflected in the shorter operating times [20, 31, 42]. Eliminating the transperitoneal dissection of seminal vesicles may shorten operative time by 50 minutes [49]. Comparable surgical results between extraperitoneal and transperitoneal LRP have been published [20, 50–54]; some authors emphasize the advantages of the extraperitoneal approach (i.e. no bowel lesions, ileus, and peritonitis) [44, 49], whereas others found no differences [53, 54].

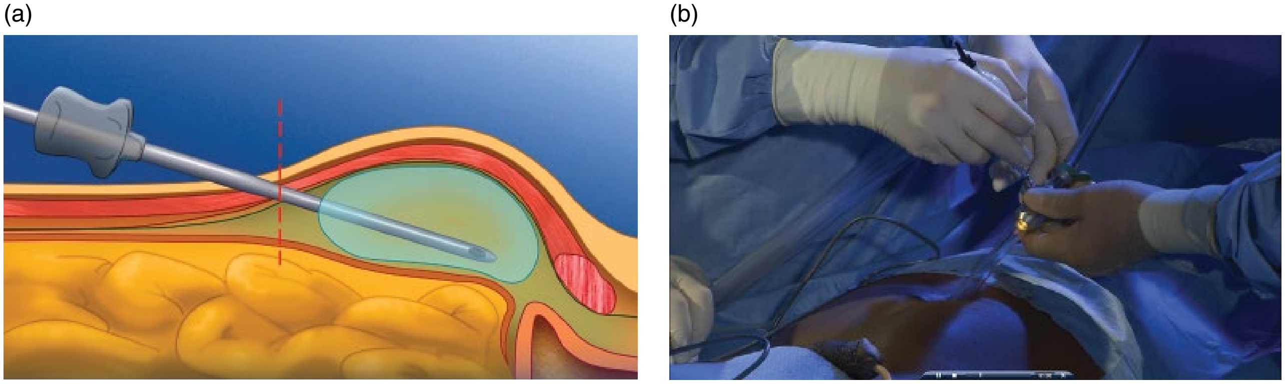


**Figure 100.4** Balloon dissection of the space of Retzius under endoscopic control. (a) Schematic view. (b) Introduction of the telescope via the balloon trocar.

**Table 100.3** Advantage and disadvantage of extraperitoneal versus transperitoneal laparoscopic radical prostatectomy.

| Advantages extraperitoneal | No advantage one technique over the other | Advantages transperitoneal |
|---|---|---|
| No contact with bowel<br>Previous abdominal surgery<br>Fewer problems with urine extravasation<br>Gross obesity<br>Simultaneous inguinal hernia repair | Operating time<br>Morbidity<br>Complication rate<br>Positive surgical margin<br>Continence | Larger room<br>Less tension on anastomosis<br>Minimal risk of lymphocele in case of extended lymph node dissection |

## Routes of dissection

The antegrade technique starts at the bladder neck. The Foley catheter is used as a retractor to expose and cut the posterior wall of the bladder neck (Figure 100.5a). Subsequently, the vesicoprostaticus muscle is divided, exposing the vas deferens and seminal vesicles. Using the vas as a retractor, Denonvilliers' fascia is incised to dissect the posterior surface of the prostate. Proximal pedicles are clipped and divided (Figure 100.5b). Following apical dissection the dorsal vein complex (DVC) is sutured and divided. Finally, the urethra is transected (Figure 100.5c).

The retrograde technique starts at the apex with suturing and dividing of the DVC. Thereafter, the urethra is incised (Figure 100.6a). The Foley catheter is used as a retractor during prostatic posterior dissection (Figure 100.6b). Subsequently, it serves as a retractor to expose the bladder neck, which is incised to reach the vas and seminal vesicles and to control the proximal pedicles (Figure 100.6c).

### Retrograde versus antegrade technique

Although the retrograde technique is more popular in open surgery [45, 55–57], laparoscopic and robotic surgeons favor the antegrade approach [15, 22]. The early control of prostatic pedicles and late division of the DVC ensure minimal bleeding.

## Technical aspects for early continence

Long-term continence exceeds 90% in most laparoscopic and robotic series; however, initially early continence (i.e. at three months) used to be still in the range of 40–50% [3]. Several strategies have been proposed [40, 58–65]:

- preservation/reconstruction of the puboprostatic ligaments;
- suspension of the DVC;
- dissection of a long urethral stump;
- preservation of the bladder neck;
- preservation and reconstruction of the rectourethralis muscle.

Recently, Takenaka et al. [58] introduced the strategy of preservation of the puboprostatic collar. We have added the preservation of the levator fascia to this strategy, yielding excellent short-term continence results.

### Heilbronn technique for early continence (see Videos 100.1 and 100.2)

#### *Conventional technique*

Following lateral incision of the endopelvic fascia, the levator fascia is perforated, creating a dissection plane along the levator ani muscle (Figure 100.7). The levator ("periprostatic") fascia is incised secondarily to perform an interfascial nerve-sparing technique [66–69]. This

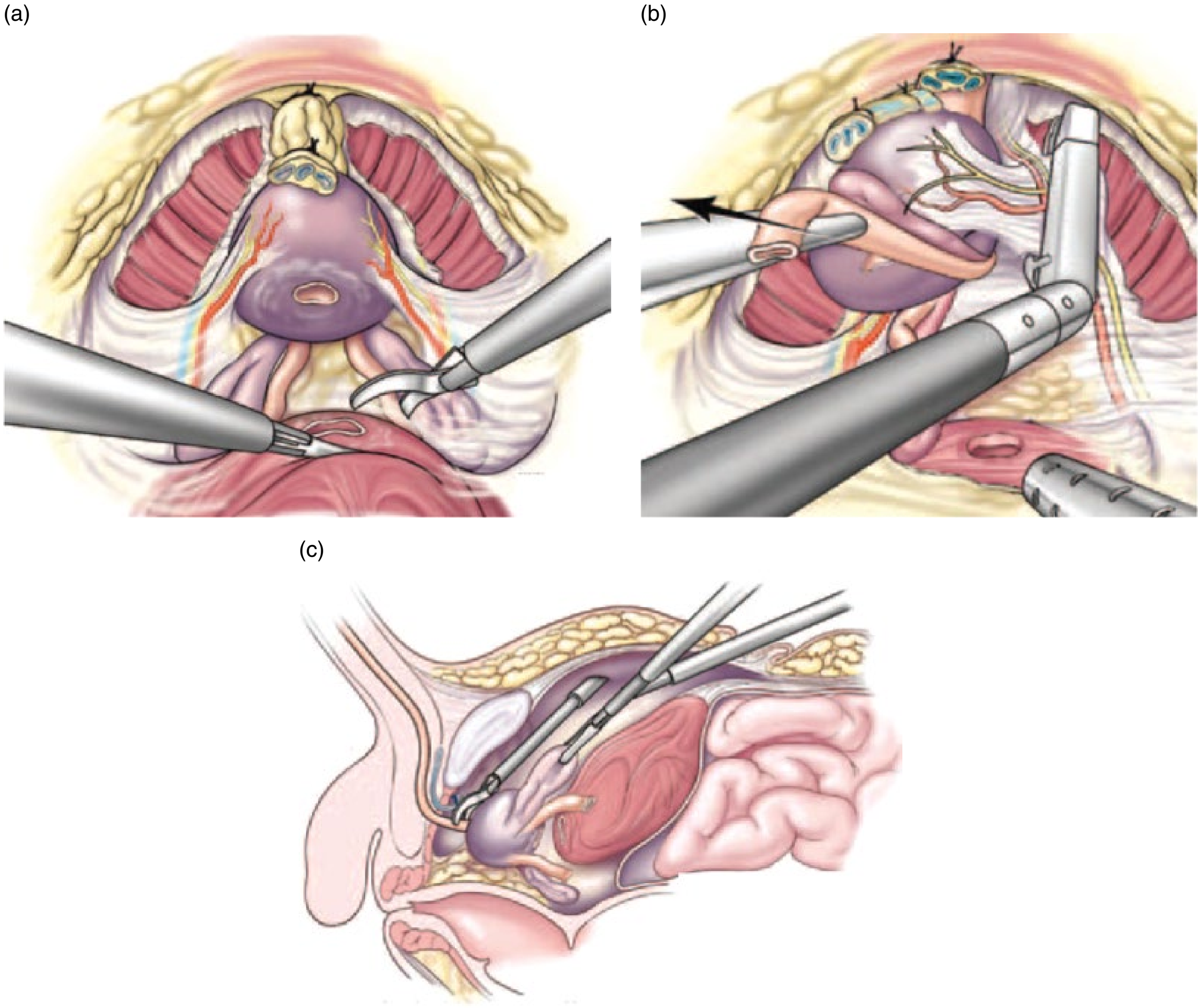


**Figure 100.5** Antegrade technique of laparoscopic radical prostatectomy according to Ukimura et al. [21]. (a) Opening of the bladder neck and dissection of the vas deferens and seminal vesicles. (b) Dissection of the posterior surface and control of prostatic pedicles using the vas deferens as a retractor. (c) Division of the urethra.

approach also includes division of both puboprostatic ligaments and distal ligation of the DVC (Figure 100.8).

#### *Preservation of levator fascia and puboprostatic collar*

Following medial incision of the endopelvic fascia below the puboprostatic ligaments, the avascular plane between the levator and prostatic fascia is developed (Figure 100.7). Thus, the intrapelvic branch of the pudendal nerve remains covered by levator fascia. The DVC is sutured over the mid part of the prostate to preserve the puboprostatic collar. For division of the DVC a 120° endodissector is placed over the prostatovesical junction (Figure 100.8), rotating the prostate towards the urethra, and the anterior striated sphincteric complex is reached. The urethra is transected just distal to the verumontanum, preserving the rectourethralis muscle. Whenever indicated, we perform a bladder neck-sparing technique. After dividing the bladder neck, the prostatovesicle muscle is incised close to the prostate to be used for posterior reconstruction of the anastomosis.

#### Non-nerve-sparing technique

If nerve sparing is contraindicated, the neurovascular bundles are clipped distal to the urethra using 10 mm titanium clips. No Hem-o-lok clips are used to avoid migration into the anastomosis. The proximal pedicles are clipped pararectally to minimize the risk of positive margins.

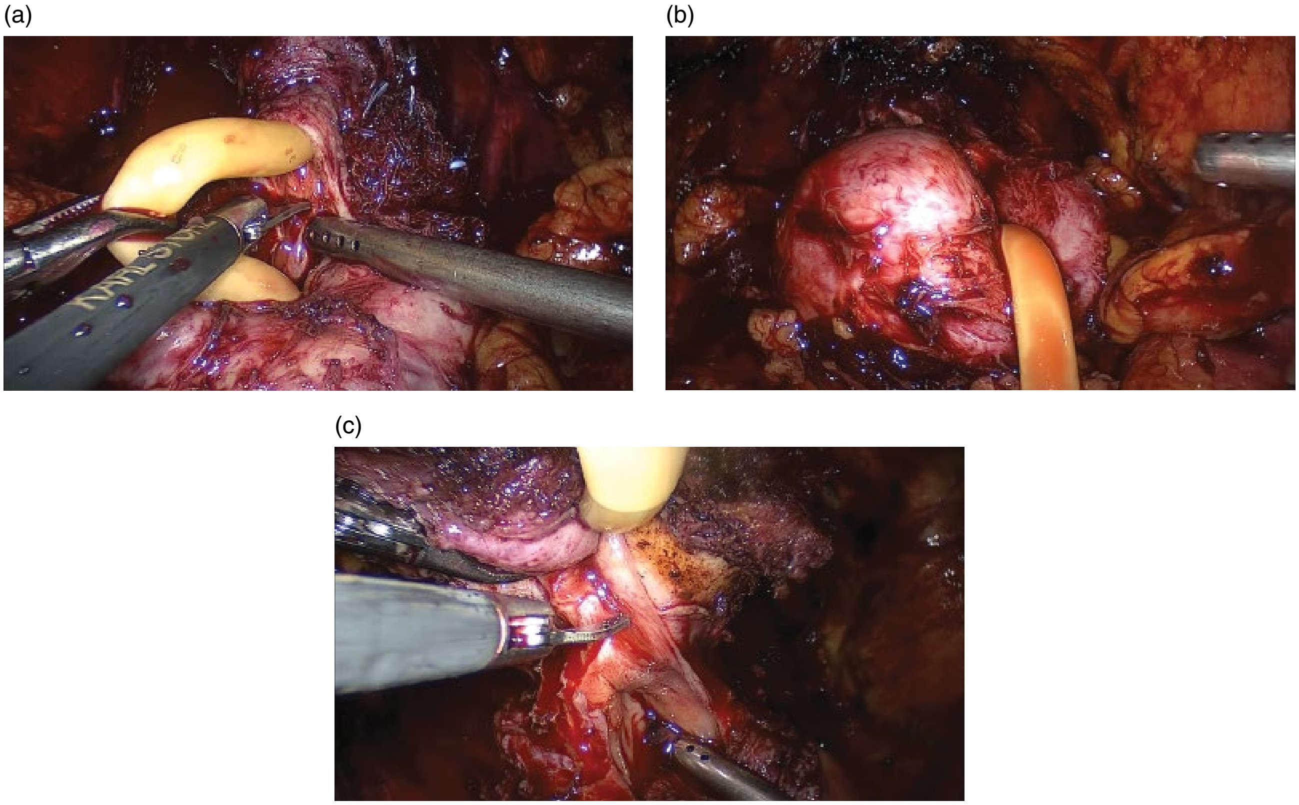
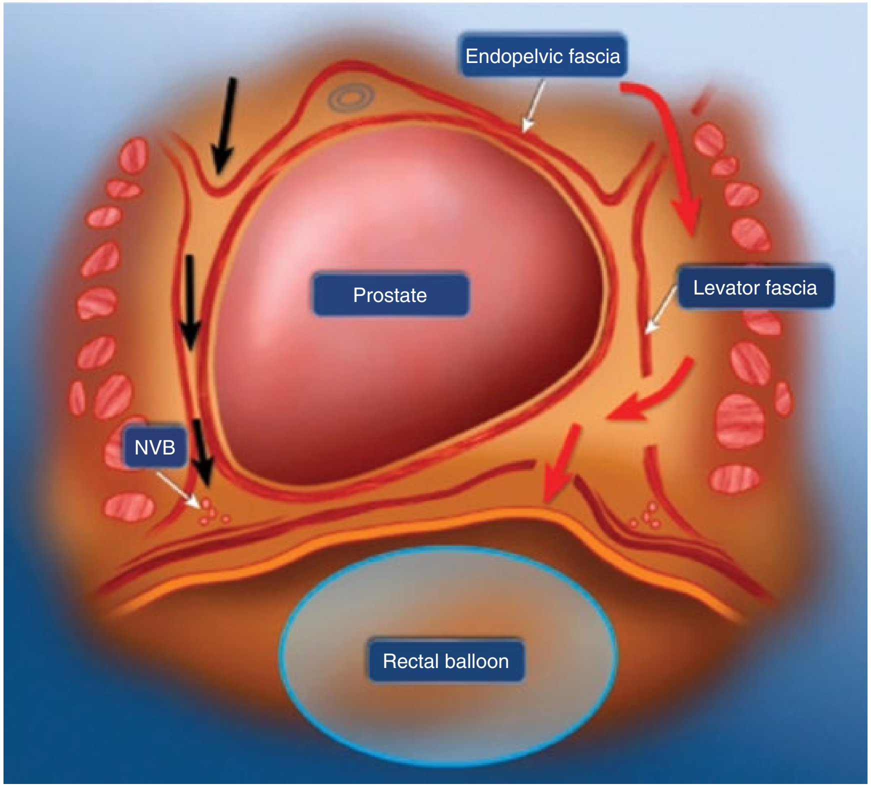


**Figure 100.6** Retrograde technique of laparoscopic radical prostatectomy (Heilbronn technique). (a) Division of the urethra. (b) Posterior dissection using the Foley catheter as a retractor. (c) Bladder neck incision using the loop of the catheter as a retractor.

**Figure 100.7** Incision of the endopelvic fascia. Red arrows: without preservation of the levator ani fascia (conventional technique). Black arrows: with preservation of the levator ani fascia. NVB, neurovascular bundle.


Endopelvic fascia
Prostate
Levator fascia
NVB
Rectal balloon

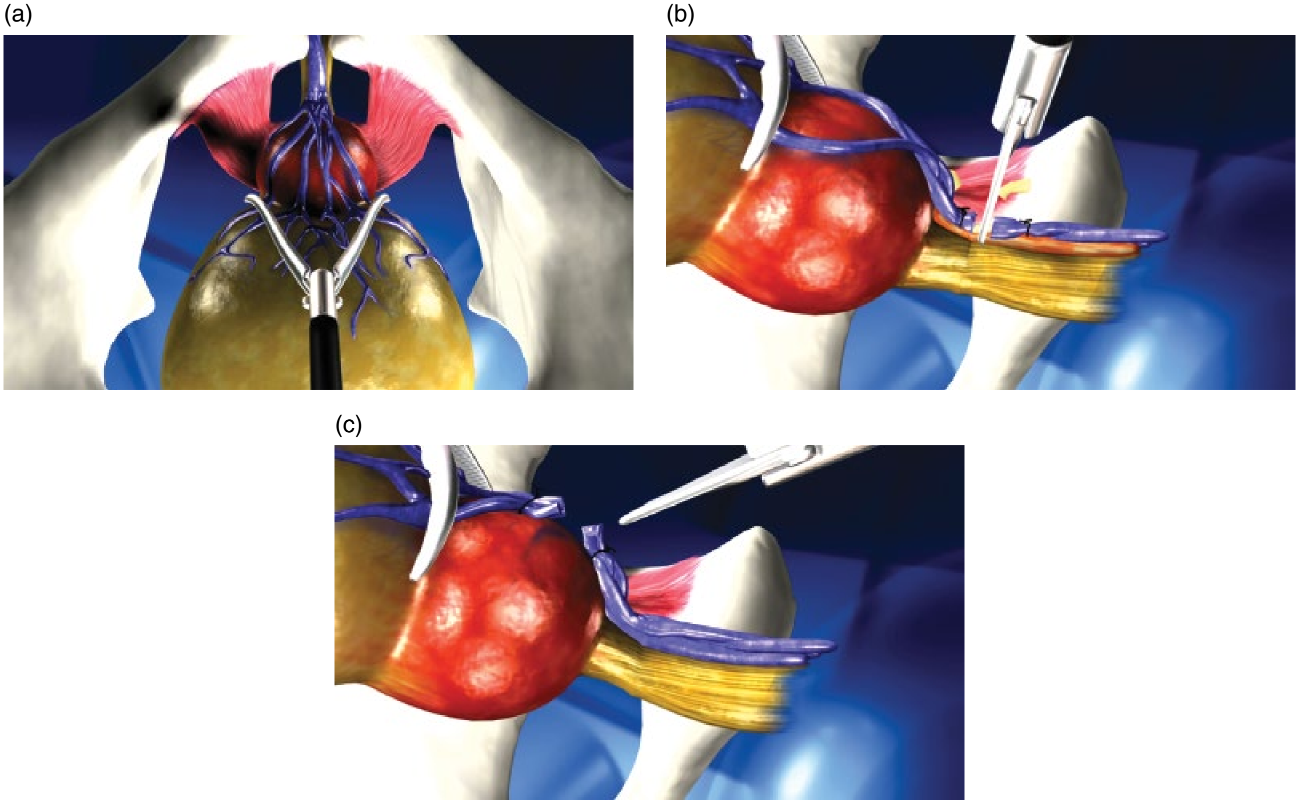


**Figure 100.8** Division of the dorsal vein complex (DVC). (a) A 120° endodissector is placed over the prostatovesical junction. (b) Conventional technique: distal suturing and division of the DVC. (c) New technique: division of the DVC at the mid prostate.

### Nerve-sparing techniques

Preservation of the neurovascular bundles can be performed using an antegrade or retrograde technique [69–71].

#### *Antegrade technique*

Antegrade dissection starts with the division of the proximal pedicle and release of the neurovascular bundles at the base of the prostate [8]. Finally, the bundles can be separated bluntly from the apex. The neurovascular bundles cannot easily be visualized without initially incising the levator fascia and developing the lateral neurovascular bundle groove [69]. Gill et al. proposed intraoperative transrectal ultrasound monitoring to identify the course of the neurovascular bundle [66]. Interfascial neurovascular bundle dissection uses the prostatic fascia as a visible landmark, starting with its separation lateromedially [31, 69].

#### *Retrograde technique*

Retrograde dissection reproduces the open technique with earlier release of the neurovascular bundles [70–72]. The space between the urethra and the neurovascular bundles is dissected bluntly until Denonvilliers' fascia can be identified. The rectal balloon is inflated with 40–60 ml of air. The prostatic fascia is incised and small branches to the neurovascular bundles are controlled with 5 mm titanium clips (Figure 100.9a). The same is achieved during posterior dissection after incision of the urethra. Following division of the bladder neck, the course of the neurovascular bundles is visualized to exactly determine the clip position to control the proximal pedicle (Figure 100.9b).

#### *Antegrade versus retrograde nerve sparing (Table 100.4)*

All steps can be performed using either technique, and in the meantime hybrid techniques using steps of both approaches have been described [73]. Commonality exists with regard to accomplishing an interfascial dissection and early visualization of the neurovascular bundles, use of task-specific instrumentation such as fine right-angled and curved dissectors, and avoiding thermal energy during steps relevant to neurovascular bundle preservation [69, 71, 74].

### Entrapment of the specimen

The specimen is entrapped in the self-opening extraction bag (Karl Storz, Tuttlingen, Germany) by pulling the purse-string out onto the skin surface via the left 10 mm port. Thereafter, the port is reinserted parallel to the bag.

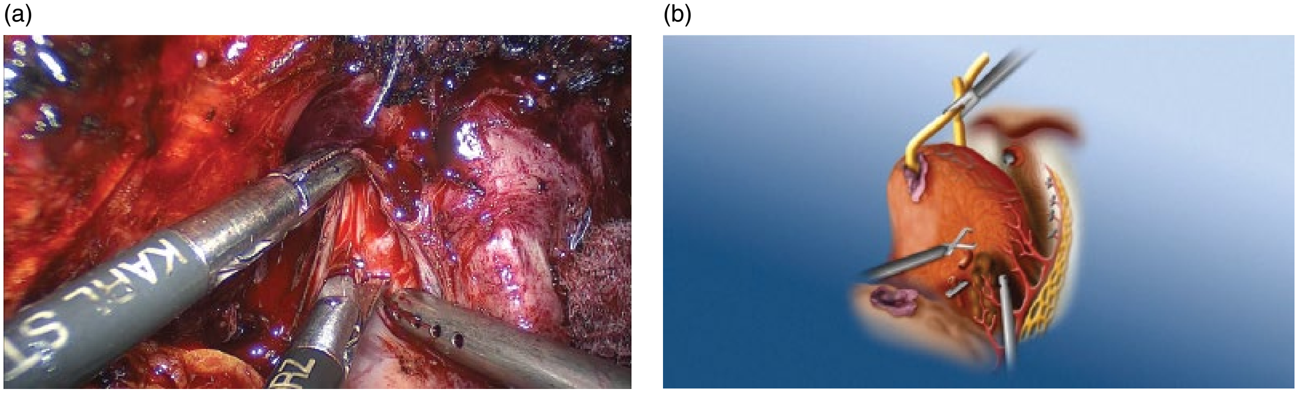


**Figure 100.9** Retrograde nerve-sparing technique. (a) Early release of the neurovascular bundles at the apex using 5 mm titanium clips. (b) Controlled division of the proximal pedicle.

## Urethrovesical anastomosis

For the urethrovesical anastomosis, the right medial port and left lateral port are used to provide an optimal angle (25–35°) between the instruments (Figure 100.10a). The anastomosis can be accomplished by the interrupted, continuous, or single-knot technique [64].

### Posterior reconstruction

Rocco and Rocco reported significant improvement of early continence following adaptation of the prostatovesicle muscle to the rectourethralis muscle [65] (Figure 100.10a–c). However, Menon et al. did not find any advantage over a single-knot technique alone [75]. Using the described technique, Rocco suture did not improve early continence. However, it did release tension on the anastomosis as well as the neurovascular bundles.

### Van Velthoven single-knot technique (see Video 100.1)

Anastomosis is performed using two bicolored sutures (17 cm PDS 3-0 and Biosyn; RB1-needle) knotted together [76, 77]. At this stage it is important that the assistant pushes the perineum with the urethral stump towards the surgeon ("perineal push"). We start at the 6 o'clock position on the bladder neck, subsequently taking the posterior urethra. Once the posterior part of the anastomosis is accomplished, the sutures are pulled to adapt the bladder neck and urethra (winch mechanism) (Figure 100.10d–f). An 18 Fr catheter is inserted and the anastomosis is completed. In difficult situations, a special bougie allows insertion of a guidewire for safe placement of the catheter.

### Reconstruction of the bladder neck

Posterior bladder neck reconstruction is necessary when the orifices are close (<5 mm) to the resection line (i.e. in cases of a large mid lobe). Anterior reconstruction may become necessary when bladder neck preservation is not possible or indicated.

### Anterior reconstruction

Based on anatomical studies Tewari et al. promoted the anterior reconstruction of the dorsal vein plexus and the reattachment of the arcus tendineus and puboprostatic

**Table 100.4** Advantages and disadvantages of retrograde versus antegrade neurovascular bundle preservation during laparoscopic radical prostatectomy.

| Technique | Advantages | Disadvantages |
|---|---|---|
| Retrograde | Earlier identification of neurovascular bundles (NVB) (i.e. hemostasis at dorsal vein plexus)<br>Exposure of NVB during every step<br>Direct transfer of existing techniques of open radical prostatectomy | Technical difficulty<br>Late control of proximal pedicle |
| Antegrade | Early control of prostatic pedicle, resulting in minimal bleeding<br>Early control of seminal vesicle arteries<br>Better working angle for the instruments<br>Dissection proceeds along surgeon's natural line of site | Later identification of NVB still covered by levator fascia (compensated by early incision of endopelvic fascia)<br>Suboptimal exposure of prostatic base during control of prostatic pedicles |

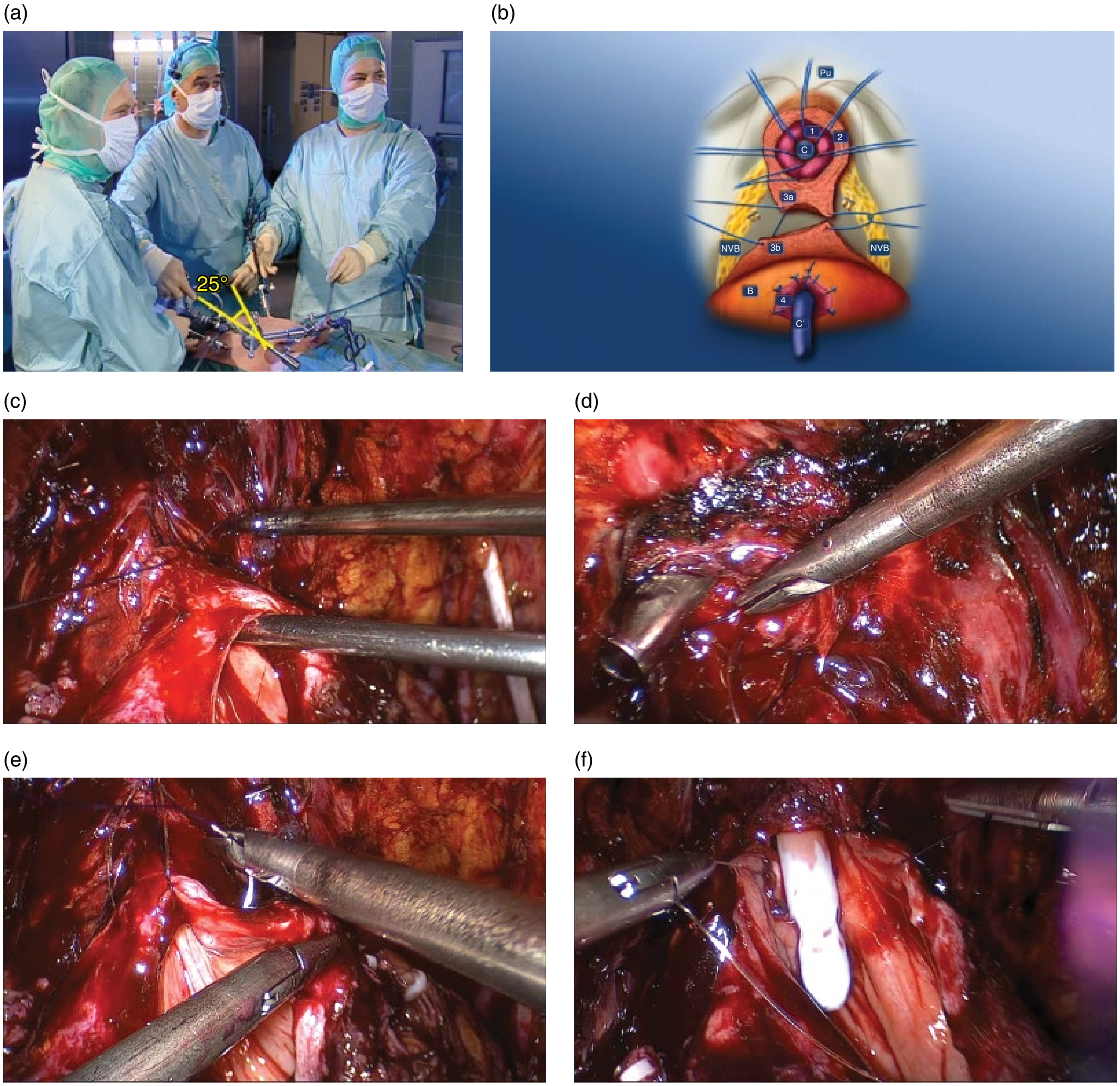


**Figure 100.10** Urethrovesical anastomosis. (a) Suturing using the right medial port for the needle driver to achieve an appropriate angle between the instruments. (b) Schematic posterior reconstruction according to Rocco and Rocco [65], with adaptation of the vesicoprostatic muscle to the rectourethralis muscle and posterior plate. B, bladder; NVB, neurovascular bundles; C, catheter; Pu, periurethral plate (prostate-vesical muscle and central raphe); 1–4, position of stitches. (c) Rocco stitch. (d) Single-knot technique according to van Velthoven using a bicolored suture. Urethral stitch (inside–outside). (e) Bladder neck stitch (outside–inside) at 4 o'clock. (f) Adaptation of the posterior part of the anastomosis using the winch principle.

plate to the bladder neck [78]. Even if other authors could not confirm its positive effect on early continence [75], the concept of total reconstruction of the urethrovesical junction seems to be an appealing concept. Early continence may depend more on other factors, such as preservation of the levator fascia minimizing the trauma to the branches of the pudendal nerve, but total reconstruction of the urethrovesical junction has a significant impact on the healing process of the anastomosis.

## Retrieval of the specimen

After placing the drainage tube via the right medial 10 mm port, the bag is extracted via the periumbilical incision.

## Results

A systematic literature search using the terms "laparoscopic radical prostatectomy," "ergonomics," "comparative studies," and "robot-assisted radical prostatectomy" was performed in Medline, Embase, and Pubmed. Inclusion criteria were randomized controlled trials (RCT) or observational series and reviews of good quality. Primary outcome parameters focused on the impact of ergonomics on performance and learning curve of the different techniques. Secondary outcome parameters were functional and oncologic outcomes after radical prostatectomy. In Heilbronn, we have performed 3505 LRPs since March 1999, including 869 with da Vinci.

Twenty-seven comparative studies were identified: 23 compared LRP with RRP and 4 compared LRP with RALP: one randomized controlled trial [79]; 12 nonrandomized prospective studies [45, 54, 80–101]; seven retrospective studies compared to contemporary series [91–96]; and four retrospective studies using historical series as controls [97–100]. Furthermore, there are robust long-term data from major centers as well as from recent meta-analyses [2, 3, 56, 101–104]. Based on this, there is an increasing body of evidence that laparoscopic and robot-assisted radical prostatectomy provide advantages with respect to surgical complications such as risk of transfusion and postoperative pain without deterioration of oncologic and functional outcomes [105, 106].

## Perioperative data

Comparison of early laparoscopic series to relevant contemporary series of RRP [8, 54, 56, 81, 86, 87, 92, 93] includes a major bias related to the different levels of surgical experience. Based on today's training programs, about 50 cases are necessary to learn LRP [47, 50].

### Operating times

Increased operating times (180–330 minutes) was one of the criticisms leveled against LRP (compared to RRP, 105–197 minutes; Table 100.5A). However, Frede et al. showed a decrease in operative time from 332 minutes for the first 50 cases to 196 minutes for the last 50 cases after 1000 procedure [47]. Similar decrease in operating time was seen with the extraperitoneal approach [107, 108]. Nowadays, at experienced centers mean duration of the operation ranges between 150 and 200 minutes.

### Blood loss and transfusion rates

Compared to RRP, LRP demonstrated a significantly lower blood loss (189–1100 ml vs. 550–1550 ml) and transfusion rate in cumulative analysis (Table 100.5B). In one study comparing 1134 LRP versus 3458 RRP cases, the transfusion rate was 4% versus 55% [109]. The study by Hu also revealed a 20% transfusion rate for RRP versus 4% for minimally invasive techniques [110].

### Postoperative pain

Most of the studies used a visual analog scale or the morphine equivalent requirement [3]. Pain scores were slightly lower during postoperative day 1 in patients undergoing LRP [79]. There was no statistically significant difference in the required morphine sulfate equivalent. The level of postoperative pain might be affected by epidural infusion of analgesic following RRP [109].

### Catheter times and hospital stay

Overall, catheterization times ranged between 6 and 14 days after LRP and 5 and 22 days after RRP [45, 54, 80–90]. The catheter was withdrawn early in a higher percentage of LRP patients compared to RRP. Length of stay in hospital was significantly shorter for LRP patients [45, 54, 80–96]. However, there is a wide variation in length of stay due to the differences in economic health systems and cultural background.

## Complications

We classified complications according to the modified Clavien system [111] (Table 100.6). In a study with follow-up of 37 months, Rabbani et al. reported 19.9% Clavien I–II complications following RRP compared to 37.3% after LRP [109]. However, they listed transfusion rates of 55% after RRP and 4% after LRP separately. Therefore, many patients receiving transfusions were not registered as Clavien II. Novara et al. observed 19% Clavien I–II (including 5.3% transfusions), similar to the rates in our series (21.7% including 10.4% transfusions) [3, 109, 112]. In Rabbani et al.'s series, Clavien III–V complications occurred in 6.4% after RRP and 8.9% after LRP, compared to 11.4% in our series (Table 100.6).

The low conversion rates (1.9–2.2%) in all major series reflect the careful introduction of LRP [20, 79]. In a multicenter study, technical reasons or unclear anatomy of the tumor were the reasons for conversion to open surgery [113]. A single retrospective study reported a lower rate of anastomotic strictures in LRP compared to RRP [93]. No differences were found between LRP and RALP [102, 103, 114].

### Predictive factors for complications (Table 100.7)

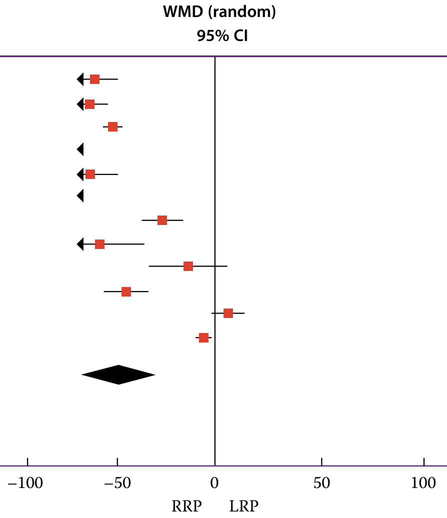
Novara et al. identified prostate volume greater than 50 cm as an independent predictor of complications [114], but Zorn et al. did not find any impact of prostate

**Table 100.5A** Comparison of intraoperative outcome following laparoscopic and retropubic radical prostatectomy: operating times.

| Study or sub-category | N | RRP Mean (SD) | N | LRP Mean (SD) | Weight % | WMD (random) 95% CI |
|---|---|---|---|---|---|---|
| Salomon (2002) | 145 | 197.00 (56.00) | 137 | 285.00 (87.00) | 8.38 | −88.00 [−105.18, −70.82] |
| Anastasiadis (2003) | 70 | 179.00 (40.00) | 230 | 271.00 (78.00) | 8.49 | −92.00 [−105.76, −78.24] |
| Artibani (2003) | 50 | 105.00 (17.00) | 71 | 180.00 (20.00) | 8.64 | −75.00 [−81.62, −68.38] |
| Bhayani (2003) | 24 | 168.00 (33.00) | 33 | 348.00 (72.00) | 7.91 | −180.00 [−207.89, −152.11] |
| Rassweiler (2003) | 219 | 196.00 (74.00) | 219 | 288.00 (98.00) | 8.41 | −92.00 [−108.26, −75.74] |
| Roumeguere (2003) | 77 | 168.00 (52.00) | 85 | 288.00 (67.00) | 8.33 | −120.00 [−138.38, −101.62] |
| Atallah (2004) | 115 | 161.00 (37.50) | 59 | 201.00 (46.20) | 8.49 | −40.00 [−53.64. −26.36] |
| Remzi (2005) | 41 | 195.00 (72.00) | 39 | 279.00 (70.00) | 7.74 | −84.00 [−115.12, −52.88] |
| Remzi (2005) | 41 | 195.00 (72.00) | 41 | 217.00 (51.00) | 7.95 | −22.00 [−49.01, 5.01] |
| Guazzoni (2006) | 60 | 170.00 (34.20) | 60 | 235.00 (49.90) | 8.44 | −65.00 [−80.31, −49.69] |
| Poulakis (2007) | 70 | 150.00 (30.00) | 72 | 144.00 (36.00) | 8.56 | 6.00 [−4.89, 16.89] |
| Touijier (2008) | 818 | 188.00 (41.00) | 612 | 199.00 (47.00) | 8.67 | −11.00 [−15.66, −6.34] |
| Total (95% CI) | 1730 | | 1658 | | 100.00 | −71.20 [−97.35, −45.05] |

Test for heterogeneity: Chi$^2$ = 635.31, df = 11 ($P < .00001$), I$^2$ = 98.3%

Test for overall effect: Z = 5.34 ($P < .00001$)

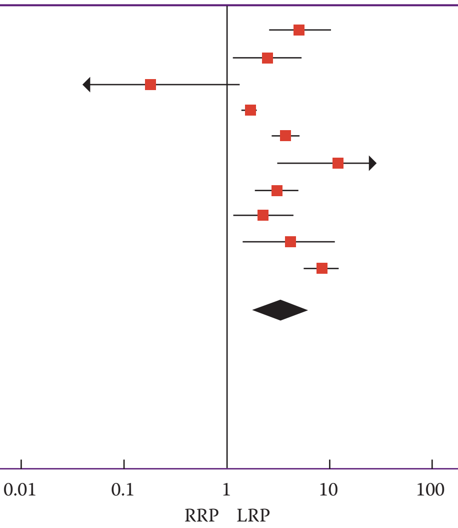


Meta-analysis according to Ficarra et al. [3].

RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy; WMD, weighted mean difference.

**Table 100.5B** Comparison of intraoperative outcome following laparoscopic radical prostatectomy and retropubic radical prostatectomy: transfusion rates.

| Study or sub-category | RRP n/N | LRP n/N | RR (random) 95% CI | Weight % | RR (random) 95% CI |
|---|---|---|---|---|---|
| Salomon (2002) | 38/145 | 4/137 | | 10.46 | 8.89 [3.29, 24.48] |
| Anastasiadis (2003) | 6/70 | 6/230 | | 10.09 | 3.29 [1.09, 9.87] |
| Artibani (2003) | 0/50 | 8/71 | | 4.64 | 0.08 [0.00, 1.41] |
| Rassweiler (2003) | 122/219 | 66/219 | | 12.61 | 1.85 [1.46, 2.34] |
| Rassweiler (2003) | 122/219 | 21/219 | | 12.28 | 5.81 [3.80, 8.87] |
| Brown (2004) | 31/60 | 1/60 | | 6.94 | 31.00 [4.37, 219.84] |
| Guazzoni (2006) | 32/60 | 8/60 | | 11.57 | 4.00 [2.01, 7.95] |
| Jurczck (2007) | 21/240 | 5/163 | | 10.64 | 2.85 [1.10, 7.41] |
| Poulakis (2007) | 13/70 | 2/72 | | 8.74 | 6.69 [1.57, 28.56] |
| Touijier (2008) | 338/818 | 14/612 | | 12.04 | 18.06 [10.69, 30.51] |
| Total (95% CI) | 1951 | 1843 | | 100.00 | 4.72 [2.20, 10.14] |
| Total events: 723 (RRP), 135 (LRP) | | | | | |
| Test for heterogeneity: Chi$^2$ = 108.91, df = 9 ($P$ < .00001), I$^2$ = 91.7% | | | | | |
| Test for overall effect: Z = 3.98 ($P$ < .0001) | | | | | |



Meta-analysis according to Ficarra et al. [3].
RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy; RR, relative risk.

**Table 100.6A** Complication rates in consecutive cases ($n = 2200$) of laparoscopic radical prostatectomy at a single center.

| | Clavien classification[a] | Within 6 weeks | | Within 50-month follow-up | |
|---|---|---|---|---|---|
| No reinterventions necessary | I | 6.8% | = 21.7% | – | = 21.7% |
| | II | 14.9% | | – | |
| Reinterventions necessary | IIIa | 3.6% | = 5.1% | – | = 9.8% |
| | IIIb | 1.5% | | 4.7% | |
| | IVa | 1.5% | = 1.6% | – | = 1.6% |
| | IVb | 0.1% | | – | |
| | V | 0.1% | = 0.1% | – | = 0.1% |

[a] Clavien I: any deviation from the normal intraoperative or postoperative course, including the need for pharmacologic treatment other than antiemetics, antipyretics, analgesics, diuretics, electrolytes, or physiotherapy; Clavien II: complications needing only the use of intravenous medications, total intravenous nutrition, or blood transfusion; Clavien IIIa: complications needing surgical, endoscopic, or radiologic intervention under local anesthesia; Clavien IIIb: complications needing surgical, endoscopic, or radiologic intervention under general anesthesia; Clavien IVa: life-threatening complications requiring intensive care unit (ICU) management: single organ dysfunction; Clavien IVb: life-threatening complications requiring ICU management: multiorgan dysfunction; Clavien V: death of the patient.

volume for RALP [115]. In addition, operating time longer than 4 hours, non-nerve-sparing technique, and transperitoneal access predicted a higher rate of complications. However, there is a relationship between the institutional learning curve and these factors, with the number of cases performed by the surgeon being a predictive factor [115].

## Oncologic results

### Positive margins

Comparative and cumulative studies have provided data of positive surgical margin (PSM) rates ranging from 11% to 37% after RRP, 11–30% after LRP, and 9.6–26% after RALP (Table 100.8). Guazzoni et al. demonstrated overlapping PSM rates [79]. No differences were

**Table 100.6B** Comparison of complication rates of laparoscopic and retropubic prostatectomy in the literature.

| | | Rabbani et al. 2010 [109] | | Literature [110] | |
|---|---|---|---|---|---|
| **Complication** | **Present series LRP (%)** | **RRP (%)** | **LRP (%)** | **RRP (%)** | **LRP (%)** |
| Urinoma/urinary leak | 1.4 | 2.9 | 8.7 | 0.2–6.7 | 1.0–13.6 |
| Bladder neck contracture | 4.6 | 5.5 | 0.7 | 1.0–17.9 | 0.2–5.3 |
| Urinary retention | 3.0 | 3.6 | 3.0 | 0.6–2.0 | 0.8–5.9 |
| Hydronephrosis | 0.8 | 0.9 | 1.9 | 0.2–1.0 | 0.0–0.4 |
| Ureteral injury | 0.1 | 0.5 | 0.2 | 0.1–0.8 | 0.2–0.5 |
| Bladder calculus/suture/clip | 0.15 | 0.6 | 0.2 | N/A | 0.8 |
| Lymphocele | 0.7 | 3.0 | 5.4 | 0.1–6.9 | 0.0–1.1 |
| Abscess | 0.1 | 0.7 | 1.7 | 0.4–1.7 | 0.0–0.7 |
| Rectal/bowel injury | 2.1[a] | 0.7 | 0.4 | 0.4–4.9 | 0.0–1.4 |
| Wound infection | 0.5 | 2.3 | 3.8 | 0.6–13.8 | 0.0–1.0 |
| Cardiac ischemia | 0.15 | 0.2 | 0.4 | 0.0–1.0 | 0.0–0.7 |
| Cardiac arrhythmia | 0.2 | 0.9 | 0.7 | 0.2–4.8 | N/A |
| Respiratory distress | 0.3 | 0.6 | 0.6 | 0.5–1.2 | 0.2–0.7 |
| Pneumonia | 0 | 0.3 | 0.4 | 0.2–1.4 | 0.0–0.3 |
| Ileus | 0.3 | 0.3 | 2.1 | 0.3–3.0 | 0.3–5.3 |
| Acute renal insufficiency | 0.05 | 0.7 | 1.0 | 0.2–0.4 | 0.0–0.3 |
| Venous thromboembolism | 0.5 | 1.9 | 2.0 | 0.4–1.3 | 0.0–2.4 |
| Urinary tract infection | 2.1 | 2.8 | 7.8 | 0.1–3.0 | 1.0–2.4 |
| Anemia needing transfusions | 14.8 | 55.0 | 4.0 | N/A | N/A |
| Total | 33.1[b] | 27.5[c] | 39.0[c] | N/A | M/A |

RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy;

[a] 1.4% of cases were managed conservatively (intraoperative suture of superficial bowel/rectal injury followed by parental nutrition for several days and prolonged catheterization time).

[b] Including blood transfusions. Excluding patients with anemia as only complication, total complication rate amounts to 22.7%.

[c] Excluding blood transfusions.

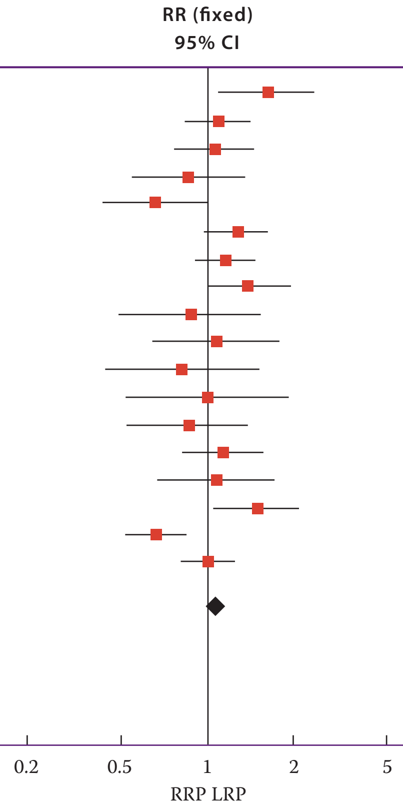
**Table 100.7** Significant prognostic factors predictive for complications of laparoscopic radical prostatectomy.

| **Factor** | | **% Without complications** | **% Clavien I–II** | **% Clavien III–V** | ***P*** |
|---|---|---|---|---|---|
| Weight of specimen (g) | ≤50 | 68.5 | 19.9 | 11.6 | .002 |
| | >50 | 61.7 | 27.2 | 11.1 | |
| Nerve sparing | Non-nerve sparing | 63.5 | 22.7 | 13.8 | <.001 |
| | Unilateral nerve sparing | 69.9 | 18.7 | 11.4 | |
| | Bilateral nerve sparing | 75.0 | 16.3 | 8.7 | |
| Access | Transperitoneal | 65.5 | 21.4 | 13.1 | .005 |
| | Extraperitoneal | 72.9 | 17.6 | 9.5 | |
| Operating time (h) | ≤4 | 73.6 | 17.5 | 8.9 | .023 |
| | >4 | 66.6 | 20.7 | 12.7 | |

**Table 100.8** Comparison of positive surgical margins after laparoscopic (LRP) and retropubic radical prostatectomy (RRP).

| Study or sub-category | RRP n/N | LRP n/N | Weight % | RR (fixed) 95% CI |
|---|---|---|---|---|
| Fremont (2002) | 36/139 | 19/139 | 3.67 | 1.89 [1.15, 3.14] |
| Salomon (2002) | 46/145 | 39/137 | 7.75 | 1.11 [0.78, 1.59] |
| Anastasiadis (2003) | 20/70 | 61/230 | 5.50 | 1.08 [0.70, 1.65] |
| Artibani (2003) | 12/50 | 21/71 | 3.35 | 0.81 [0.44, 1.49] |
| Egawa (2003) | 14/49 | 17/34 | 3.88 | 0.57 [0.33, 1.00] |
| Rassweiler (2003) | 63/219 | 46/219 | 8.89 | 1.37 [0.98, 1.91] |
| Rassweiler (2003) | 63/219 | 52/219 | 10.05 | 1.21 [0.88, 1.66] |
| Roumeguere (2003) | 31/77 | 22/85 | 4.04 | 1.56 [0.99, 2.44] |
| Brown (2004) | 10/60 | 12/60 | 2.32 | 0.83 [0.39, 1.78] |
| Martorana (2004) | 13/50 | 12/50 | 2.32 | 1.08 [0.55, 2.14] |
| Remzi (2005) | 8/41 | 10/39 | 1.98 | 0.76 [0.34, 1.73] |
| Remzi (2005) | 8/41 | 8/41 | 1.55 | 1.00 [0.42, 2.41] |
| Guazzoni (2006) | 13/60 | 16/60 | 3.09 | 0.81 [0.43, 1.54] |
| Jurczok (2007) | 47/240 | 27/163 | 6.22 | 1.18 [0.77, 1.82] |
| Poulakis (2007) | 16/70 | 15/72 | 2.86 | 1.10 [0.59, 2.05] |
| Silva (2007) | 37/89 | 22/90 | 4.23 | 1.70 [1.10, 2.64] |
| Terakawa (2008) | 52/220 | 54/132 | 13.05 | 0.58 [0.42, 0.79] |
| Touijier (2008) | 92/816 | 69/612 | 15.24 | 1.00 [0.75, 1.34] |
| Total (95% CI) | 2655 | 2453 | 100.00 | 1.08 [0.97, 1.19] |

Total events: 581 (RRP), 522 (LRP)
Test for heterogeneity: Chi$^2$ = 37.42, df = 17 (*P* = .003), I$^2$ = 54.6%
Test for overall effect: Z = 1.38 (*P* = .17)



Meta-analysis according to Ficarra et al. [3].
RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy; RR, relative risk.

found between LRP and RALP, considering early and more advanced phases of the RALP learning curves [102, 116, 117].

### Prostate specific antigen recurrence

There are still only few long-term studies [118–122]. Guillonneau et al. reported an overall actuarial biochemical progression-free survival rate of 90.5% at 3 years [118–120]. The rates were 92% for pT2a, 88% for pT2b, 77% for pT3a, and 44% for pT3b. Our data revealed overall 10-year PSA-recurrence-free survival of 65%, including 80% for pT2 and 51% for pT3–4 (Figure 100.11a). Compared to RRP [123–134], the oncologic outcome was similar (Table 100.9). Also in T3 stages oncologic outcome was favorable, although this was based on a multimodal approach [28, 29] as previously published for open surgery [134–138].

The multicenter study published by Vickers analyzed the learning curve of LRP based on PSA recurrence-free status [139]. In an earlier RRP study, it was identified that 250 cases needed to be performed by a surgeon to achieve a plateau. In the LRP series including more than 5000 patients, this plateau was reached after 750 patients. However, there was an ongoing improvement (Figure 100.12), indicating some advantages attributed to video-endoscopic surgery.

### Survival data

Clinical progression-free 10-year survival was 97% for pT2 and 81% for pT3 (Figure 100.11b). We observed a local recurrence in 3% of pT2 and 13% of pT3/4 cases managed mostly by early adjuvant irradiation. Overall, 10-year survival was 96.8% for pT2 and 92.2% for pT3 (Figure 100.11c) [28, 29].

## Functional results

Evaluation of functional results after radical prostatectomy is difficult, because only a few comparative studies have used validated questionnaires [3, 97].

### Continence

To determine early continence, we introduced the urine loss ratio (URL) based on a micturition protocol following

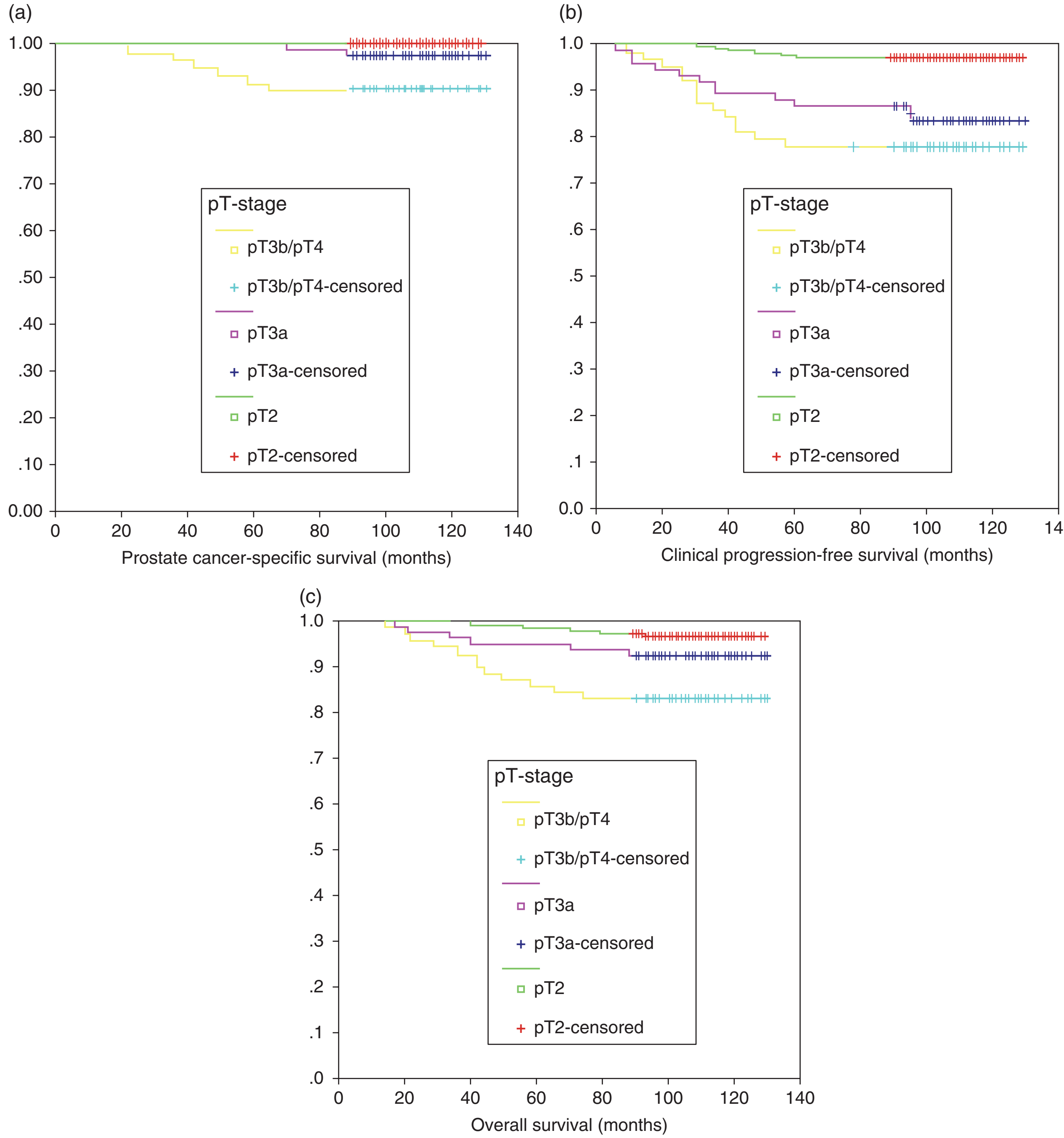


**Figure 100.11** Oncologic outcome of laparoscopic radical prostatectomy at 10 years follow-up (Heilbronn experience). (a) Prostate specific antigen (PSA) recurrence. (b) Clinical progression-free survival. (c) Overall survival.

catheter removal [140]. If URL is below 0.05, the probability that the patient will be continent after three weeks is 89%. Using URL, we compared our previous technique with and without posterior reconstruction and found no impact on URL (52% vs. 54%). When using the Heilbronn approach, the rate of minimal urine loss increased to 92% (Table 100.10).

One comparative study has shown higher long-term continence rates in RRP patients [89]. When evaluating the learning curve of LRP, continence recovery was better after RRP. Patients undergoing LRP had a twofold higher risk of being incontinent. In major series from referral centers, however, 12-month continence rates (66–95% vs. 60–93%) overlapped for RRP, LRP, and

**Table 100.9** Comparison of oncologic outcome of laparoscopic and retropubic radical prostatectomy.

| Positive margin (%) | | | | PSA recurrence-free survival | | | | | | | | | Clinical progression-free | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. pts | pT2 | pT3 | | pT2 | | | | pT3 + pT4 | | | | Prostate-confined disease | | | Extraprostatic disease | | |
| Authors (year) | | | | Authors (year) | 3 yr | 5 yr | 8 yr | 10 yr | 3 yr | 5 yr | 8 yr | 10 yr | Authors (year) | 5 yr | 10 yr | Authors (year) | 5 yr | 10 yr |
| **Laparoscopic radical prostatectomy** | | | | | | | | | | | | | | | | | | |
| Guillonneau et al., 2003 [107] | 350 | 11.1% | 37.3% | Salomon et al. 2002 [91] | 90.4% | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Stolzenburg et al., 2004 [108] | 300 | 9.2% | 30.3% | Guillonneau et al. 2003 [118] | 90.4% | – | – | – | 77.7% | | – | – | – | – | – | – | – | – |
| Rozet et al., 2005 [116] | 599 | 14.6% | 25.6% | Secin et al. 2006 [119] | – | 81.0% | – | – | – | 53.0%$^{b}$ | – | – | – | – | – | – | – | – |
| Martinez-Pineiro et al., 2006 [104] | 604 | 19.2% | 53.2% | Goeman et al. 2006 [122] | – | 89.7% | – | – | – | 58.6%$^{c}$ | – | – | – | – | – | – | – | – |
| Lein et al., 2006 [121] | 1000 | 14.9% | 54.5% | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Touijer et al., 2007 [98] | 485 | 8.2% | 17.2% | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Rassweiler et al. 2003 [93] | 2200 | 6.7% | 41.3% | Rassweiler et al. 2010 [106] | 94.1% | 88.3% | – | 82.9% | 80.0% | 64.9% | – | 53.0% | Rassweiler, 2003 [93] | 97% | 97% | Rassweiler, 2010 [106] | 84%$^{b}$ | 81%$^{b}$ |
| **Retropubic radical prostatectomy** | | | | | | | | | | | | | | | | | | |
| Huland et al., 2001 [123] | 789 | 14.9% | 36.5% | Catalona et al. 1998 (RRP) [126] | 92.5% | 90.0% | – | – | 78.7% | 68.7% | – | – | Trapasso et al. 1994 [131] | 93% | – | Gerber, 1997 [134] | 72% | 32% |
| Artibani et al., 2003 [89] | 50 | 14% | 43.6% | Ward et al. 2004 [127] | – | 82.0% | – | 73.0% | – | 58.0% | – | 39.0% | Catalona et al. 1994 [126] | 96% | 70% | Van der Ouden, 1998 [135] | 59% | 31% |
| Swindle et al., 2005 [124] | 1389 | 7% | 23% | Haukaas et al. 2005 [128] | 86.0% | 76.0% | – | – | 57.0% | 46.0% | – | – | Ohori et al., 1994 [132] | 94% | 90% | Ward, 2005 [136] | 85% | 73% |
| Guazzoni et al., 2006 [79] | 60 | 18.3% | 31.2% | Chun et al. 2006 [129] | – | 87.1% | 80.2% | – | – | 44.2% | 34.5% | – | Walsh et al., 1994 [133] | 97% | 85% | Carver, 2006, [137] | 86% | – |
| Estham et al., 2007 [125] | 2242 | 7% | 22% | Carini et al. 2008 [130] | – | 91.1% | 84.1% | – | – | 73.8% | 69.9% | – | – | – | – | Hsu, 2007$^{a}$ [138] | 96% | 85% |

$^{a}$ Only pT3a, $^{b}$ pT3a + pT3b + pT4, $^{c}$ pT3a + pT3b.

RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy.

RALP (Table 100.11). Comparing our previous technique with the described technique of preservation of levator fascia and puboprostatic collar, we found a significant improvement with respect to early continence (Figure 100.13).

### Erectile function

Two studies have used validated questionnaires such as the International Index of Erectile Function (IIEF) [85, 141]. Three studies have compared RRP and LRP [85, 87, 89] and none showed any advantage favoring LRP. A single retrospective study comparing historical series after LRP and RALP demonstrated a statistically insignificant trend in favor of RALP [116]. No comparative study showed any significant advantage for LRP at 12 months (42–76% vs. 10–93%).

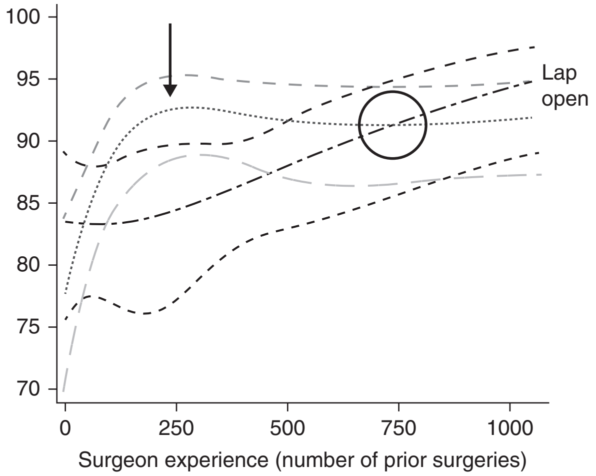


**Figure 100.12** Comparison of learning curves of laparascopic and retropubic radical prostatectomy [115]. Open surgeon reaches plateau of performance after 250 cases; laparoscopic surgeon requires 750 cases to reach similar level, but still improves beyond this level during the next 250 cases.

## Cost-effectiveness

Various cost calculations from the United States are available [142–146]. They suggested that LRP was more expensive than RRP (RRP US$5253–8596; LRP US$5058–10414). However, with the use of nondisposable instruments, completing LRPs in 3.4 hours, and discharging patients on postoperative day 2, cost equivalence between the two could be achieved [143]. Lotan et al. included RALP in their analysis and found a cost advantage of RRP of US$487 and US$1726 over LRP and RALP, respectively [144]. The shorter operative time (140 minutes vs. 160 minutes) and length of stay (1.2 days vs. 2.5 days) did not compensate for

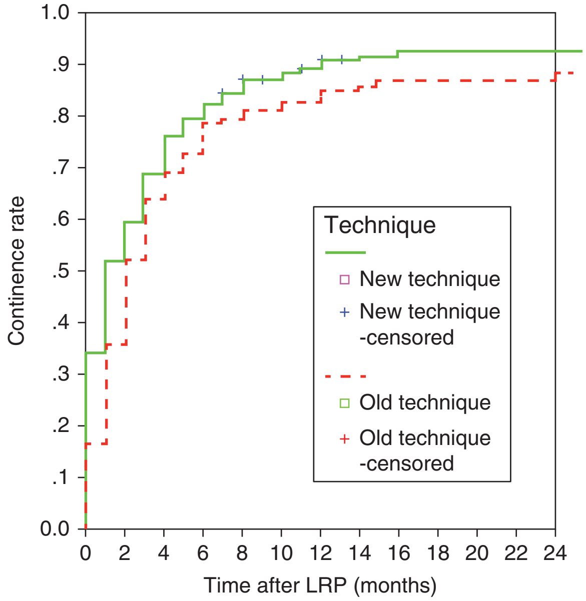


**Figure 100.13** Comparison of development of continence using the technique of preservation of puboprostatic collar (green) and levator fascia versus the standard technique (red). Kaplan–Meier curves demonstrate significantly higher rate of earlier continence. LRP, laparoscopic radical prostatectomy.

**Table 100.10** Impact of posterior reconstruction versus preservation of puboprostatic collar and levator ani fascia on early continence based on the urine loss ratio (ULR) following catheter removal (same surgeon, <70 years, pT2/3, bilateral nerve sparing).

| ULR[a] | No posterior reconstruction No preservation of puboprostatic collar | Posterior reconstruction No preservation of puboprostatic collar | Posterior reconstruction Preservation of puboprostatic collar |
|---|---|---|---|
| <0.02 | 55.2% | 52.3% | 92.3% |
| <0.05 | 22.7% | 18.2% | 7.7% |
| <0.11 | 9.4% | 18.2% | – |
| <0.16 | 6.4% | 9.1% | – |
| Total | 92.7% | 97.8% | 100% |

[a] Urine loss weight in pads/micturition volume (according to Ates et al. 2007 [140]).

the added expense of RALP. Moreover, in Germany the diagnosis-related group (DRG)-reimbursement system might be split into laparoscopic (pure or robot-assisted) and open prostatectomy. In such a scenario, LRP may become a very reasonable cost-effective alternative. This could be triggered by the end of the monopoly of Intuitive Surgical with introduction of other robotic systems [146].

## Perspectives on laparoscopic radical prostatectomy

### Ergonomic deficiencies

During LRP, surgeons suffer from high levels of mental and physical stress. After 4–5 hours, the fatigue syndrome sets in, characterized by mental exhaustion and reduced dexterity and capacity for good judgment [147, 148]. Back pain is common [148]. The force required to control the laparoscopic instruments can be six times greater compared to open surgery, and the problem is magnified further by the non-ergonomic design of the handles [149]. The assistant is also in a high-risk ergonomic position, created by the left leg bearing 70–80% of body weight over time [150]. Even if the da Vinci system has optimized the ergonomics of laparoscopic surgery, it still has limitations and is not cost-effective. Therefore, a significant effort needs to be invested to improve the ergonomics of laparoscopy.

### Technical advances

**Improvement in video-technology**

The introduction of HD video-technology to surgical theatre procedures at the beginning of this century

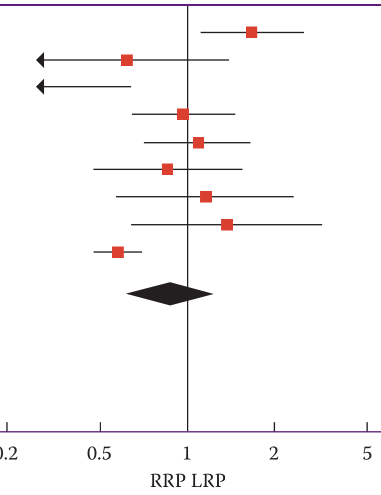
**Table 100.11A** Comparison of continence after laparoscopic and retropubic radical prostatectomy. Meta-analysis according to Ficarra et al. [3].

| Study or sub-category | RRP n/N | LRP n/N | RR (random) 95% CI | Weight % | RR (random) 95% CI |
|---|---|---|---|---|---|
| Anastasiadis (2003) | 16/70 | 25/230 | | 13.01 | 2.10 [1.19, 3.71] |
| Artibani (2003) | 3/14 | 0/20 | | 0.25 | 0.54 [0.17, 1.67] |
| Egawa (2003) | 3/41 | 14/34 | | 0.09 | 0.18 [0.06, 0.57] |
| Rassweiler (2003) | 22/219 | 22/219 | | 13.07 | 1.00 [0.57, 1.75] |
| Rassweiler (2003) | 22/219 | 19/219 | | 12.86 | 1.16 [0.65, 2.08] |
| Roumeguere (2003) | 9/56 | 10/52 | | 10.79 | 0.84 [0.37, 1.89] |
| Remzi (2005) | 8/41 | 6/39 | | 9.57 | 1.27 [0.48, 3.32] |
| Remzi (2005) | 8/41 | 5/41 | | 9.05 | 1.60 [0.57, 4.48] |
| Touijier (2008) | 56/222 | 100/193 | | 15.30 | 0.49 [0.37, 0.63] |
| Total (95% CI) | 923 | 1047 | | 100.00 | 0.87 [0.54, 1.39] |

Total events: 147 (RRP), 209 (LRP)

Test for heterogeneity: Chi$^2$ = 35.59, df = 8 ($P$ < .0001), I$^2$ = 77.5%

Test for overall effect: Z = 0.59 ($P$ = .56)



RRP, retropubic radical prostatectomy; LRP, laparoscopic radical prostatectomy; RR, relative risk.

**Table 100.11B** Comparison of continence after laparoscopic and retropubic radical prostatectomy. Continence according to first-day urine loss ratio (ULR) according to Ates et al. [140].

| | Continence | | | |
|---|---|---|---|---|
| | Continence time | | | |
| First-day ULR | Early continent | Midterm continent | Late continent | Incontinence |
| 0–0.049 ($n = 339$) | 303 (89.4%) | 29 (8.5%) | 3 (0.9%) | 4 (1.2%) |
| 0.05–0.149 ($n = 313$) | 230 (73.5%) | 59 (18.9%) | 8 (2.5%) | 16 (5.1%) |
| 0.15–1 ($n = 287$) | 122 (42.5%) | 85 (29.6%) | 22 (7.7%) | 58 (20.2%) |

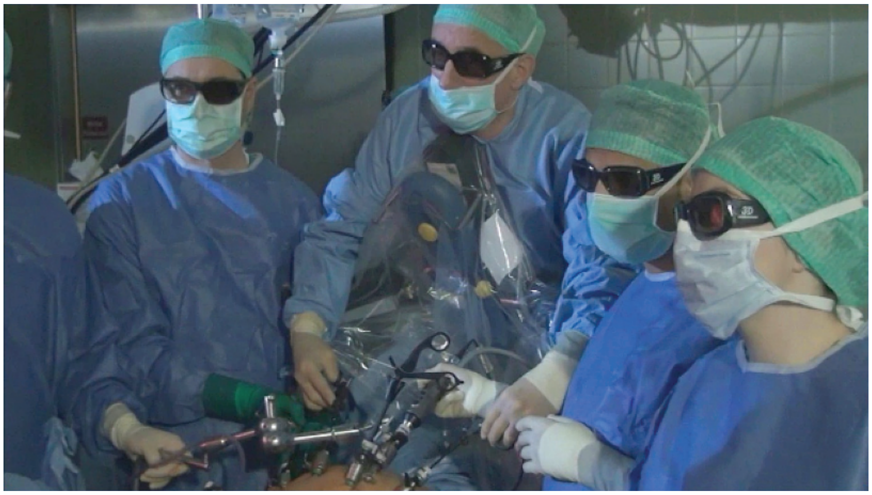


**Figure 100.14** ETHOS™ platform (ETHOS Surgical, Seattle, USA) to improve ergonomics during laparoscopic surgery. The surgeon sits over the patient's head during laparoscopic pelvic surgery. The armrest significantly improves ergonomics during suturing.

resulted in a considerable improvement in image quality (including resolution, brightness, depth, and magnification) compared with three-chip charge-coupled-device (CCD) technology or even one-chip technology, and enabled surgeons to safely perform complicated laparoscopic procedures, such as radical prostatectomy.

However, technology is under continuous development and 4K ultra-HD televisions are already being used in the consumer entertainment industry. In the last year first use of 4K in endoscopy and arthroscopy has been started (4K Arthrex, Munich, Germany; Olympus-Europe, Hamburg, Germany). These systems are a derivation of 4K digital-cinema standard, providing slightly lower resolution than a multiplex cinema at 3840 × 2160 pixels compared with 4096 × 2160 pixels, respectively. Consequently, 4K video-technology shows 8 million pixels compared with the 2 million pixels that full HD provides, enabling finer anatomical details and greater tissue texture than full HD, and a quasi-photographic emulsion of smoothness of the image [26].

Currently, 3D HD video-technology is available for 0° and 30° endoscopes, but polarized glasses, with a consequent reduction of brightness of the image, are still required. However, HD technology might partly compensate for this loss of brightness. The use of six degrees-of-freedom (6-DOF) instruments (i.e. Radius, Dexteritè) require 3D video-technology for optimal application, because the third dimension (i.e. using a 6-DOF needle driver) cannot be completely perceived by the operating surgeon [26, 151].

#### Ergonomic platform

In 1999, a special chair was proposed with pedal switches to improve the ergonomics [152]. Since 2005, we have used a surgical support during LRP to reduce the stress on the knee joints; however, during anastomosis the surgeon needs to stand up. Recently, a specially designed ergonomic body support consisting of a platform with foot pedal, a semi-standing support, a remote control, and a chest support was presented [153]. Electomyography results showed an average reduction of stress on the muscle of 44% for the erector spinae, 20% for the semitendinosus, and 74% for the gastrocnemious muscle when using the chest support. The average reduction of stress on the muscle using the semi-standing support was 5%, 12%, and 50%, respectively. In 2010, first experiences were published for the use of a platform (ETHOS™, ETHOS, Seattle, USA) that allows the surgeon to sit over the patient's head [154, 155]. This may overcome all physical stress problems concerning rotation, unstable standing, and weight balance (Figure 100.14). In a study published in 2015 comparing the ergonomics of standard laparoscopy with laparoscopy using the second-generation ETHOS chair or using the da Vinci system, the use of the ETHOS chair improved ergonomics significantly. Surgeon's muscle pain score (i.e. neck pain, shoulder pain, wrist pain, back pain) was 32 for standard laparoscopy versus 16 for the use of ETHOS versus 4 for the da Vinci system ($P < 0.05$) [155]. A further study confirmed these findings for retroperitoneal surgery as well [156].

#### Image-guided surgery

Surgical therapy for a clinically localized prostate cancer has undergone a significant transition in the past several decades. With wide application of minimally invasive radical prostatectomy, there has been a renewed interest in image-guided navigation techniques that could potentially be used to supplement the tumor resection and visualization/preservation of neurovascular bundles. Although this area of research is still in its infancy, these imaging techniques hold significant promise in achieving ultimate goals of radical prostatectomy [157–159].

Recently, an augmented reality (AR) navigation system that conveys virtual organ models generated from transrectal ultrasonography (TRUS) onto a real laparoscopic video during radical prostatectomy was described (Figure 100.15). This system uses custom-developed needles with colored pins inserted into the prostate as

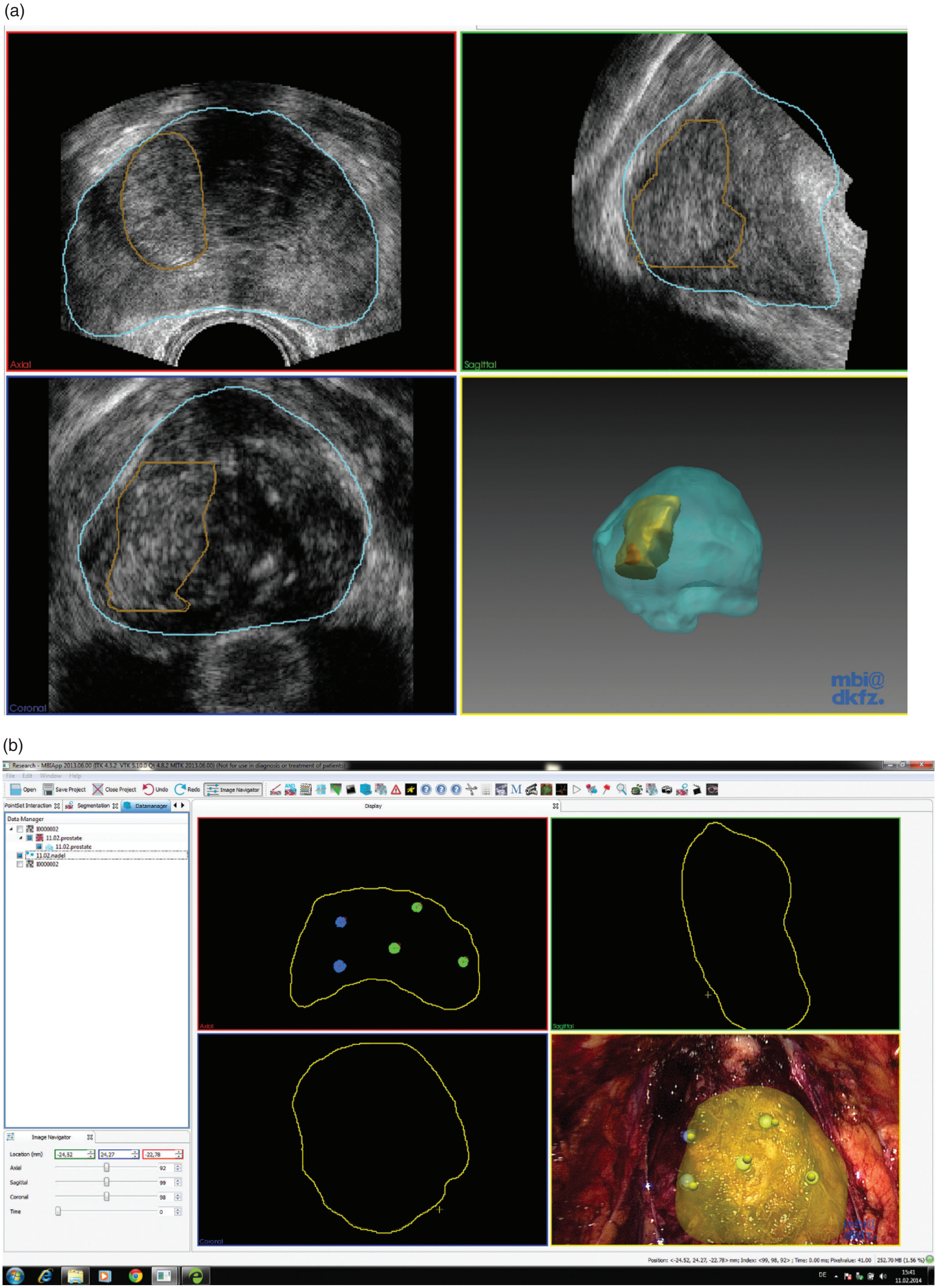

(a)
Axial
Sagittal
Coronal
mbi@
dkfz.
(b)
Research - MBIApp 2013.06.00 (ITK 4.3.2 VTK 5.10.0 Qt 4.8.2 MITK 2013.06.00) (Not for use in diagnosis or treatment of patients)
File Edit Window Help
Open
Save Project
Close Project
Undo
Redo
Image Navigator
PointSet Interaction
Segmentation
Datamanager
Display
Data Manager
I0000002
11.02.prostate
11.02.prostate
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Image Navigator
Axial
Sagittal
Coronal
DE
15:41
11.02.2014

Location (mm) -24.52 24.27 -22.78

Axial 92

Sagittal 99

Coronal 98

Time 0

Position: <-24.52, 24.27, -22.78> mm; Index: <99, 98, 92> ; Time: 0.00 ms; Pixelvalue: 41.00   252.70 MB (1.56 %)

**Figure 100.15** Marker-based navigation during laparoscopic radical prostatectomy. (a) Segmentation of intraoperative 3D-TRUS image identifying suspicious areas and position of inserted needle (navigation aids). (b) Calculation of endoscopic visualized markers and virtual markers as shown in the 3D-TRUS. (c) Real-time projection of virtual 3D image on HD image (right monitor). If the virtual markers and real markers are exactly overlaying, the virtual anatomy fits to the real endoscopic image. For performance of laparoscopic surgery a monitor without overlay is necessary.

(c)

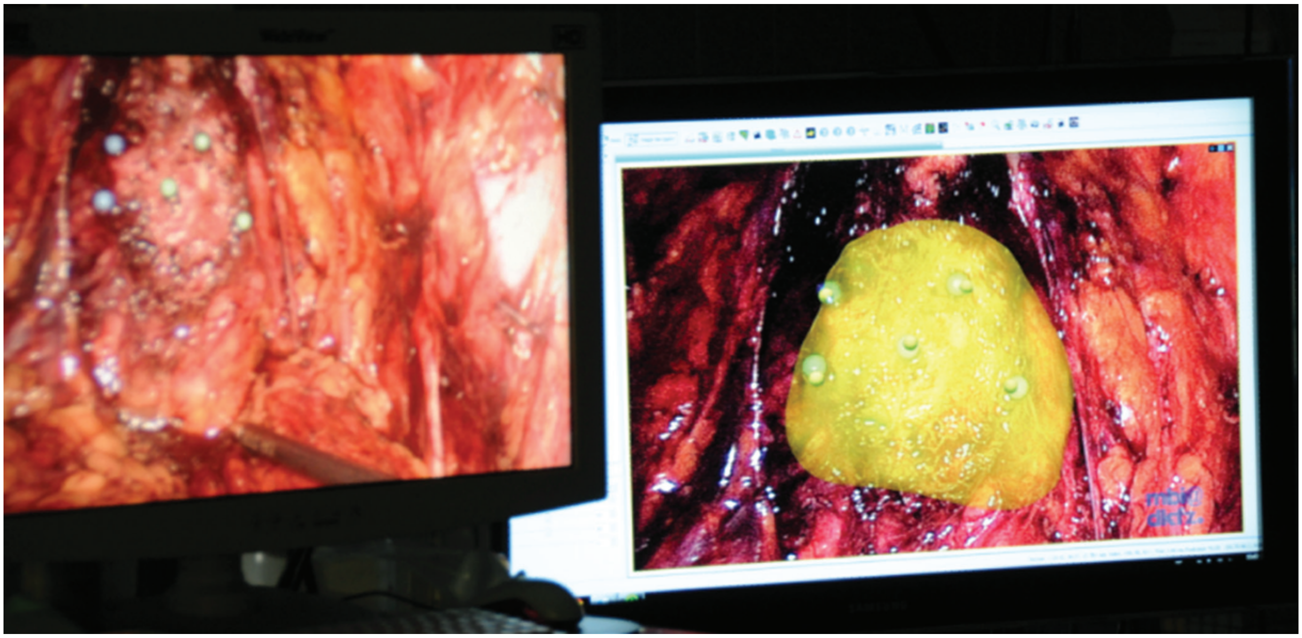

**Figure 100.15** (Continued)

soon as the organ surface is uncovered. By tracing the navigation aids in real-time, it allowed a registration between TRUS image and laparoscopic video based on the 2D–3D point correspondences. With this registration, the system correctly superimposed TRUS-based 3D information on an additional AR monitor placed next to the normal laparoscopic screen. First initial *in vivo* human application of the surgical navigation system in LRP was successful. No complications occurred, the prostate was removed together with the navigation aids, and the system supported the surgeons as intended with AR visualization in real-time [158, 159].

### Laparoendoscopic single-site surgery radical prostatectomy

Laparoendoscopic single-site (LESS) surgery has received significant attention in general surgery, where transvaginal cholecystectomy is increasingly performed. There are also reports of LESS radical prostatectomy using a periumbilical incision for port placement [160]. Interestingly, marketing also plays an important role in offering an "incision-less" removal of the gallbladder or prostate. The development of robotic systems for LESS surgery will significantly impact the ergonomics of this approach [161].

## Conclusions

There is no doubt that LRP has lost the race against RALP in the United States. Nevertheless, LRP has proven to be safe and provides at least similar functional and oncologic outcomes to RRP [162]. It will be interesting to see if future improvements, particularly concerning the ergonomics of the procedure, will impact on the role of LRP worldwide.

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# Robot-assisted Laparoscopic Radical Prostatectomy

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## Evolution of minimally invasive radical prostatectomy

Laparoscopic radical prostatectomy (LRP) was first described in 1997 by Schuessler et al. [1], 10 years after the arrival of laparoscopic surgery in 1987. Widespread adoption of LRP did not occur immediately, however, out of concern around the challenging vesicourethral anastomosis. Furthermore, there was no discernible advantage of LRP compared to open radical prostatectomy, suggesting that refinement of the technique was necessary. Additional development of the transperitoneal LRP approach was championed by Guillonneau and Vallancien in France in 2000, demonstrating a more reproducible and teachable technique, with operative times of a more acceptable 3 hours [2]. After concluding that LRP could be performed with comparable oncologic and functional outcomes, it started to be disseminated throughout Europe and select centers in the United States. The learning curve for LRP, however, remained high, primarily due to the technical challenge of the vesicourethral anastomosis. As a result, LRP was a daunting challenge for the novice laparoscopist and was performed only by skilled laparoscopic surgeons with sufficient experience to overcome the technical hurdles.

Soon after the advent of robotic surgery, the first robot-assisted laparoscopic radical prostatectomy (RALRP) was performed in 2000. This marked the beginning of a rapid shift in the surgical management of prostate cancer [3]. Use of the dominant robotic platform, the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), spread quickly throughout the field of urology, promising magnified 3D stereoscopic visualization, wristed instrumentation, and four robotic arms that proponents believed enhance the surgeons' ability to visualize the complex anatomy, retract, and suture. The seven degrees of freedom provided by the robotic arms simplified suturing of the complex vesicourethral anastomosis, in contrast to the technical challenge of pure laparoscopic suturing. Adoption of the da Vinci Surgical System was rapid and wide-ranging, including both large-volume tertiary care centers and smaller community hospitals. Without sufficient evidence to claim superiority of RALRP over LRP or open radical prostatectomy, the widespread use of the da Vinci system was driven by its popularity among surgeons and patients rather than proven benefit.

## Trends in practice patterns

Between 2003 and 2013 there was a 376% increase in the number of RALRPs performed, accounting for 22% of all radical prostatectomies in 2003 and 85% of all radical prostatectomies in 2013 [4, 5]. The dramatic shift also led to significant changes in practice patterns by urologists; LRP was largely replaced by RALRP and a growing number of urologists were no longer performing open radical prostatectomies. In 2013, 53.3% of urologist treating prostate cancer in the United States were exclusively performing RALRPs, a figure expected to rise [4], raising concerns about limited training opportunities for open radical prostatectomy. Furthermore, despite successful dissemination of robotic technology, practice patterns of urologists reflect a centralization of care for RALRP. Currently, the majority of open radical prostatectomies are performed by low-volume urologists, whereas RALRPs tend to be performed at high-volume tertiary care hospitals [6]. Despite the absence of randomized studies, current trends suggest that RALRP will continue to evolve into the predominant form of radical prostatectomy.

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## Outcomes

Since the introduction of RALRP to the urologic community there has been considerable and continuous debate in the literature comparing open radical prostatectomy versus RALRP. In large part this controversy exists as a result of the absence of prospective randomized trials. As a result, reported outcomes typically arise from observational studies and single-center experiences with inadequate follow-up and poor methodologic quality [7]. Only recently have sufficient long-term oncologic and functional results been published, further validating the robotic approach to radical prostatectomy.

### Perioperative outcomes

Although long-term data are limited, perioperative trends for RALRP are well described. RALRP operative times are significantly greater than those for open radical prostatectomy and depend on surgeon experience [8]. Operative times during the early RALRP experience were in the 4–5 hour range [3], but as surgeon and operating room staff experience improved, operative times decreased significantly to 2–3 hours at centers of excellence [9, 10]. Nonetheless, some experienced robotic surgeons demonstrate operative times equivalent to those of open radical prostatectomy [9, 10].

RALRP also has significantly less blood loss than open radical prostatectomy, which results in a 4–7 times lower rate of perioperative blood transfusion [11–13]. As with LRP, pneumoperitoneum tamponades venous bleeding, which is the primary source of blood loss during radical prostatectomy. Other advantages to RALRP cited as factors optimizing hemostasis include improved visualization of bleeding, particularly at the prostatic apex and neurovascular bundles (NVBs), more precise ligation of the dorsal venous complex (DVC), and improved hemostatic energy sources [12, 14].

Postoperatively, there also appears to be a trend showing a reduced hospital length of stay, averaging 2–3 days for open radical prostatectomy and 1–2 days for RALRP in the United States [13]. Large series and meta-analysis have confirmed this trend of earlier discharge after RALRP in both the United States and Europe, but centers of excellence have actually demonstrated shorter lengths of stay with open radical prostatectomy [14–16]. Early experiences in the United States have also identified a significant reduction in postoperative pain for minimally invasive radical prostatectomy relative to open radical prostatectomy, reflected both as patient-reported pain score and narcotic requirement [17, 18]. When further examined with higher quality prospective data, the postoperative pain difference was of little clinical significance, signifying that both RALRP and open radical prostatectomy are well tolerated [18].

### Oncologic outcomes

Oncologic control remains the primary goal of any radical prostatectomy, which involves complete removal of the prostate and seminal vesicles with curative intent of clinically localized disease. To date, no randomized prospective study has been performed to compare oncologic outcomes of open radical prostatectomy and RALRP. However, since the introduction of the RALRP in 2001, a considerable amount of research points to RALRP, open radical prostatectomy, and LRP having equivalent long-term oncologic outcomes.

Surrogates of oncologic control of prostate cancer include positive surgical margin (PSM) status and biochemical recurrence rates. Early experience with RALRP was confounded by mixed results in the literature examining rates of PSMs. Many single-center experiences of RALRP identified worse PSMs compared to those from open radical prostatectomy [19], while other studies asserted that RALRP had superior rates of PSMs [20]. However, more comprehensive meta-analyses have favored RALRP as having lower PSM rates [11, 21], strengthened by lower rates of adjuvant radiation therapy and androgen deprivation therapy [21]. Tewari et al. and Novara et al., in large systematic reviews, reported mean PSM rates of 10.7% and 11% for pT2 disease, respectively [14, 15]. These studies were unable to detect a significant difference compared to open radical prostatectomy. Conversely, Pearce et al., in a matched comparison of 96 935 men who underwent RALRP and open radical prostatectomy from the National Cancer Data Base, identified RALRP as having a reduced risk of PSMs and use of adjuvant radiation [22], leading some to declare RALRP as having superior oncologic results [23]. Proponents cite improved visualization and dissection of the prostatic apex, where PSMs are more likely to occur [24]. In general, PSM rates are highly dependent on the experience of the surgeon [25] and patient characteristics. Known patient predictors of PSM for RALRP are identical to those seen in open radical prostatectomy: clinical stage, Gleason score, prostate volume, body mass index (BMI), and prostate specific antigen (PSA) [11, 15, 26, 27].

Biochemical recurrence and disease-specific survival, however, are more accurate assessments of oncologic outcomes. Overwhelmingly, RALRP has been shown to provide equivalent and durable oncologic outcomes relative to open radical prostatectomy at both intermediate [28, 29] and long-term [30, 31] follow-up. Novara et al., in a meta-analysis including five large series with 3–5 year follow-up, identified no difference in biochemical recurrence-free survival (BCRFS) rates when comparing open radical prostatectomy and RALRP [15]. Only recently has long-term oncologic data become available which has provided solace to skeptics of RALRP citing incomplete oncologic outcomes. In a series of 483 men, Diaz et al. demonstrated 10-year BCRFS rates of 85.7%, 62.4%, and 43.2% in low-, intermediate-, and high-risk patients, respectively, which is comparable to results from contemporary open radical prostatectomy cohorts [30, 32]. In a multi-institutional study of 1100 patients at 10-year follow-up, Abdullah published similar results [31].

### Functional outcomes

The primary functional endpoints of interest after radical prostatectomy, regardless of the approach, are rates of erectile dysfunction and urinary incontinence. These complications pose a significant impact on a patient's quality of life post prostatectomy and need for further intervention. Advocates of RALRP cite evidence of improved functional outcomes with RALRP, owing to enhanced visualization and dissection of relevant anatomy.

In the 3–6 months post prostatectomy, there is considerable improvement in urinary continence which appears to stabilize within 1 year. Significant evidence suggests that there is an earlier return to continence in men after RALRP compared to open radical prostatectomy, however no significant difference existed at 1 year [33–35]. In a large population-based study, O'Neil et al. revealed that men after RALRP experienced significantly improved urinary continence at six months compared to open radical prostatectomy [35]. No difference was found at 12 months. Findings of earlier return of urinary control in RALRP have been replicated in a number of other studies [11, 17].

As with other outcomes, many of the data examining potency for RALRP are highly influenced by the definition of potency, patient self-reporting, timing of evaluation, and use of erectile dysfunction medications. Despite these limitations, trends in the literature suggest RALRP confers superior preservation and earlier return of erectile function relative to open radical prostatectomy [17, 33] and LRP [36]. Ficarra et al., in a meta-analysis of studies reporting potency rates, revealed improved 12-month potency rates after RALRP compared to open radical prostatectomy (OR 2.84; 95% CI 1.46–5.43; $P = 0.002$) [37]. A combined cohort of 2438 men similarly identified significantly improved sexual function for RALRP at both 6 and 12 months. The RALRP cohort had lower rates of erections insufficient for intercourse, fewer poor quality erections, and less significant sexual bother compared to open radical prostatectomy [35].

## Complications

Compared to open radical prostatectomy and LRP, the types of complications for RALRP are similar; however, the complication rates may differ depending on the approach. A large meta-analysis of 15 studies published between 2008 and 2011 revealed an average overall complication rate of 9% for RALRP (ranging from 3% to 26%), 2% of which were complications grade 3 or greater [15]. Compared to open radical prostatectomy and LRP approaches, RALRP appears to demonstrate fewer overall complications [38, 39], although other studies have shown the opposite [40]. Not surprisingly, surgeon experience greatly influences the rates of complications, with a significant reduction seen after the learning curve [41]. Complications are also influenced by patient characteristics such as BMI [42], prostate volume [43], and tumor characteristics [15].

## Positioning and insufflation

Many of the early complications unique to RALRP were based on patient positioning; these are related to prolonged operative times, Trendelenburg and lithotomy positioning, and $CO_2$ insufflation. Lower extremity neuropathy (LEN), primarily from prolonged compression of the femoral and common peroneal nerves, has been reported at a rate of 1.3% [44].

Prolonged $CO_2$ insufflation and steep Trendelenburg have also been associated with complications such as increased intraocular pressure [45], increased intracranial pressures [46], and subcutaneous emphysema [47]. Hemodynamic and respiratory effects of $CO_2$ insufflation have been well described and include hypercarbic acidosis from $CO_2$ absorption and unintended consequences from increased intra-abdominal pressure, such as hypoxemia due to impaired mechanical ventilation, cardiovascular depression due to impaired venous return and vasodilation, and oliguria from decreased renal perfusion.

## Intraoperative complications

Intraoperatively, trocar placement and robotic instrument exchange have the potential for vascular and bowel injuries. Care must be taken to place and adjust robotic trocars and instruments under direct vision. Prompt recognition and repair of a bowel or vessel injury are vital to prevent serious bleeding and avoid more serious complications.

Rectal injuries, although rare, can occur at the apex during urethral transection and posterior dissection.

Two large meta-analyses of RALRP complications report rates of rectal injuries to be between 0.2% and 0.5% [14, 15, 39], however some early single-center series report rates as high as 1.5% [39]. Tewari et al. found significantly lower rates of rectal injuries during RALRP compared to LRP, but no difference existed relative to open radical prostatectomy [14]. Repair typically can be performed robotically and often involves a two-layer primary closure. However, more serious injuries may require open conversion or bowel diversion. If left unrecognized, rectal injuries can result in abscess formation and, more seriously, rectourethral fistula.

Ureteral injury, a rare complication occurring at a rate of 0.1–0.2% [14, 15], predominantly occurs during the dissection of the posterior vesicoprostatic junction and during approximation of the posterior wall of the vesicourethral anastomosis. Ureteral orifices must be identified, particularly in patients with a large median lobe, which often can be perilously close to the bladder neck and future anastomosis.

Open conversion has been reported at rates of 0.3–0.9% [14, 48] and is associated with significantly worse perioperative and functional outcomes. Patients who have had open conversion report greater rates of overall perioperative complications, prolonged hospital stay, and worse functional outcomes [49].

## Perioperative and delayed complications

In the immediate perioperative period, complications include anastomotic leak and thromboembolic events. Compared with open radical prostatectomy and LRP, RALRP provides improved dexterity and visualization of the anastomosis during suturing, which may explain why there tend to be fewer urine leaks and, later, fewer bladder neck contractures [14]. Proponents believe the reduction of anastomotic leak to be related to superior watertight approximation of bladder and urethra. Urine leaks and bladder neck contracture occurred on average in 1.8% and 1.4% of patients, respectively; this is significantly less than open radical prostatectomy [15, 50].

Because thromboembolic events are infrequent, the American Urological Association (AUA) continues to advise against routine use of perioperative prophylactic anticoagulation for radical prostatectomy [51]. Published series report deep vein thrombosis (DVT) occurring in 0–0.7% of patients [15]. In the setting of DVT, lymphocele which may be compressing the external iliac vein must also be ruled out with pelvic imaging. Treatment of DVT in the setting of lymphocele includes anticoagulation as well as drainage of the lymphocele, typically performed by interventional radiology. Asymptomatic and incidentally found lymphoceles do not require drainage.

## Perioperative care

### Patient selection

Indications for RALRP are the same as those for open radical prostatectomy and LRP, which is clinically localized prostate cancer. Few absolute contraindications exist; patients who are unable to tolerate pneumoperitoneum due to cardiopulmonary comorbidities and those unable to tolerate Trendelenburg positioning, including those with increased intracranial pressure, are contraindicated. Patients who pose a greater operative challenge include those with prior benign prostatic hyperplasia surgery, prior pelvic surgery or radiation therapy, prior inguinal hernia operations with or without mesh, and prior hormonal therapy. These patients often have significant adhesions and complex anatomy, requiring longer operations at a higher rate of both intraoperative and perioperative complications. Salvage RALRP is a particularly challenging procedure due to higher rates of tissue adhesions and dense fibrosis. Patients undergoing salvage RALRP should be counseled about higher rates of anastomotic leaks, challenging recovery of urinary continence and potency, and higher rates of rectal injury [52, 53].

### Bowel preparation

Prior to surgery, patients are typically managed with a form of mechanical bowel preparation, often based on institutional preference, to decompress the bowel and optimize visualization. Most commonly this is in the form of a fleet enema or oral laxative. Patients are often limited to a clear liquid diet 24 hours prior to surgery.

### Extraperitoneal versus intraperitoneal approach

Although there may be advantages and disadvantages to each approach, the decision to choose intraperitoneal versus extraperitoneal RALRP is heavily based on surgeon preference. Although early experiences with extraperitoneal RALRP suggested reduced operative time, shorter hospital stay, and improved functional outcomes, further evidence has shown no difference in outcomes compared to transperitoneal RALRP [54]. Overall, the transperitoneal approach is most commonly performed by robotic surgeons. Relative advantages of the transperitoneal approach include greater working space, less complex trocar placement, and less $CO_2$ absorption [55]. The major advantages to the extraperitoneal approach are related to being separated from significant adhesions from prior abdominal surgery and ease of simultaneous inguinal hernia repair with mesh [56]. Disadvantages include a smaller working space and challenging access in patients who have had prior extraperitoneal mesh during hernia repairs. Although there is a prevailing opinion that extraperitoneal pelvic lymph node dissection (PLND) is more difficult, lymph node yield has been shown to be equivalent for limited and standard PLND compared to the transperitoneal approach [57]. While an extended PLND has been described extraperitoneally, no study has compared the two approaches.

## Operative steps

### Patient positioning

Patients are positioned supine with arms tucked to the side on an operating table capable of steep Trendelenburg position. Eggcrate cushions are placed on either side of the arms to prevent compression injury to ulnar and median nerves. Use of shoulder rests should be avoided to avoid brachial plexus injury. The patient's legs are placed in low lithotomy in padded spreader bars with sequential compression devices to access the patient's perineum and provide space for robotic docking for the da Vinci S or Si models. For the da Vinci Xi model, the patient's legs are placed in a regular supine position. Tape or a securing strap should be placed across the patient's upper chest to keep him secured to the operating room table while in steep Trendelenburg position. Next, the patient is prepped and draped in the sterile fashion and a 16 Fr indwelling Foley catheter placed to drain the bladder.

### Pneumoperitoneum and trocar placement

#### Transperitoneal approach

The majority of urologic surgeons prefer the transperitoneal approach which affords greater working space relative to the extraperitoneal approach. Access into the peritoneum is obtained through a number of potential routes and is often dictated by surgeon preference. Veress needle placement, typically inserted at the level of the umbilicus, can be used to obtain pneumoperitoneum to a $CO_2$ insufflation pressure of 12–15 mmHg. Next, a skin incision is made for placement of the 12 mm trocar at the midline just above or below the umbilicus. For those with a high likelihood of abdominal adhesions, placement of the 12 mm trocar can be done under direct laparoscopic vision with a Visiport (Medtronic, Minneapolis, MN, USA) or with a dissecting trocar. Alternatively, open access and trocar placement via the Hassan technique is an effective and safe route to gain access under direct vision. The decision to place the trocar above or below the umbilicus is dependent on the length of the torso, with the optimal working distance 15 cm above the pubic symphysis.

The remaining ports should be placed under direct vision from the robotic laparoscope midline port. The Veress needle should be inspected to ensure no signs of bowel or vascular injury during initial placement and removed. Two 8 mm robotic ports are placed symmetrically two fingerbreadths below and 8–10 cm from the midline port. The minimum 8 cm distance between ports is required to prevent robotic arm clashing. With the da Vinci four-arm configuration, an additional 8 mm robotic port is placed on the left side 2–3 cm superior and medial to the anterior superior iliac spine (ASIS), approximately 8–10 cm from the left robotic trocar. Similarly, a 12 mm assistant port is placed on the right side, a similar 2–3 cm medial and superior to the ASIS and 8–10 cm from the right robotic trocar which is used for clip and suture access. On the right, a 5 mm assistant port for suction and irrigation is placed between the camera port and the right robotic trocar cranially. Either of the assistant ports can be used with the AirSeal (SurgiQuest, Milford, CT, USA) trocar for maintaining constant insufflation pressures. For obese patients, ports are placed more cephalad, paying special attention to the trajectory of the port during insertion into the abdomen to avoid skiving. Once the ports are in place, the lens can be switched to either a 0° or 30° down lens, depending on surgeon preference.

The robot is then docked to the patient, approaching the patient between the legs for S and Si models, or on the patient's side for Xi model. The ports are attached to each robotic arm, positioning the arms to avoid clashing outside of the patient. Robotic instruments are then advanced carefully under direct vision with monopolar cautery scissors in the right robotic arm, bipolar Maryland forceps in the left robotic arm, and ProGrasp forceps in the left lateral robotic arm. The bedside assistant is positioned on the patient's right, using the medial assistant 5 mm port for suction/irrigation and the lateral 12 mm assistant port for clip and suture access.

#### Extraperitoneal approach

Gaining access into the extraperitoneal space requires adequate understanding of the abdominal wall anatomy to avoid entering the peritoneum. A midline 1.5 cm infraumbilical incision is made followed by blunt dissection down to anterior rectus sheath with a mosquito or Kelly clamp. Using a Visport dissecting trocar under direct vision with a 0° laparoscope, sharp dissection is performed slightly left or right from midline until reaching the posterior rectus sheath. Next, the angle of the trocar is flattened and then advanced along and parallel to the posterior rectus sheath toward the pubis until entering the space of Retzius. Blunt dissection with the trocar is performed to each side. A balloon dilating trocar is advanced along the same tract and inflated under direct vision until the balloon edge reaches the lateral pelvic walls. Trocar placement is performed in a pattern similar to the transperitoneal approach, staying along a line drawn from the midline port to the ASIS on each side. For the extraperitoneal approach, however, there is only a single lateral 12 mm assistant port. Care must be taken to avoid entering the peritoneum during trocar placement to avoid insufflating the peritoneal space. Often, the lateral edges of the space of Retzius must be developed manually with a grasping instrument prior to docking of the robot. If the peritoneum is violated, a Veress needle or 5 mm port can be placed in the abdomen to vent the pneumoperitoneum.

## Posterior dissection

Access to the seminal vesicles (SVs) and vasa can be performed either anteriorly after transecting the bladder neck or posteriorly through a transperitoneal incision between the plane of the bladder and rectum into the pouch of Douglas. Using a 0° lens, the peritoneum is incised horizontally with the monopolar scissors in the midline. Blunt dissection is performed in the midline until the vasa and SVs become visible. The assistant or robotic fourth arm ProGrasp can aid in the retraction of the peritoneal fold and prostate with the suction device anteriorly. The vasa are divided and, slightly more laterally, the SVs can be freed out with electrocautery, Weck clips, and blunt dissection. It is important to stay medially during this dissection to avoid injuring the ureters inserting into the trigone laterally. The vessels at the tip of the SVs are divided with a clip. The ProGrasp can be used to expose the posterior plane of the prostate by retracting the SVs superiorly. Denonvilliers' fascia is entered just posterior to the SVs and the posterior plane is further developed between the prostate and Denonvilliers' fascia (anteriorly) and the perirectal fat (posteriorly) until the prostatic apex is reached. Alternatively, instead of a posterior approach, the SVs and vasa can be reached anteriorly after transection of the bladder neck. In the setting of a large median lobe, a posterior approach is preferred because the median lobe can obscure access to the SVs and vasa anteriorly.

## Bladder mobilization

After interfering abdominal adhesions are lysed, the space of Retzius is entered by cutting a U-shaped peritoneal incision that is extended laterally, transecting the medial umbilical ligaments until the vasa are encountered. The median umbilical ligament is also cauterized with the bipolar forceps and ligated. The peritoneal edge is retracted posteriorly and kept on tension while the extraperitoneal space is developed with monopolar electrocautery to drop the bladder and expose the anterior prostate. Blunt dissection of the extraperitoneal areolar tissue should be kept to a minimum to avoid venous bleeding into the operative field. When exposing the anterior prostate, the superficial dorsal vein is encountered and cauterized with bipolar electrocautery. The anterior periprostatic fat is removed to expose the anterior prostate and endopelvic fascia laterally to optimize visualization and is sent for pathologic evaluation.

On the lateral edge of the prostate, the endopelvic fascia is sharply incised from the prostatic base and extended toward the apex to the urethra. The Maryland forceps or ProGrasp can be used to retract the prostate cranially and medially to provide tension to the endopelvic fascia during dissection. As the fascia is cut, the muscle fibers of the levator ani should be preserved and brushed laterally. The use of electrocautery is minimized to reduce collateral injury to the nearby NVBs. Next, the puboprostatic ligament is incised, exposing the deep dorsal venous confluence. Care must be taken to avoid entering the DVC, which can result in bleeding that obscures the operative field.

## Dorsal vein stitch

Once the prostatic apex is exposed laterally, the dorsal vein can be ligated to minimize venous bleeding. After exchanging the left and right arms for needle drivers, a barbed deep dorsal stitch is advanced underneath the DVC and anterior to the urethra. The stitch should be placed as far distally from the prostatic apex to prevent violation of the prostate during apical dissection. The Foley catheter should be manipulated to ensure it is not incorporated in the suture. A second, more superficial bite across the DVC is made and the suture is tied to obtain hemostasis. Alternatively, the dorsal vein can be ligated with a laparoscopic stapling device in a similar fashion, but with a higher cost.

## Pelvic lymph node dissection

If a patient's preoperative risk of lymph node metastasis is sufficiently high, a bilateral PLND is performed at the surgeon's discretion. Typically, a PLND is unnecessary if the patient is low risk or if a preoperative nomogram predicts the risk of lymph node metastasis is less than 2%. The European Association of Urology (EAU) and National Comprehensive Cancer Network (NCCN) recommend an extended lymph node template, but the AUA lists this as an option. The dissection begins with the identification of the external iliac vein and, with gentle lateral traction of the vein, the lymph nodes are separated from the lateral pelvic sidewall as they course inferiorly to the vein. The obturator nerve is identified posteriorly as the lymph node packet is retracted medially. Dissection is carried out toward the obturator fossa caudally and the iliac bifurcation cranially. Hem-o-lok clips (Teleflex Medical, Research Triangle Park, NC, USA) are placed on the distal and proximal ends of the lymph node packet, paying particular attention to avoid entrapment or injury to the obturator nerve.

### Bladder neck transection

Identification of the bladder neck is performed primarily with repetitive retraction of the Foley catheter by the assistant at bedside and observing the border between the bladder and prostate. In addition, visual cues from palpating the Foley balloon with the robotic arms can further help locate the bladder neck. With monopolar electrocautery, a horizontal incision is made at the midline of the anterior bladder neck while maintaining traction on the bladder with the ProGrasp arm. The incision is continued until the Foley balloon is reached, staying medially to avoid bleeding from the lateral pedicles. The balloon is deflated and the tip is clutched by the ProGrasp forceps and retracted anteriorly toward the abdominal wall. The assistant provides countertraction on the Foley catheter to lift the prostate to expose the posterior bladder wall. The presence of a median lobe is identified at this time as well as the relative location of the ureteral orifices to avoid ureteral injury during both bladder neck transection and vesicourethral anastomosis creation. The posterior bladder neck is incised, navigating around any median lobe. Once through the posterior bladder wall, dissection of the posterior bladder neck off the prostate is performed by grasping the cut bladder edge with the Maryland forceps and developing a plane posteriorly at a downward 45° angle until reaching the SVs. Careful dissection is performed to avoid a positive margin on the prostate edge and to prevent buttonholing the bladder wall on the bladder edge. Sparing of the bladder neck should be attempted; however this may not be possible if a large median lobe or large-volume prostate is encountered.

If performing an early posterior approach, the SVs and vasa have already been freed and the ProGrasp arm can use the SVs as the new handle to retract the prostate anteriorly for managing the lateral pedicles. During an anterior approach, the vasa and SVs are encountered immediately after transection of the posterior bladder wall. While the assistant provides downward retraction of the bladder lip, the vasa are ligated and SVs are skeletonized. Care must be taken to reduce electrocautery use due to the close proximity of the NVBs laterally. The posterior dissection toward the apex is carried out in an identical fashion to the posterior approach.

### Lateral pedicles

Dissection and hemostatic control of the lateral pedicles is performed primarily in small tissue packets using Hem-o-lok clips. Electrocautery use should be minimized to prevent injury to the NVBs. Tension is maintained on the pedicle via lateral retraction of the bladder by the assistant to facilitate the separation of the lateral pedicle into packets with blunt dissection from either the scissor or closed Maryland grasper. Once the assistant places the clip in the defined packet, being careful to stay close to the prostate, the clip is released sharply with scissors. After the lateral pedicle is transected, attention is turned to preservation of the NVBs that course along the posterolateral aspect of the prostate as described by Walsh. The interfascial plane between the prostatic fascia and levator fascia is identified. With a combination of sharp cutting and blunt dissection, the NVBs are released along the fascial plane from the prostate toward the apex. Any significant arterial or venous bleeding can be controlled with careful placement of small Hem-o-lok clips, being careful to avoid entrapment of the NVB. Some authors, with hopes of preserving greater erectile function, have advocated a "high release" of the NVBs because of evidence suggesting that cavernosal nerves can course more anterior to the prostate than previously thought. In this situation, the lateral prostatic fascia is incised along the ventrolateral aspect of the prostate in a similar fashion with hopes of optimizing nerve preservation and revealing the so-called "veil of Aphrodite."

### Apical dissection

With the NVBs released, the DVC is incised with monopolar electrocautery scissors until the anterior urethra is reached, being careful to avoid capsular violation of the prostate. The Foley catheter is reinserted and the urethra is divided sharply a few millimeters distal to the prostate with hopes of preserving urethral length. Next, the posterior wall of the urethra is transected under direct vision, completely freeing the specimen. The specimen is inspected laparoscopically to ensure adequate margins.

### Vesicourethral anastomosis

Two barbed sutures are tied together at the tails and passed to the robotic arms, which have been exchanged for bilateral needle drivers. The anastomosis begins posteriorly with each suture coursing anteriorly on either side of the anastomosis, ensuring bladder and urethral mucosa are incorporated in each throw. The initial posterior throw of each needle is out-to-in on the bladder edge to keep the knot external to the anastomosis. During the posterior approximation of the anastomosis, the assistant can provide perineal pressure to facilitate placement of the urethral sutures. The running anastomosis is continued anteriorly, cinching the barbed suture after each throw by pulling the suture anteriorly to avoid tearing. The urethral catheter tip is passed into view by the assistant before each urethral throw to provide the best view of the urethral mucosal edge. Once the sutures meet anteriorly, they are tied together. Additional throws may be required to further approximate the bladder neck. The anastomosis is tested with the final 18 Fr catheter filled with sterile normal saline and the balloon is filled to 15 ml. Prostate and pelvic lymph node specimens are bagged with a specimen bag.

### Closure and postoperative management

After hemostasis is obtained, the robot is undocked and the ports are removed under direct vision to identify any bleeding from the trocar sites. The specimen bag is extracted through the midline port followed by fascia and skin closure. The 12 mm assistant port fascia can be closed with a Carter–Thomason suture. For the majority of cases, a pelvic drain is inserted through a 5 mm trocar site which is removed just before discharge if no urine or lymph leak is present. Narcotics are used only as needed and ketorolac is used frequently. Patients are typically discharged home within 1–2 days and catheter removal is planned within 10 days without a cystogram if an anastomotic leak is not present. On the night of surgery, patients are given a clear liquid diet followed by full liquid diet and regular fat-free diet for breakfast and lunch, respectively, on post-op day 1.

## Conclusion

Since the introduction of the RALRP, initial skepticism has been replaced with widespread adoption and belief that RALRP may soon become the new gold standard for radical prostatectomy. Supported by long-term functional and oncologic data, the RALRP provides equivalent outcomes. As future advances in robotic technology continue, minimally invasive radical prostatectomy will certainly continue to go through phases of transformation requiring additional studies to ensure patients are appropriately treated.

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## 102

# Optimizing Outcomes During Laparoscopic and Robot-assisted Radical Prostatectomy

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## Introduction

Optimization of the robot-assisted laparoscopic radical prostatectomy (RALP) principally focuses on three main outcomes: cancer control, continence, and erectile function. Innovations that address these areas have been applied preoperatively, intraoperatively, and postoperatively. Although the primary purpose of RALP is the safe removal of cancer, advances in our understanding of pelvic anatomy have allowed RALP to cause the least amount of collateral damage possible. Furthermore, the innovation of the robot-assisted technique allows for higher magnification and vision of tissues as well as increased range of motion with which to manipulate them. Consequently, the past two decades have seen several advances in radical prostatectomy technique, including in bladder neck dissection, prostatic nerve sparing, and urethral anastomosis.

## Preoperative optimizations

### Preoperative waiting period

A delay of six weeks following biopsy has traditionally been recommended to allow inflammation to subside. One single-surgeon retrospective study showed the surgeon was less able to perform bilateral nerve sparing when the procedure was performed within six weeks compared to waiting the six-week period, without seeing any differences in operative outcomes [1]. On the other hand, a large retrospective study showed no increase of adverse events or efficacy of surgery when performed prior to the conclusion of the six-week waiting period [2]. Further studies have shown that a six-week delay is unlikely to adversely affect patient outcomes. A large retrospective study found that adverse pathological outcomes did not develop by delaying prostatectomy until 150 days after biopsy for patients with Gleason <6 and prostate-specific antigen (PSA) 0–10, 60 days for patients with Gleason 7 and PSA >20, and 30 days for patients with Gleason 8–10 and PSA 11–20 [3]. Accordingly, given data showing no worse outcomes within six weeks of biopsy and the desire to avoid unnecessary stress and psychological harm to the patient, prostatectomy may be performed as soon as possible following biopsy.

### Preoperative magnetic resonance imaging

As advances in technology have rapidly progressed, utilization of pelvic magnetic resonance imaging (MRI) has taken on an important role in preoperative planning for patient counseling and surgical preparation. If undertaken post-biopsy, MRI is generally performed 6–8 weeks following biopsy to decrease artifact from hemorrhage [4]. Preoperative MRI, through the use of the Likert scale, can assess for the presence of clinically significant cancer, and can predict both biochemical recurrence and prostate cancer-specific mortality [5, 6]. Furthermore, information for the surgery itself can be gleaned from the MRI and utilized to predict surgical complexity [7]. The use of MRI preoperatively can also be used by the surgeon to assess the location and involvement of nerves and the likelihood of extracapsular spread and seminal vesicle invasion [4, 8]. This knowledge can then be used to direct intraoperative frozen-section analysis to reduce the rate of positive surgical margins (PSMs), though recent data suggests this advantage may only appear in cT1 tumors [9, 10]. Figure 102.1 shows a 3 tesla pelvic MRI with a right-sided lesion abutting the prostatic capsule, providing valuable clinical information about where

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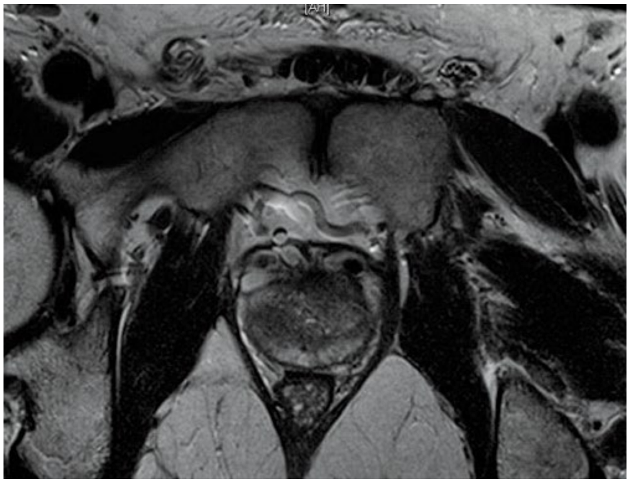

**Figure 102.1** A 3 T T2 signal MRI showing Prostate Imaging Reporting and Data System (PI-RADS) 5 lesion abutting the prostatic capsule on the right transition/peripheral zone.

a wider dissection may be required. Despite the advantages of MRI, it does have certain limitations. The presence of post-biopsy inflammation can impair interpretation, and the sensitivity and specificity of the MRI is radiologist dependent [4]. The complexity of interpretation of the study strengthens the need for specifically trained radiologists interpreting the MRI. An additional limitation is the significant cost associated with the study, and availability and accessibility of high-quality MRI machines. Given its multitude of advantages, pelvic MRI has become an important tool for preoperative optimization.

## Weight loss counseling and preoperative activity level

Preoperative exercise and increased activity are recommended for several reasons. First, several studies have pointed to increased complications and surgical difficulty in patients with greater body mass index (BMI) [11, 12]. The second reason is the desire to limit venous thromboembolism (VTE) by increasing physical activity and avoiding stasis. Finally, patients with higher baseline activity levels preoperatively have comparatively improved quality of life following radical prostatectomy [13]. Increasing preoperative mobility may also help motivate the postoperative patient to resume normal activities more quickly.

## Smoking cessation

Smoking is a demonstrable risk factor for surgical site infections in addition to its other detrimental effects on the body [14, 15]. As a result, cessation counseling should always be provided prior to surgery. Even abstinence of smoking in a current smoker in the perioperative period can lead to decreased risk of infection [15]. There has also been some controversy as to whether smoking cessation has an impact on biochemical recurrence, though the most recent data demonstrate that smoking must be stopped at least 10 years prior to surgery to have an effect on disease recurrence [16].

## Erectile function evaluation

Preoperatively, it is also important to quantify baseline erectile function status for several reasons. First, quantification of baseline establishes realistic expectations for postoperative potency. A recent study demonstrated that even returning to baseline does not always lead to patient satisfaction, making preoperative counseling vital to postoperative satisfaction [17]. Furthermore, patients undergoing RALP have higher expectations with regards to recovery of erectile function than following an open procedure [18]. Preoperative erectile function can be evaluated at the time of biopsy to avoid the psychogenic influences of the immediate preoperative period [19, 20]. Potency and sexual function can be quantified using one of the many validated questionnaires of sexual health such as the International Index of Erectile Function (IIEF).

## Pelvic floor muscle exercises/training

Postoperative urinary incontinence is a potential outcome following RALP and should be approached proactively. A recent meta-analysis demonstrated that preoperative pelvic floor muscle exercises (PFME) might shorten time to recovery of continence. The meta-analysis demonstrated equivalent return to continence at one and six months, but a 36% reduced risk of incontinence at three months with usage of PFME at three months. Most suggested regimens involve physiotherapist guidance beginning 2–6 weeks preoperatively [21]. Yet, several of these studies suffer from biases including improper postoperative comparisons, limited postoperative PFME, or inconsistent continence criteria. Hoping to address this, a prospective randomized clinical trial found reduced risk of incontinence at both one and three months postoperatively for those undergoing 30 days of biweekly therapy [22]. However, in a 180-patient randomized clinical trial, conflicting results were found showing that three weeks of preoperative therapy had no improvement of continence following prostatectomy [23]. The discrepancy between the studies' findings may stem from the difference in definition of continence, with the first using patient's voiding diary and the second using a more stringent definition of 3 consecutive days of 0 g urine loss on a 24-hour pad. Although the data are not conclusive, many of the studies suggest a potential benefit of preoperative PFME without any significant clinical downside.

### Outpatient versus inpatient procedure

Though RALP has traditionally involved a mandatory inpatient admission, efforts have been made in recent years to test the feasibility of performing the RALP as an outpatient procedure. Two small studies conducted by experienced surgeons with carefully selected patients showed that >90% of the patients treated by these surgeons were able to undergo outpatient RALP without any observed detriment to surgical outcomes or patient satisfaction [24, 25].

### Choice of antibiotics

The American Urological Association (AUA) Best Practice guidelines recommend 24 hours of treatment with antibiotics to be started preoperatively for RALP. First-line therapy involves a first- or second-generation cephalosporin or an aminoglycoside or aztreonam with either metronidazole or clindamycin. Second-line antibiotics are ampicillin/sulbactam or a fluoroquinolone.

### Venous thromboembolism prophylaxis

A significant though rare source of morbidity and mortality following RALP stems from VTE, a term comprising both deep venous thromboembolism (DVT) and pulmonary embolism (PE). RALP patients are at risk for VTE due to the extended time spent in lithotomy position. Several studies have identified additional common risk factors for VTE including prior VTE diagnosis, smoking, obesity, and extended operating room time and requirement for lymph node dissection. Accordingly, in complex cases expert consultation is warranted. Studies examining the occurrence of VTE postoperatively found 17% prevalence of asymptomatic VTE and 0.5–2% symptomatic VTE. Critically, most symptomatic VTE events occurred following discharge, with peak occurrence occurring 2–4 weeks following surgery [26, 27]. Consequently, patients should be warned about the signs and symptoms of DVT and PE prior to discharge as well as their potentially catastrophic consequences. A 2009 AUA Best Practice Guideline suggests that all patients should have mechanical prophylaxis and patients with multiple risk factors should be treated with both mechanical and pharmacological prophylaxis. This includes both intermittent compression pneumatic boots as well as either low molecular weight heparin (enoxaparin 40 mg subcutaneous daily) or unfractionated heparin (5000 units every 8 hours subcutaneous starting during or after surgery) [28].

### Choice of equipment in the operating room and safety precautions

The choice of Foley catheter used in the RALP procedure has been shown to have significant postoperative effects. In particular Yee reported decreased stricture rate with the usage of 18 Fr compared to 22 Fr urinary catheters [29]. The extended time spent in Trendelenburg also poses an increased risk for facial edema and corneal abrasions, which can be prevented with the usage of patient safety goggles or other eye protection [30].

## Perioperative optimization

Although preoperative considerations are critical to optimize postoperative outcomes, careful and methodical technique within the operating room is also essential in providing patients with the best chance for a full recovery. All possible measures should be taken to maximize oncologic therapy as well as quality-of-life measures. As cancer control is the most critical component requiring successful treatment during RALP, it will be discussed throughout the following sections since its impact should be incorporated in all steps of surgery.

### Prostatic anatomy

At each step of RALP there is opportunity to optimize outcomes. This process begins with a thorough knowledge of all steps involved in RALP as well as the relevant pelvic anatomy. Although a detailed overview of surgical steps can be found in preceding chapters, the anatomy of the prostate and its nerve supply warrant additional discussion as their preservation is paramount in achieving rapid return to continence and erectile function.

The periprostatic nerve supply has been shown to form a hammock of neurovascular support extending around the base of the prostate and across its posterolateral aspect down to the apex. The hammock is comprised of the proximal neurovascular plate (PNP), predominant neurovascular bundle (PNB), and accessory distal neural pathways (ANP). All of these structures should be preserved to achieve ideal nerve sparing in any patient undergoing RALP, although oncological implications can sometimes make this impossible [31].

The PNP provides a source for integration of neurons surrounding the prostate. It courses lateral to the bladder neck and seminal vesicles before moving posteriorly along the base of the prostate to join the cavernous nerve. The PNB can be found in the lateral pelvic fascia (LPF) and is responsible for the nerve supply of the cavernosal tissue, urethral sphincter, and levator ani.

Since the LPF also contains the ANP lateral and posterior to the prostate, additional care should be taken with any manipulation of this region during dissection [31].

Care also needs to be taken during the apical and posterolateral dissection as this is the area most likely to have positive margins during RALP [32, 33]. A specific technique has been described for apical dissection whereby the conventional approach of ligating the dorsal venous complex (DVC) early is avoided as it can be detrimental to visualization. In one series, 209 patients were treated with a synchronous urethral transection through a retroapical approach and compared to 1665 that had previously undergone traditional anterior urethral transection after DVC ligation. The patients who underwent the novel technique had a lower apical PSM rate (1.4% vs. 4.4%; $P = 0.04$) despite those patient's having a higher incidence of >pT3a prostate cancer (16% vs. 10%; $P = 0.027$) [34].

## Bladder neck preservation

Bladder neck preservation through meticulous dissection of the muscle wall between the bladder and prostate has been shown to improve early return to continence in patients undergoing RALP. One retrospective analysis was completed with 599 patients who underwent RALP and had the level of bladder neck sparing graded from 1–4 with higher numbers denoting more aggressive bladder sparing. There were a higher proportion of patients in groups 3 and 4 compared to groups 1 and 2 who were continent at their three-month postoperative visit. However, by the 1-year mark there was no longer any statistically significant difference in continence [35]. A prospective study examined 1067 men who underwent RALP, 791 of whom had bladder-sparing surgery and 276 of whom did not. The group who underwent bladder neck sparing had less leakage ($P = 0.009$). Cancer control as defined by positive margins and biochemical recurrence was equivalent between both groups [36]. Nyarangi-Dix et al. completed a prospective, single-blinded randomized trial of 208 men who were assigned to either complete bladder neck sparing with urethra–urethral anastomosis or standard RALP. At 3, 6, and 12 months postoperatively patients who underwent bladder neck sparing were shown to have improved continence compared to controls (84.2% vs. 55.3%; 89.5% vs. 74.8%; 94.7% vs. 81.4%, respectively). The men who underwent bladder neck sparing also reported higher quality-of-life (QOL) scores at each visit. Furthermore, there was no significant difference between the two groups with positive margins (12.5% vs. 14.7%; $P = 0.65$) [37]. Bladder neck preservation is a safe technique with regards to oncological outcomes and can facilitate early return to continence.

## Preservation of puboprostatic ligaments

One area of debate during RALP is preservation of puboprostatic ligaments (PPL). Jarow described a reconstruction where the PPL are maintained in normal anatomic position to bolster support of the anterior urethra following radical retropubic prostatectomy (RRP) [38]. An additional study examined postoperative continence in 43 men following RRP where 25 had traditional apical dissection and the remaining 18 had preservation of the PPL. Postoperative questionnaires were completed showing a median time to continence of 6.5 weeks in the ligament-sparing group versus 12 weeks in the standard dissection group [39]. However, another study examined 149 men who underwent either PPL preservation alone, bladder neck preservation alone, or both and found that those who underwent either bladder neck preservation alone or in conjunction with PPL preservation had an earlier return to continence than those who had PPL suspension alone. This study also showed no significant difference in oncologic outcomes between the above techniques [40]. Figure 102.2 displays an intraoperative visualization of PPL sparing.

Another technique to preserve anterior attachments and space of Retzius includes a posterior approach to RALP. Galfano et al. completed 200 RALPs with avoidance of the Retzius structures in favor of dissection through the pouch of Douglas. Although this study was an internal comparison designed to assess the learning curve for this surgical approach, it achieved promising results with regard to continence and erectile dysfunction. Continence was achieved immediately in >90% of patients with 1-year continence rates of 96%. Erectile function had returned after one month in 40% of patients

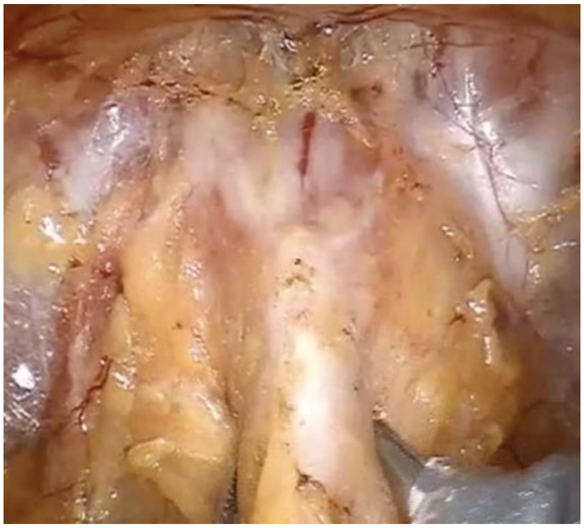

**Figure 102.2** Anterior view of bladder with sparing of puboprostatic ligaments prior to incision of bladder neck.

and by 1 year 70–80% of previously potent men had regained erectile function [41]. Further study into the posterior approach is certainly warranted and many robotic surgeons now champion this technique.

### Preservation of endopelvic fascia

Sparing of the endopelvic fascia (EPF) is another technique with promising results. Khoder et al. performed 231 RRPs for clinically localized prostate cancer without incision into the EPF and found earlier return to continence and potency with preservation [42]. Stolzenburg et al. performed 150 endoscopic, extraperitoneal radical prostectomies without incision into the EPF with 12-month continence rates of 94.3%. They describe a method by which the dissection plane is directly on the prostatic capsule, freeing the prostate laterally and preserving the EPF and PPF as well as the neurovascular bundles (NVBs) [43]. Preservation of the EPF should be attempted in patients where oncologic outcomes are not being sacrificed.

### Preservation of urethral length

Another operative technique to improve both time to and overall rate of continence is preservation of urethral and sphincter length (Figure 102.3). Multiple studies have examined the anatomic relationship between urethral length and continence. Paparel et al. examined 64 men who had undergone MRI before and after radical prostatectomy. Postoperative MRI was completed to assess for local recurrence. Increased mean urethral length was shown to have superior continence as graded on a 1–5 scale by patients. In addition, patients with more periurethral fibrosis were found to have worse continence rates [44]. Nguyen et al. described a new technique for anterior and total reconstruction of the urethra and bladder neck. He examined 274 men who had pre- and post-RALP MRI assessing urethral sphincter length found that in those with urethral sphincters >14 mm, 83% had return to continence (no pads or liner for security reasons) and 99% with the total reconstruction [45].

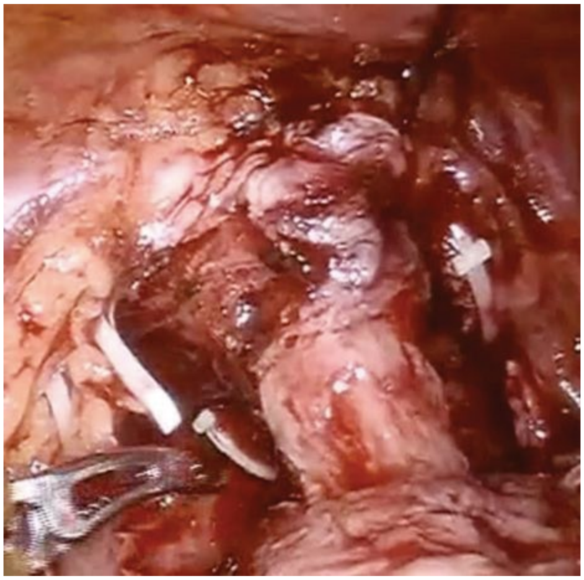

**Figure 102.3** Preservation of maximum urethral length in effort to promote postoperative continence.

### Neurovascular structure-adjacent frozen-section examination (NeuroSAFE)

Nerve sparing during RRP has long been an accepted principle for good functional outcomes after surgery. A relatively new technique, however, involves the utilization of frozen sections in the operating room to ensure that oncological outcomes are not compromised with nerve-sparing technique. The initial study by Schlomm et al. examined 11 069 patients who underwent RRP. During surgery, the entire lateral and rectal border of the prostate specimen was submitted for frozen-section analysis to determine surgical margin status. Of those patients who underwent NeuroSAFE, 1368 had positive margins, with subsequent negative margins being detected in 86% of those patients upon secondary resection. Overall rate of nerve sparing in these patients was significantly higher at all disease stages than without utilization of NeuroSAFE (97% vs. 81%; $P < 0.0001$). Furthermore, NeuroSAFE was found to have no increase in rates of biochemical recurrence [46]. Other studies have confirmed the ability of NeuroSAFE to detect positive margins and convert these patients to having negative margins with improved ability to complete appropriate nerve sparing [47]. Furthermore, the NeuroSAFE technique has also been found to be a feasible alternative specifically for RALP [48].

### Graded approach to nerve sparing

The oncological principles of NeuroSAFE can be augmented through combination with a graded approach to nerve sparing during RALP. A technique for standardized categorization of nerve sparing during RALP has been successfully utilized. Within this categorization, nerve sparing is graded 1–4, where grade 1 requires dissection immediately outside the prostatic capsule medial to the venous plane, grade 2 involves dissection outside the venous layer adjacent to the prostatic capsule (perivenous plane), grade 3 includes dissection through the lateral aspect of the LPF with some adipose tissue visualized on the prostate specimen, and grade 4 involves a wide dissection of the LPF and Denonvilliers' fascia (Figure 102.4). Grade 1 is reserved for patients with

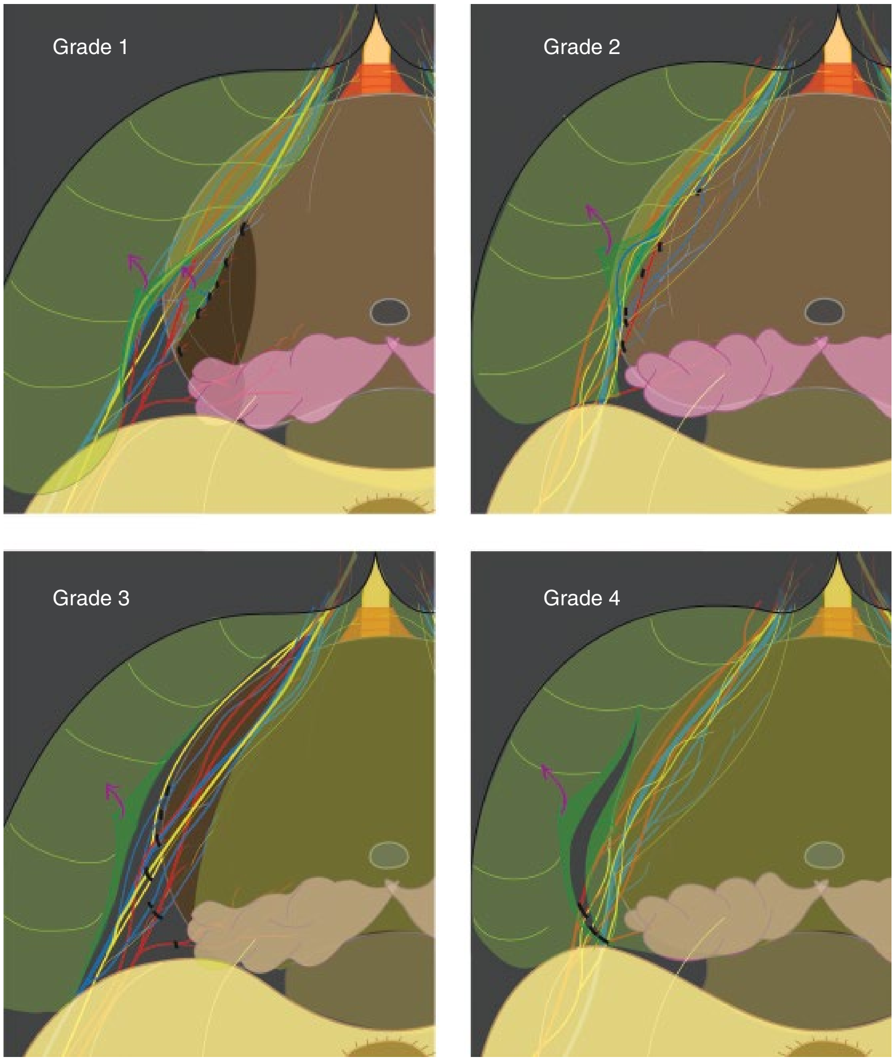

**Figure 102.4** Nerve-sparing grades. Grade 1: nerve sparing immediately lateral to prostatic capsule sparing all nerves. Grade 2: within the venous layer with sparing the majority of nerves. Grade 3: lateral to the venous layer with sacrifice of some nerve trunks. Grade 4: Non-nerve sparing. Key: Nerve fibers (yellow), venous plexus (blue), arterial plexus (red).

minimal risk of extraprostatic extension (EPE), grade 2 for patients with low risk of EPE, grade 3 in patients with moderate risk of EPE since some medial neural trunks are removed, and grade 4 for patients with known EPE. This grading system was retrospectively validated and, when utilized with NeuroSAFE, was able to establish better grades of nerve sparing without any compromise in cancer control [49]. Figure 102.5 shows an anatomic representation of the prostatic fossa following RALP with nerve sparing.

## Periurethral suspension and posterior musculofascial reconstruction

Another means by which some urologic surgeons feel they augment continence involves reconstruction of the bladder neck and urethra (Figure 102.6). In 1992, Klein examined 60 patients who had fascia posterior to the urethra incorporated into their vesicourethral anastomosis with complete continence (no need for pads) achieved in 83% of patients at three months and 88% at last follow-up [50]. Rocco et al. felt a combination of caudal retraction of the urethral sphincter and disruptions of the median posterior raphe were the main contributors to post-prostatectomy incontinence. In 2006 they reported a new technique to combat this problem where the posterior aspect of the sphincter was connected to residual Denonvilliers' fascia and tacked to the posterior bladder wall above the bladder neck. The "Rocco stitch" was examined in 161 patients who underwent RRP and compared to previous 50 patients in whom a traditional anastomosis was completed. The study showed a 90-day

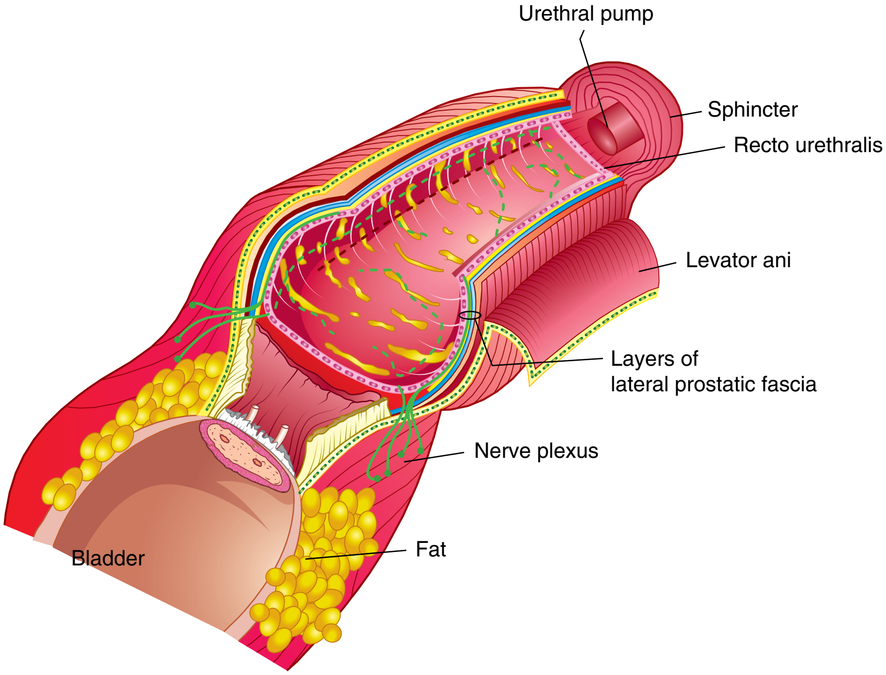

**Figure 102.5** Anatomic diagram of prostatic fossa after complete nerve sparing during robot-assisted laparoscopic radical prostatectomy.

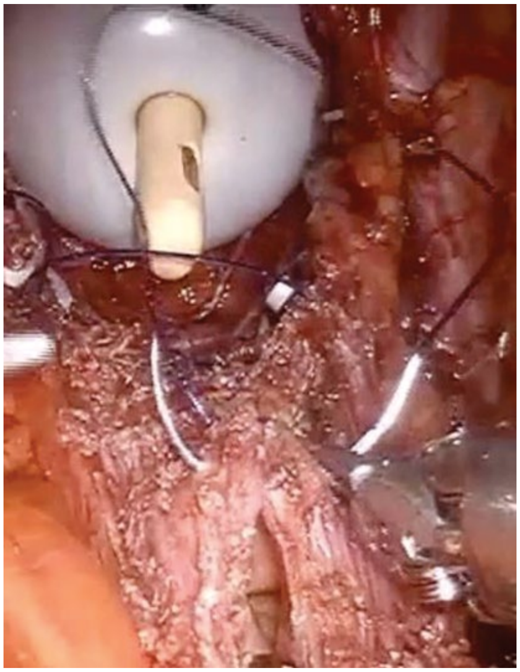

**Figure 102.6** Reconstruction of the bladder neck and posterior myofascial plane to promote postoperative continence.

continence rate of 86.3% in men who received the modified technique versus 46% in those who underwent standard reconstruction [51]. Nguyen et al. examined the effectiveness of posterior reconstruction of Denonvilliers' musculofascial plate and found a greater continence three days after catheter removal with the new technique, as well as an increase on average of 2 mm in postoperative urethral length [52].

At least four randomized trials have also been conducted studying the effect of modified reconstructive techniques on postoperative continence. A prospective, randomized trial of 60 men by Noguchi et al. examined a novel periurethral suspension technique and found the newer procedure had augmented continence at one (53% vs. 20%), three (73% vs. 40%), and six months (100% vs. 83%), respectively [53]. Menon et al. studied 116 men who were randomized to either a single-layer closure or double-layer urethrovesical reconstruction using the anterior and posterior rhabdosphincter for reconstruction. Continence was then examined at day 1, 2, 7, and 30 following catheter removal. The two-layer closure showed improved continence at every interval with the exception of the day 2 measurement. Despite impressive results with regard to continence in both groups, these results were not statistically significant [54]. Another prospective study examined 72 men who were randomized to either standard RALP or RALP with anterior suspension and posterior reconstruction. They found improved continence at one and three months in the modified reconstruction group (7.1% vs. 26.5%, $P = 0.047$; 15.4% vs. 45.2%, $P = 0.016$) with no significant difference in PSM or complications [55]. Finally, Sutherland et al. randomized 94 patients undergoing RALP to either standard running vesicourethral anastomosis or posterior rhabdosphincter reconstruction followed by standard anastomosis. There was no significant improvement in postoperative continence demonstrated with the modified reconstructive technique [56]. Although not all trials have demonstrated improvements in continence with posterior musculofascial reconstructive techniques, there is a potential benefit with early continence without evidence of increased complications. Similarly promising results with regard to periurethral suspension and reconstruction technique have been reported in other trials, further supporting the notion that implementing a similar strategy can optimize postoperative outcomes in patients undergoing RALP [57].

### Avoidance of traction and electrocautery

Throughout the dissection and reconstruction during RALP, great care should be taken to avoid excessive electrocautery. Multiple studies have shown histological and clinical damage is increased when a thermal technique is utilized. Ahlering et al. compared 125 men undergoing NVB preservation with and without the use of electrocautery and found that cases without electrocautery had a more rapid return to potency. Although patients who received electrocautery during dissection did regain potency two-thirds of the time, it generally took at least 12–18 months to recover function [58]. Mandhani et al. compared bipolar to monopolar electrocautery for RRP. They monitored temperature of the prostatic NVB during 25 cases of radical prostatectomy with a rise of 53.6 °C with monopolar and 60.9 °C with bipolar electrocautery, as well as an additional 3 seconds required to return to baseline temperature with bipolar electrocautery. Although the preceding difference was not statistically significant, it may give some credence to avoiding bipolar use during nerve-sparing components of RALP in favor of monopolar when electrocautery is required [59]. Despite other studies failing to show significant difference in return to potency with athermal technique, it is prudent to avoid extensive cautery during NVB dissection [60].

Avoidance of excessive traction is another critical component of RALP. Continuous pressure on the NVB can result in neuropraxia, axonotomesis, and even neurotmesis in severe instances. Wall et al. examined the effects of excessive stretch on tibial nerve fibers in a rabbit model and found that while 6% strain showed 70% return to normal function within 1 hour and complete regaining of function over longer time periods, 12% strain resulted in minimal return of nerve functioning after both 1 hour and the longer study periods [61]. One study examined the effects on 610 men undergoing RALP with and without assistant countertraction at the dissection of the NVB. The group who did not have assistant countertraction showed improved potency at five months (45% vs. 28%), although this difference disappeared by 12 months, suggesting that any nerve paralysis was temporary [62].

### Regional hypothermia

Hypothermia protocols have been used broadly in medicine to decrease inflammatory response and metabolic activity. Thorlacius et al. examined the effect of cooling on microvascular perfusion in hamsters and found that by reducing perfusion by decreasing temperature 8 °C, an inflammatory response in the tissue was avoided with a normal return to perfusion following a warming period [63]. Another study examined the effect of tissue cooling on microvascular response to tumor necrosis factor-alpha (TNF-α) and showed that decreasing tissue temperature by 10 °C for 60 minutes inhibited TNF-α-induced failure of capillary perfusion as well as leukocyte reaction to local injury [64].

Within the realm of prostate cancer specifically, several studies have examined the effect of local hypothermia on postoperative metrics. Finley et al. examined 47 patients undergoing RALP who received pelvic cooling with cold irrigation and endorectal cooling balloon. These patients underwent intraoperative temperature measurement and were compared to controls that underwent standard RALP without cooling. With a median temperature of 25.5 °C, the experimental group had a higher continence rate at three months (86.8% vs. 68.6%) and a faster median return to continence (39 days vs. 59 days) compared to the control group [65]. A follow-up study showed a 1-year pad-free continence rate of 96.3% compared to 86.6% in controls. In addition, there was a significant improvement in potency rates at the 15-month mark (83% vs. 66%; $P = 0.045$) in the hypothermic cooling group [66].

### Autologous nerve grafts and amniotic wraps

A more recent development in the effort to preserve erectile function and promote return to continence after RALP is the use of amniotic tissue around the NVB following dissection. Autologous nerve grafts using both the genitofemoral nerve and sural nerve have been attempted to restore cavernous nerve supply in radical prostatectomy patients without significant success [67, 68]. However, novel therapies with nerve wraps from amniotic tissue have demonstrated benefits with regard to preservation of continence and potency after prostate surgery. Patel examined the use of amniotic wrap around the neurovascular bundle during RALP to assess for possible acceleration of return to continence and potency in men with good preoperative measures in both categories. The study included 58 men who received dehydrated human amnion/chorion membrane (dHACM) wrap around the NVB who were then computer matched with 58 similar patients who did not receive treatment with dHACM wrap. The study showed improvements in time to continence (1.21 months vs. 1.83 months; $P = 0.033$) and potency (1.34 months vs. 3.39 months; $P = 0.007$). Although the dHACM group had higher continence and potency at the eight-week postoperative visit, those results were not statistically significant [69]. In the future, nerve grafts and wraps may provide a novel technique for further augmenting continence and potency following RALP.

## Postoperative optimization

Techniques to improve postoperative continence and potency do not end when the patient enters the recovery room. There are multiple methods by which patients can improve their outcomes after surgery through pharmacology, mechanical devices, and physical therapy.

### Pharmacologic therapy

The first study to examine the impact of medical pharmacology on post-RRP potency utilized intracavernosal injections (ICI) of alprostadil. In 1997, a prospective, randomized trial examined 30 potent men with clinically localized prostate cancer (Gleason 7 or greater) who underwent RRP with nerve sparing. Fifteen men were randomized to receive alprostadil injections three times per week for 12 weeks while the other group received no therapy. The group receiving alprostadil had a significant improvement in potency as defined by spontaneous erections satisfactory for intercourse at six months (67% vs. 20%; $P < 0.01$) [70].

Initial studies in animal populations have shown significant benefits in erectile function with phosphodiesterase 5 (PDE-5) inhibitors. Ferrini et al. examined fibrosis and loss of corporal smooth muscle in rats that underwent either sham operation, bilateral corporal nerve resection, or bilateral corporal nerve resection with postoperative vardenafil therapy and found corporal veno-occlusive dysfunction (CVOD) and decreases in inducible nitric oxide synthase (iNOS) in rats with corporal nerve resection. However, iNOS increased and CVOD improved in those rats treated with vardenafil compared to those who only received surgery [71]. These studies have been repeated with similar results in other animal studies utilizing sildenafil [72, 73].

Oral therapies have also been tested in the post-prostatectomy patient to determine their efficacy in improving potency after surgery. A randomized, double-blinded, placebo-controlled study examined the effect of nightly sildenafil treatment on patients who had undergone RRP with nerve sparing. Patients were given no therapy or one of two different dosages (50 mg or 100 mg) of sildenafil starting four weeks after surgery. Patients were then given 36 weeks of placebo or treatment and an eight-week treatment-free period. The treatment group showed 27% of patients who had experienced satisfactory sexual activity, while the placebo group showed only 4% of patients with that response. However, the extremely low rate of return to potency in untreated men compared to established levels in previously published literature caused a low overall response rate and early study closure [74]. Another randomized double-blinded study was completed in men who underwent bilateral nerve-sparing RRP and were treated with either placebo, nightly vardenafil, or on-demand vardenafil. The IIEF was used to assess patient's potency postoperatively and showed an improvement with on-demand vardenafil when compared to placebo [75].

Intraurethral suppositories have also been examined for potential efficacy with regards to treating erectile dysfunction after RRP. Raina et al. prospectively studied 91 males who underwent RRP with nerve sparing and were treated postoperatively with either Medicated Urethral System for Erection (MUSE) three times per week or on-demand PDE-5 inhibitors for desired sexual intercourse. Sexual Health Inventory for Men (SHIM) was used to assess potency and found that after six months, 74% of men who continued on MUSE had successful intercourse while only 37% of the on-demand group had achieved the successful intercourse. The study was flawed, however, with 32% of men in the MUSE group stopping therapy early secondary to penile aching or burning [76]. Another prospective, randomized trial compared men who underwent nerve-sparing RRP and were treated with either MUSE or sildenafil postoperatively. IIEF was completed in all patients at six months and 1 year, with a significant return to potency in the MUSE group at six months. By 1-year follow-up, however, there was no statistically significant difference between the two treatment modalities [77]. Although both MUSE and oral PDE-5 inhibitors appear beneficial in a return of erectile function following surgery, the discomfort associated with MUSE therapy in addition to its higher cost may make oral PDE-5 inhibitors a better option for patients who have undergone RALP.

PDE-5 inhibitors and local vasodilators are not the only medications with benefits in postoperative potency. Hong et al. prospectively analyzed 50 men without hypercholesterolemia who had prostate cancer and underwent RRP with nerve preservation. The patients were all given sildenafil postoperatively, with the second group also being prescribed atorvastatin 10 mg.

The experimental group exhibited higher sexual satisfaction as defined by IIEF scores ($P = 0.003$) at six-month follow-up [78]. There were minimal side-effects reported with the patients taking atorvastatin and this regimen should be considered in otherwise healthy men who undergo RALP for clinically localized prostate cancer.

Erythropoietin (EPO) injections are another pharmacologic intervention that has shown promising results with regard to erectile function in patients undergoing RALP. Initial animal studies have shown the expression of EPO receptors on neuronal and vascular tissue. They have also exhibited a more rapid recovery of erectile tissue function following cavernous nerve injury [79]. The presence of EPO receptors has been confirmed in human neurovascular prostate and penile tissue samples through immunohistochemical studies [80]. A retrospective analysis of 15 patients who received EPO prior to undergoing RRP with nerve preservation and were prescribed "on-demand" PDE-5 inhibitors showed higher IIEF-5 scores at 3-, 6-, and 12-month postoperative visits ($P = 0.05$) regardless of PDE-5 usage. The experimental group also exhibited a higher percentage of patients performing sexual activity, although those results were not statistically significant [81]. Other animal and retrospective analyses have shown benefits associated with angiotensin II receptor blockers (ARBs) in patients treated with these medications who underwent RRP with nerve sparing [82, 83]. Although these results appear promising, further examination with prospective, randomized trials is warranted to elucidate whether preoperative treatment with EPO and ARBs are warranted in all healthy, potent men undergoing RALP with nerve sparing.

## Mechanical therapy

Pharmacological therapy is not the only postsurgical treatment utilized to preserve potency. Vacuum erection devices (VED) have been employed with significant effect at promoting return of erectile function. One trial randomized 28 men who had good preoperative erectile function (IIEF >11) and underwent RALP with nerve sparing to either early VED use (one month) following surgery or late use (six months) after surgery for 10 minutes per day. The early-use group had higher IIEF scores at both three months (11.9 vs. 1.8; $P = 0.008$) and six months (12.4 vs. 3.0; $P = 0.012$) postoperatively. In addition, the patients who had early VED utilization showed a preservation in stretched penile length at six months while the late-use group showed a decrease in stretched length of approximately 2 cm ($P = 0.013$) during the same time period [84]. Other studies have also shown the preservation of penile length through early utilization of VED as well as potential increase in partner sexual satisfaction and return of potency [85, 86].

## Pelvic floor muscle training and electromyograph biofeedback

Many studies have examined the impact of postoperative physical rehabilitation on return to continence after radical prostatectomy. A Cochrane review was completed examining 50 distinct, randomized trials of patients who underwent radical prostatectomy, transurethral resection of prostate (TURP), or either RRP or TURP. These trials collectively included 4717 men, of whom 2736 had a conservative intervention. Although the authors concluded that there was not sufficient evidence to suggest that conservative interventions after RRP are effective at treating postoperative incontinence, most of their critiques were concerned with lack of standardization in outcome measures rather than the quality of individual studies. The main criticism revolved around the inability of most studies to blind participants and personnel [87]. Despite these deficits, many of the studies which specifically examined pelvic floor muscle training (PFMT) in post-RRP patients alone did show a benefit.

One study randomized 66 men (49 of whom completed the study) who underwent laparoscopic radical prostatectomy to either physical therapy with resistance, flexibility training, and Kegel exercises for 12 weeks to controls who did not complete these exercises. The experimental group reported an improvement in continence (73.1% vs. 43.5%; $P = 0.035$) at the study's conclusion [88]. A larger study randomized 300 consecutive patients who underwent RRP for clinically localized prostate cancer to a structured regimen of PFMT or a control group given no formal training in PFMT following catheter removal. After one and six months, the experimental group showed 19% and 94.6% continence, respectively, while the control group rates were significantly lower at 8% and 65% ($P < 0.001$). At the 12-month postoperative visit, however, there was no statistically significant difference in continence between the two groups [89]. Another randomized, controlled trial found significant benefit to preoperative training session in PFMT with close postoperative follow-up when compared to patients who only received a folder of written instructions on PFMT [90].

Goode et al. conducted a prospective, randomized controlled trial to examine post-RRP patients who were still experiencing incontinence 1 year after undergoing surgery. The trial included 208 men with persistent incontinence 1–17 years after RRP who were randomized to eight weeks of PFMT, PFMT with additional electromyograph (EMG) biofeedback and daily home pelvic floor electrical stimulation, or delayed treatment (control group). Bladder diaries completed by participants showed a 55% and 51% reduction in incontinence episodes in those patient's undergoing PFMT without and with EMG biofeedback/electrical stimulation, respectively, while the control group showed only a 24% reduction in incontinence episodes ($P = 0.001$). There was no significant difference between the two treatment groups [91].

EMG biofeedback has also been proven an effective treatment for post-RRP urinary incontinence. Yamanishi et al. completed a randomized, placebo-controlled trial where 56 men with severe incontinence were randomized to EMG biofeedback or a sham procedure. The active treatment group displayed a statistically significant improvement in continence compared to the group who underwent a sham procedure at one, three, and six months (36% vs. 4%; 63% vs. 16%, and 81% vs. 44%, respectively). Although continence rates were equivalent at 1 year, the results propose an additional method for prompting an earlier return to continence [92].

Electrical stimulation techniques have also demonstrated benefits in post-prostatectomy potency. A randomized, prospective trial of 68 men with prostate cancer who underwent nerve-sparing RRP included an experimental group who started stimulation of the frenulum with a penile vibratory device (PVD) for one week prior to surgery. IIEF-5 scores were higher in the experimental group 12 months after surgery (18 vs. 7.5; $P = 0.09$) [93].

## Conclusions

RALP is a dynamic operation which is continuously evolving. The process by which we optimize patients' postoperative status must incorporate a multifaceted approach to achieve both oncological cures as well as management of erectile dysfunction and urinary continence. Through preoperative planning, including smoking cessation and weight loss counseling, in addition to antibiotic and VTE prophylaxis we can build a solid foundation. With careful anatomic dissection, bladder neck, PPL, and EPF preservation we can further improve our patients' outcomes. Postoperatively, treatment with PDE-5 inhibitors, statins, and other medications in combination with VEDs, PMFT, and biofeedback can provide the best possible opportunity for our patients to maximize early return to full continence and potency. The above interventions, along with novel techniques such as hypothermia protocols and amniotic nerve wraps, make this an exciting time for urologists as well as an encouraging era for patients undergoing surgical treatment for prostate cancer.

See accompanying Video 102.1.

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# 103

# Laparoscopic and Robotic Reconstructive Ureteral Surgery: Basic Principles

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## Introduction

Urological reconstructive surgery is performed for a variety of benign and malignant conditions, and has traditionally been performed using open surgical techniques. The transition toward minimally invasive surgery began when Schuessler et al. performed the first laparoscopic pyeloplasty in the 1990s [1]. The introduction of robot-assisted laparoscopic surgery has increased the use of minimally invasive technique for complex reconstructive urologic surgery [2]. The benefits imparted to the surgeon include enhanced 3D visualization, improved dexterity, greater precision, increased range of motion, and reproducibility.

Initial urologic experience with robotics was largely limited to prostatectomy, and by 2013 nearly 85% of prostatectomies in the United States were performed robotically [3]. As surgeon comfort and experience with robotic prostatectomy grew, robotic technology was adapted to reconstructive surgery, first with robot-assisted pyeloplasty and then by reports of robotic ureteroureterostomy, ureterolysis, ureteroneocystostomy, ureterocalicostomy, and others [4–9]. These procedures have maintained the benefits of minimally invasive surgery, including decreased postoperative pain, short length of hospitalization, and reduced postoperative recovery time, while demonstrating success rates comparable to those for the conventional open approach. Despite these successful series, minimally invasive, and specifically robot-assisted, reconstructive surgery can be technically challenging, which has limited its universal applicability [10–13].

Our institution has been performing robotic upper urinary tract surgery for over 10 years, and at the writing of this chapter we have completed over 300 reconstructive urologic cases [14]. Box 103.1 gives a summary of the common robotic instruments used in robotic reconstructive cases. The essential principles of robotic reconstructive surgery are surgical magnification, precise suturing techniques, well-vascularized tissue, watertight anastomosis, and judicious use of supportive tissues flaps. We continue to advance the field of reconstructive surgery utilizing new techniques such as buccal mucosa for ureteral reconstruction [15], the use of near-infrared fluorescence with indocyanine green (ICG) and dynamic ureteroscopy during robot-assisted ureteral reconstruction to help delineate the borders of ureteral pathology [16–18].

## Patient selection

Prior to bringing a patient to the operating room, the surgeon should determine if the obstructive ureteral pathology is extrinsic or intrinsic, document the length of the involved segment, and identify any surrounding pathology. Preoperative imaging is essential to illustrate the disease process, including length of the defect, and allow for accurate planning of the surgical approach. We advise the use of a three-phase computed tomography scan or magnetic resonance image of the abdomen and pelvis, with dedicated arterial and urographic phases to help identify if ureteric obstruction was from an intrinsic or extrinsic source.

The use of antegrade or retrograde studies help to provide dynamic imaging and aid in the evaluation. If the diseased ureter is severely stenotic and does not allow flow of contrast, simultaneous antegrade and retrograde radiography or ureteroscopy may be necessary to evaluate stricture length. If the patient presents with a ureteral

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**Box 103.1 Robotic instrumentation and equipment list for reconstructive cases.**

**Equipment**

- da Vinci® Si or Xi HD Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA)
- EndoWrist® PK dissector (Intuitive Surgical Inc.)
- EndoWrist Maryland bipolar forceps (Intuitive Surgical Inc.)
- EndoWrist curved monopolar scissors (Intuitive Surgical Inc.)
- EndoWrist Potts scissors (Intuitive Surgical Inc.)
- EndoWrist ProGrasp™ forceps (Intuitive Surgical Inc.)
- EndoWrist needle drivers (2) (Intuitive Surgical Inc.)
- InSite® Vision System with 0° and 30° lens (Intuitive Surgical Inc.)

**Trocars**

- 12 mm trocars (1)
- 8 mm robotic trocars (3)
- 5 mm trocar (1)
- 8 mm AirSeal® Access Port (SurgiQuest, Milford, CT, USA)
- Applied Hasson balloon trocar (Applied Surgical, LLC, Birmingham, AL, USA)

**Instruments used by the surgical assistant**

- Laparoscopic needle driver
- Laparoscopic scissors
- Blunt tip bowel grasper
- Maryland dissector
- Genzyme retractor (Snowden Pencer, Genzyme; Tucker, GA, USA)
- Laparoscopic Doppler ultrasound probe (Vascular Technology Inc. Laparoscopic Doppler System, Nashua, NH, USA)
- 5 mm Ligasure device (for omental wrap) (Valleylab, Tyco Healthcare Group LP, Boulder, CO, USA)
- Ethicon harmonic scalpel (for omental wrap) (Ethicon Endo-Surgery, Cincinnati, OH, USA)
- Linear vascular stapling device (for omental wrap)
- Suction irrigator device
- Hem-o-lok® clip applier (Teleflex Medical, Research Triangle Park, NC, USA)
- Vessiloop (Getz Bros, Chicago, IL, USA)

stent in place, we prefer to remove it, and place a nephrostomy tube to allow for accurate evaluation of the affected ureter. We find that this practice decreases inflammation and allows easier identification of stricture and extent of disease.

Administration of a diuretic may be beneficial to obtain optimal ureteral imaging during the delayed urographic phase. Diuretic renal scans are useful to determine baseline function of the associated renal unit (in case nephrectomy is indicated) and to confirm obstruction in equivocal cases. Patients were considered obstructed if the $T_{1/2}$ was greater than 20 minutes after furosemide and/or if they had a delayed nephrogram on cross-sectional imaging with contrast. In some cases, patients presenting in acute renal failure or with intractable symptoms underwent a decompression procedure with a nephrostomy tube placement before a renal scan could be performed.

The indications for each procedure will be discussed in the individual procedural sections that follow.

## Preoperative preparation

Before undertaking reconstructive surgery, the urologist must be familiar with the use of numerous techniques to address any condition of the kidney or ureter that might surface at the time of surgery. The preoperative surgical plan may be modified intraoperatively when faced with unexpected findings.

Although preoperative imaging can help to guide the informed consent process, patients must be involved in an extensive discussion regarding all possible options for upper tract or lower tract reconstruction, which can include pyeloplasty, ureterocalicostomy, transureteroureterostomy, ureteroureterostomy, buccal mucosa ureteroplasty, ileal ureter, Boari flap, psoas hitch, ureteral reimplantation, autotransplant, and possibly nephrectomy. As a guide for ureteral reconstruction, defects of 2–3 cm may be managed with ureteroureterostomy, whereas defects 4–5 cm are better managed via ureteroneocystotomy; a psoas hitch works well for defects measuring 6–10 cm, a Boari flap can be used for longer defects measuring 12–15 cm in length. Buccal mucosa ureteroplasty can be placed throughout the mid and proximal ureter and lengths of up to 8 cm have been used. In addition, an ileal ureter can be used to replace any length of diseased ureter (Table 103.1).

All possible operative interventions, including open, endoscopic, laparoscopic, and robotic, are thoroughly discussed with the patient during the informed consent process. In addition to bleeding, transfusion, and infection, patients undergoing robotic ureteral reconstruction must be aware of the potential for conversion to open surgery. The possibility of recurrence of ureteral obstruction should also be discussed, in addition to the need for long-term follow-up and the possible need for reoperation. Urinalysis is performed before surgery and any urinary tract infection treated accordingly, and preoperative antibiotics are given prior to commencing the procedure.

**Table 103.1** Reconstructive techniques by location with adjunct procedure.

| Location of ureteral pathology | Surgical technique | Ureteral defect (cm) | Adjunct procedure |
|---|---|---|---|
| Proximal | Pyeloplasty | 2–3 | Downward nephropexy |
| | Ureteroureterostomy | 2–3 | Omental wrap |
| | Ureterocalcostomy | 2–3 | Autotransplant |
| | Buccal mucosa ureteroplasty | 2–6 | Bowel interposition |
| Mid | Ureteroureterostomy | 2–3 | Downward nephropexy |
| | Ureterolysis | Any length | Omental wrap |
| | Buccal mucosa ureteroplasty | 2–6 | Boari flap |
| | | | Bowel interposition |
| Distal | Ureteroneocystotomy (reimplant) | 2–3 | Omental wrap |
| | Ureteroureterostomy | 2–3 | Boari flap |
| | Ureterolysis | Any length | Psoas hitch |

In our practice, we do not routinely place ureteral stents preoperatively, to avoid ureteral edema and potential masking of an intraureteral stenosis. In addition, if a patient comes to consultation with a stent in place, we elect to remove it one week prior to surgery. We elect to place a nephrostomy tube if the patient has pain or fever.

## Selected case indications

### Upper tract reconstruction

**Pyeloplasty**

This is indicated in patients with a proximal ureteral stricture and symptoms or radiographic evidence of ureteropelvic junction obstruction.

**Ureterocalicostomy**

This is indicated in patients with a proximal ureteral stricture and a scarred renal pelvis who have failed prior antegrade or retrograde endoscopic management, or in patients with an inaccessible intrarenal pelvis.

**Ureteroureterostomy**

This is indicated in patients with proximal or mid-ureteral strictures that have been refractory to endoscopic treatments and in patients with ureteral obstruction secondary to a retrocaval ureter. The length of the stricture should be short enough, 2–3 cm, for a tension-free anastomosis.

### Pan-ureteral disease

**Ureterolysis**

Robotic ureterolysis with omental wrap can be performed in patients with ureteral obstruction secondary to retroperitoneal fibrosis. This procedure can be done unilaterally or bilaterally as dictated based on the patient's clinical scenario. It is important to rule out the presence of lymphoma or other retroperitoneal malignancy, a frozen section of the retroperitoneal tissue is sent prior to proceeding with any ureterolysis procedure.

### Lower tract reconstruction

**Ureteroneocystostomy (± Boari flap)**

This is indicated in benign or malignant pathology which entails the resection of distal ureter and the need to bridge a gap of 4–15 cm. We work in a stepwise approach; if the defect is 4–10 cm we perform a ureteroureterostomy with the addition of a psoas hitch sometimes combined with a ureteral reimplantation to ensure a tension-free anastomosis. For large ureteral defects measuring 10–15 cm, a Boari flap combined with psoas hitch may be used.

## Operative setup for robotic reconstructive surgery

Careful consideration must be given to operating room configuration due to the varied components of the procedure, including the robotic approach and the cystoscopic/ureteroscopic evaluation. Practical consideration must include positioning of the screens for the cystoscopic tower as well as the video tower for the robot.

## Patient positioning and preparation

The operating room setup depends on the location of the proposed reconstruction. For upper tract ureteral reconstructions we place the patient in a flank position similar to that used for a partial nephrectomy (Figure 103.1). This position is modified to ensure that the ipsilateral arm remains in an anatomic position. Two gel rolls are placed behind the patient, one at the upper back and the other at the lower back and buttocks, to help maintain a 45–60° angle. A bolster is placed under the patient's axilla to prevent brachial plexus injuries, and a rolled-up foam pad can be placed between the upper shoulder and neck for additional support. The patient's lower arm is placed on an arm board, and foam pads are stacked on top of it to create a place for the patient's upper arm to rest comfortably.

To improve access for the superior robotic trocar we place ipsilateral, upper arm, in a neutral position and a tape sling is placed under the elbow for support. The lower leg is flexed at the hip and knee while the upper leg is positioned straight; a pillow is placed in between the legs, and sequential compression boots are also employed for deep venous thrombosis prophylaxis. The patient is secured to the table with 3-inch silk or cloth tape. Attention is paid to ensure that all pressure points are padded. Once docked, the table is maximally rotated to allow gravitational mobilization of the bowel.

For mid-ureteral surgery a lateral to semilateral decubitus position or a lateral decubitus position with the patient in a modified low-lithotomy position is employed to provide access to the bladder for ureteroscopy or stent placement. Again we pad the patient with gel pads, axillary rolls, and do not bend the ipsilateral arm. These maneuvers protect against nerve injury while allowing for simultaneous cystoscopy and ureteroscopy. The robot is docked at a 90° angle to the operating table with the robot in line with the camera trocars.

For lower ureteral reconstructions, the patient is placed in a low-lithotomy position, with the robot docked between the patient's legs with steep Trendelenburg, similar to a robotic prostatectomy. For pan-ureteral reconstruction we usually place the patient in a lateral or semilateral decubitus position. The patient's anterior superior iliac spine is placed directly over the flexion pivot of the operating table to allow for maximal patient flexion when desired.

In all cases, the bedside assistant and scrub nurse stand contralateral to the affected ureter to facilitate the passing of instruments. The screen for the robot is placed cephalad to the robot and the cystoscope tower is placed caudad to the robot to allow both the bedside assistant and the surgeon performing ureteroscopy to see their respective screens.

It is important to note that the positioning of the table and robot can be changed intraoperatively to access other areas of pathology throughout the urinary tract. This may require placing an additional robotic trocar and changing the position of the robotic arms.

## Trocar configuration

### Upper tract port setup

Four or five trocars are used. A camera trocar is placed directly above the umbilicus and two robotic trocars are

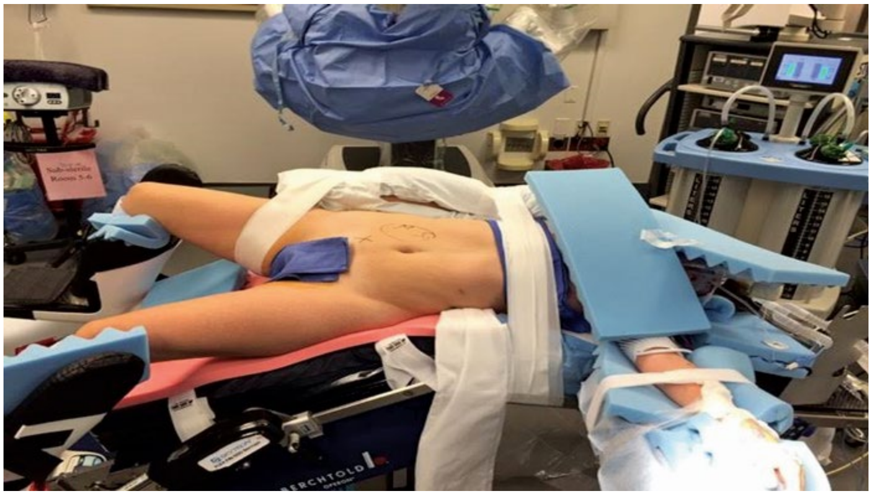

**Figure 103.1** Operating room positioning for reconstructive urology with ureteral access.

positioned 2–4 cm lateral and 8–10 cm away from the origin in either direction. These three trocars create a "V" shaped configuration. The fourth arm (optional) robotic trocar is placed in the lower quadrant 2 cm above the pubic bone in the midclavicular line, and the assistant trocar is just below the umbilicus (Figure 103.2a). For an obese patient this template is shifted laterally to ensure there is adequate access. Prior to docking, the table is maximally rotated to full flank to allow gravitational mobilization of the intestines. The robot is then brought in perpendicular to the operating table. The robot is docked at a 90° angle to the operating table with the robot in line with the camera trocars.

### Distal ureter port setup

Five trocars are used as follows. A camera trocar at the umbilicus, two robotic trocars to the left: one just lateral to the umbilicus in the midclavicular line and the other 2 cm superior to umbilicus in the anterior axillary line. We place a robotic trocar lateral and to the right of the umbilicus in midclavicular line and an assistant trocar above, between these two trocars (Figure 103.2b). The robot is then brought between the patient's legs.

Our institution uses AirSeal® (SurgiQuest, Milford, CT, USA) which provides stable pneumoperitoneum throughout the case through the assistant port. If AirSeal is not available, standard insufflation techniques may be used instead. In terms of access, we use the Hasson technique, and the Applied gel trocar (Applied Surgical, LLC, Birmingham, AL, USA).

## Specific techniques for reconstructive urology

### Cystoscopy and ureteral stent placement

If cystoscopy, with or without stent placement, or retrograde pyelography is needed we utilize the modified flank low-lithotomy position. Retrograde pyelography allows confirmation of the level and length of the compromised ureter. We also find that this helps reduce the number of inadvertent ureteral injuries during mobilization. In addition, the stent may be helpful in identifying the ureter with intraoperative ultrasonography in cases of severe fibrosis and inflammation.

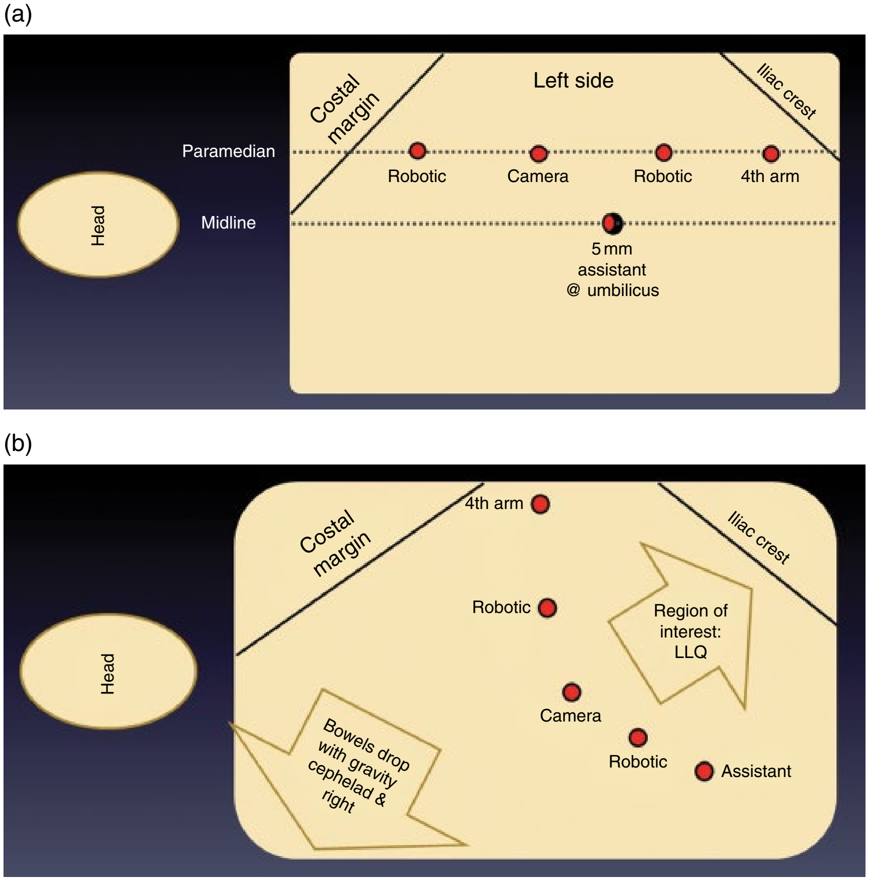

**Figure 103.2** Port placement for upper tract reconstructive urology. (a) Port placement for upper tract reconstructive urology: kidney, upper and mid ureter. (b) Port placement for bladder and distal ureter reconstructive urology.

## Surgical steps

### Exposure of ureter

Exposure of the entire ureter is of paramount importance; this is accomplished on the left by medializing the colon to the aorta from the spleen to the bladder, and on the right by medializing the colon and duodenum to the vena cava from the liver to the bladder. Having the table rotated so that the patient is in flank helps with this exposure. The console surgeon utilizes the bipolar graspers in the left hand and the curved robotic scissors in the right, while the bedside assistant uses a suction/irrigator. The amount of ureter that needs to be exposed is procedure and patient specific, but we find that this technique can easily allow exposure of the entire retroperitoneum, clearly demonstrating landmarks such as the gonadal vessels, iliac vessels, and lower pole of the kidney. We have also utilized intraoperative ultrasonography, intraureteral ICG and intraoperative ureteroscopy to identify the ureter [16–18].

### Exposure of kidney

We start by reflecting the colon medially along the white line of Toldt. The peritoneum overlying the inferior aspect of the kidney is then carefully dissected and mobilized off Gerota's fascia, which is then incised to locate the ureter which is carefully dissected free of the surrounding tissues. The ureter is traced cranially toward the renal pelvis, and meticulous efforts are made to avoid excessive handling/manipulation of the ureter and to leave tissue surrounding it to maintain perfusion. As dissection of the ureter approaches the renal pelvis, care should be taken to identify and preserve any crossing vessels.

### Exposure of the bladder

We start by dividing the urachus and developing the space of Retzius (between the medial umbilical ligaments) all the way down to the endopelvic fascia; this is very similar to a prostatectomy. Although rarely necessary, the contralateral superior bladder pedicle may be transected to increase bladder mobilization. Another technique to improve bladder mobilization is to incise the bladder horizontally and then stretch it vertically to the psoas muscle in a Heineke–Mikulicz technique. In all cases we perform a psoas hitch. We believe this minimizes tension at the anastomosis and keeps the path of the ureter lateral and away from bowel. We use 2-0 polyglactin or barbed suture on an SH needle to fix the posterior bladder wall to the psoas muscle tendon after identifying and avoiding the genitofemoral nerve. By performing a complete mobilization procedure we can insure a tension-free ureteral anastomosis.

When determining the site for ureteral reimplantation on the bladder, our goal is to always reimplant into the most posterior aspect of the bladder. We find that this prevents intermittent obstruction of the ureter during passive urine storage. To identify this we fill the bladder with 200–250 ml of saline and then split the overlying detrusor fibers to identify the mucosa. The mucosa is incised sharply and the neocystostomy is performed. In addition, a flexible cystoscopy can be used; simply dimming the light of the robotic camera and identifying the light from the cystoscope provides a clear location. Intraoperative cystoscopy is also very useful when additional bladder procedures are required, such as removal of a bladder diverticulum.

## Ureteral suturing

### Ureteral–ureteral

With the aid of da Vinci Potts scissors, we perform a spatulation of at least 10 mm. Once it is confirmed that a tension-free anastomosis can be performed, we use two 4-0 polyglactin sutures (a dyed and an undyed) on an RB-1 needle. We anchor the dyed suture laterally and the undyed suture medially. We place a double-J stent under direct visualization and the anterior anastomosis is then completed in a running fashion with the dyed suture, in a lateral to medial fashion.

### Ureteral–pelvic

Following removal of the diseased ureteropelvic junction and spatulation of the proximal ureter, we begin our anastomosis with a 4-0 polyglactin suture on an RB-1 needle placed through the apex of the spatulated ureter and at the most dependent portion of the renal pelvis. The posterior anastomosis is then performed in a running fashion. If redundant pelvis tissue has been excised, the remaining pyelotomy incision is closed using additional sutures.

### Ureteral–vesical

After the bladder mucosa has been entered we perform a running anastomosis using two 4-0 polyglactin sutures on an RB-1 needle, one for the lateral wall and one for the medial wall. This is followed with an intermittent 3-0 suture to reapproximate detrusor fibers over the neocystotomy and to obtain a watertight closure.

Following all ureteral reconstructive procedures, a closed suction drain is placed near the surgical field.

## Specific considerations

### Bilateral disease

In cases where bilateral ureteral surgery is needed (ureterolysis), we typically undock the robot, cover or close all trocar sites, move the robot to the contralateral side and reposition the patient with the contralateral side facing up. Our average repositioning time has been 20 minutes.

#### Tissue bolstering (omental wrapping or Gerota's fascia pedicle)

Bolstering the ureteral anastomosis with a well-vascularized tissue scaffold promotes healing for ureteral reconstruction. For mid or distal ureteral reconstruction we often use an omental wrap. The surgeon uses bipolar graspers in the left hand and ProGrasp™ forceps in the right, while the assistant uses atraumatic graspers to expose and isolate the omentum. Once the omentum is identified, the vessel sealer is used to harvest the omental pedicle. The most distal portion of the pedicle is brought underneath the ureter and tacked to the sidewall with a 3-0 polyglactin suture. Next, the lateral pedicle is tacked to the sidewall, allowing the entire omental flap to lay posterior to the ureter. The medial edge of the omentum, which is also medial to the ureter, is now wrapped anterior to the ureter and tacked to the sidewall. To prevent internal hernia, the window between the omentum and kidney should be closed.

We prefer to cover proximal ureter or ureterocalicostomy anastomosis with a vascularized pedicle of Gerota's fascia. We believe this improves healing, adds blood supply, and may protect from urine extravasation. As with all our ureteral reconstructions, a closed suction drain is placed near the reconstruction to detect urine leakage in the postoperative period.

#### Renal hilar control and use of intraoperative ultrasound for ureterocalicostomy

After the renal hilum is isolated, the psoas muscle is identified and the posterior surface of the kidney is dissected off the psoas. The kidney is then lifted anteriorly, placing the renal hilum on stretch. This retraction is supplied by the assistant or the fourth arm using a ProGrasp™ forceps, allowing the console surgeon to use two hands/instruments for the hilar dissection. A Doppler probe is used to identify the renal artery and vein, which is often encased in fibrotic tissue. The vessels are then dissected free from the surrounding tissue and isolated. A laparoscopic Doppler ultrasound probe is then introduced to identify the most dependent lower pole calyx. Gerota's fascia is cleared off this segment of kidney circumferentially. Prior to clamping the artery we ensure the patient is adequately volume resuscitated and administer 12.5 g of mannitol in an attempt to minimize ischemia–reperfusion injury.

#### Tension-free anastomosis

As in any reconstructive surgery, the main principles include the need to achieve tension-free, watertight anastomosis to allow for dependent drainage. If there is any concern that ureteral length is preventing a tension-free anastomosis, a downward nephropexy may be performed to allow the ureter to reach the calyx more easily and without tension. This is performed by mobilizing the kidney inferiorly and suturing it to the psoas muscle using a 2-0 barbed suture. If a tension-free anastomosis cannot be performed with this maneuver a renal autotransplant can be performed in an attempt to salvage the kidney. If kidney salvage is not possible, a simple nephrectomy should be performed. All surgical possibilities should be listed on the consent documentation, as part of the informed consent, prior to starting.

#### Exiting the abdomen

The operative site is examined for bleeding under low insufflation pressure, and hemostasis is achieved. The trocars are then removed under laparoscopic view. The robotic arm and assistant trocars generally do not require fascial closure but are simply closed subcutaneously.

## Postoperative management

Patients typically remain in the hospital for 1–2 days. On the first postoperative day, patients begin a clear diet, aggressive ambulation, and oral pain medication. The urethral catheter is removed on postoperative day 1 or 2 for a trial of void, and 8 hours later the output of the Jackson–Pratt (JP) drain is sent for creatinine analysis to rule out a urine leak. If the JP fluid analysis is consistent with serum and not urine, the drain is removed. Diet is advanced, and the patient is discharged. The stent is removed with an office cystoscopy in 4–6 weeks, and appropriate imaging studies are obtained thereafter.

## Tips and tricks

### Atraumatic ureteral traction

A Vessiloop® (Getz Bros, Chicago, IL, USA) can be placed around the ureter to aid the bedside surgeon in applying atraumatic traction on the ureter during dissection. Careful dissection is continued to free the ureter up to the area of stricture, at which point any of the above described maneuvers can be used to confirm the distal end of the stricture.

### Retrograde stent placement during ureterocalicostomy

Prior to completion of the anastomosis a wire is advanced through the open-ended stent into the pelvis. The double-J stent is placed in a retrograde fashion, under direct vision. Care must be taken if antegrade stent placement is elected, as this maneuver can creates significant tension on the anastomosis during the passage of the wire and stent.

### Obstructed kidney with concurrent stones

If stones are present, a flexible cystoscope or ureteroscope is introduced by the assistant through one of the trocars and then passed through the open lower pole calyx to examine the internal collecting system of the kidney. Any encountered stones are retrieved with a 1.9 Fr tipless nitinol basket (Boston Scientific, Natick, MA, USA).

### Use of indocyanine green during robot-assisted ureteral reconstruction

In select cases where preoperative imaging or intraoperative studies cannot fully visualize the ureteral stricture, secondary to periureteral inflammation which often coexists with the underlying pathology, the use of ICG may help to document the full extent of the ureteral disease. ICG aids in the identification of the proximal and distal ends of healthy ureteral tissue to help define the boundaries of the ureteral pathology. Specifically, this technique identifies poorly perfused ureteral tissue as dark green, and well-perfused tissue as bright green. This technique has since been used by other groups to minimize complications related to poor blood supply. [16, 17]. While ICG is used as an intravenous injection during partial nephrectomy, we use an intraureteral instillation of 5 ml for ureteral reconstruction. It must be noted that intraureteral ICG is an off-label use. ICG can be instilled either via a preexisting percutaneous nephrostomy tube or via a ureteral catheter, placed intraoperatively. We suggest that the surgeon waits 5–6 minutes after the ICG is instilled before activating the Firefly™ camera.

### Use of dynamic intraoperative ureteroscopy

Because ICG can be lost after ureteral transection, we have developed a technique which allows for dynamic ureteroscopy and concomitant fluorescent visualization, without the need for ureteral instillation. The light source filter of the ureteroscope can be changed to near-infrared setting and the Firefly camera will identify the ureteroscope's light as green, similar to the color of ICG (Figure 103.3a–d) [18]. We find this especially useful in complex cases which require significant reconstruction. Fluorescence imaging allows for confident and improved ureterolysis in the setting of significant scarring and fibrosis. This technique can be used for ureteral or renal pelvis reconstruction and we have successfully performed ureterolysis, pyeloplasty, and other robotic reconstructive cases with dynamic intraoperative ureteroscopy [19].

## Steps to avoid complications

Wide exposure is essential to identify the transition from healthy to diseased ureter as adjacent structures may be involved in the disease process. An athermal technique favoring sharp dissection is essential to avoid potential compromise of the blood supply to the already diseased ureter, which can develop into ischemia and urine leakage. The use of omentum provides vascularized tissue which promotes healing. A surgical drain helps to identify diagnosis and quantify postoperative urine leaks, which may delay urethral catheter and stent removal.

## Assessing treatment success

We use radiological imaging, renal scans, to determine postoperative success. If the postoperative renal scan identifies a $T_{1/2}$ of <20 minutes, there is no obstruction and the surgery was successful. For patients with ipsilateral preoperative renal function ≤25% that persists after surgery and a postoperative $T_{1/2} > 20$ minutes we rely on radiographic endpoints. We define radiographic success as an improvement in the drainage curve and/or improved hydronephrosis. This exception was made secondary to the fact that poor renal function can affect calculations by nuclear medicine scan. Other patients undergoing reconstructive procedures are assessed for resolution of obstruction with retrograde pyelogram and resolution of hydronephrosis with ultrasonography. Lastly, symptomatic improvement is assessed by history on follow-up visits.

## Identifying complications of robotic reconstructive surgery

### Intraoperative complications

General principles of perioperative care apply to patients having urologic reconstruction and include the use of bilateral sequential compression boots, prophylactic antibiotics, and generous padding to all pressure points. We must preface that there are limited data, from small case series, on robotic reconstructive procedures. However, overall, the intraoperative complication rate is low and there was no significant morbidity noted in published series of robotic reconstructive cases [5–9, 12, 13].

**Ureteral reimplantation**
One specific study compared open laparoscopic and robotic ureteral reimplantation in 130 patients. While there was a 5% rate of intraoperative complications in the laparoscopic group, most commonly inadvertent ureterotomies which

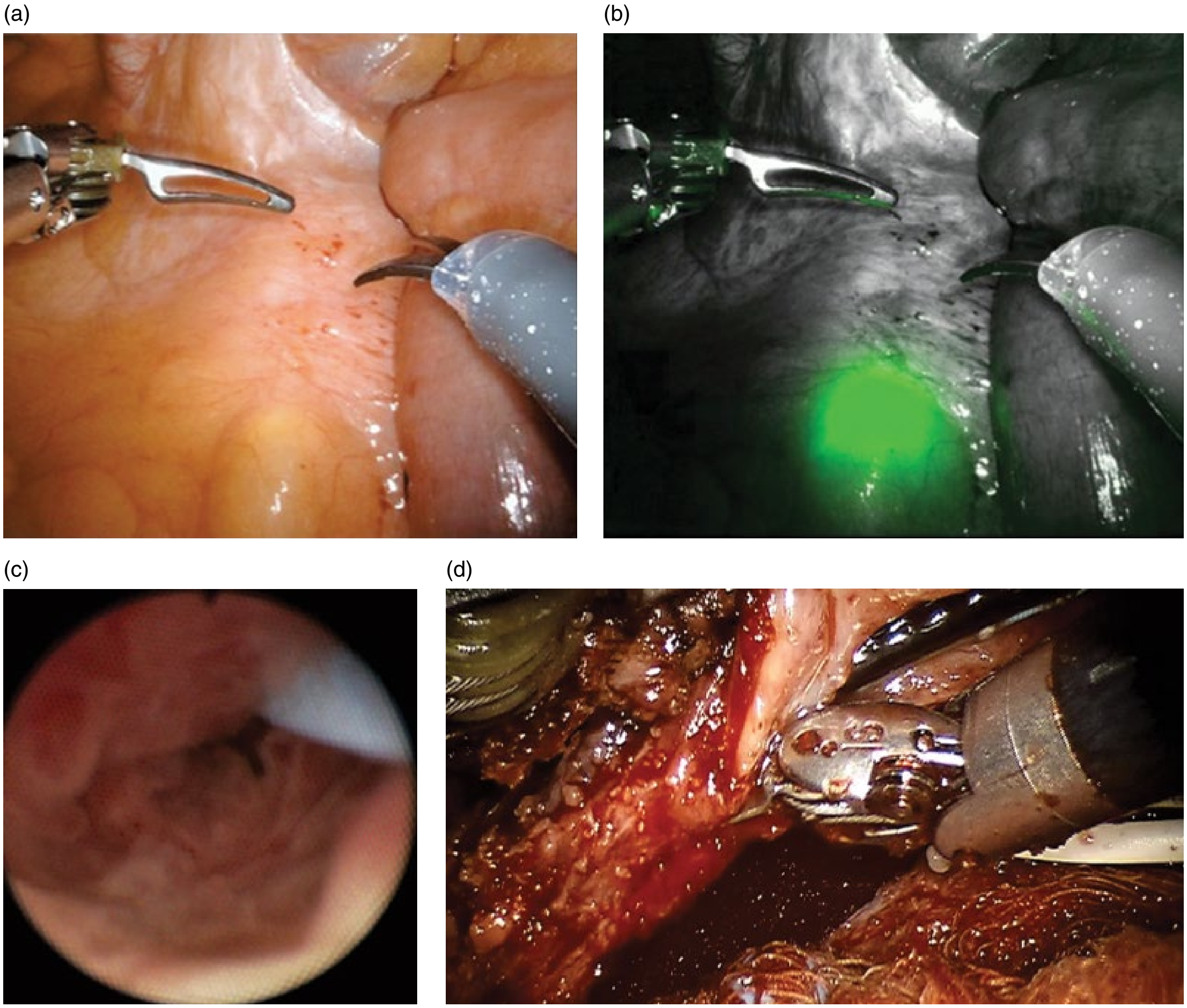

**Figure 103.3** The ureter in (a) white light and (b) fluorescence mode. The light of the ureteroscope within the ureter can easily be seen in fluorescence mode. (c) Ureteroscopic view of the strictured segment. (d) Ureteroscope seen after incision into the ureter, additionally the ureteroscope can be left in the ureter during anastomosis to prevent the misplacement of the suture into the back wall of the ureter.

were repaired intraoperatively and an enterotomy which required small bowel resection, there were no complications or conversations in the robotic cohort [12]. The authors noted the robotic approach provided superior visualization which made suturing easier and resulted in increased hemostasis and fewer complications. In addition, two studies with a total of 35 robotic procedures found significantly shorter hospital stay and reduced blood loss compared to the open surgical approach [9, 13].

**Ureterolysis**

Ureteral injury is the most common complication of ureterolysis [20]. These injuries should be repaired primarily, if possible, based on the extent and location of injury. An omental wrap or intraperitonealization should be performed to protect the ureteral anastomosis [21]. Robotic ureterolysis has been performed without morbidity and continues to be a safe technique. The magnification may facilitate identification of the ureter, and the use of limited tissue handling and the precision of robotic Pott scissors can help with dissection and prevent the risk of injury to the ureter [22].

## Postoperative complications

A review of the literature has identified that the majority of complications of robotic reconstructive surgery are postoperative [10, 11]. However it is difficult to separate the intraoperative injuries which were missed and identified in the postoperative period. The surgeon should be attentive for patient symptoms that cannot be explained by physical examination or routine studies and should be quick to investigate further. CT scans have been shown to identify a diagnosis in patients with unexplained pain, fever, or laboratory abnormalities following reconstructive surgery [23]. Documented postoperative complications of robotic ureteral reconstructive surgery include prolonged ileus, ureteral anastomotic leak, urinary retention, and port site erythema [20, 24].

#### Ureterolysis

In two studies of robotic ureterolysis involving a total of 22 procedures one perioperative ureteral leak was identified that was managed with prolonged Foley catheter drainage and ureteral stent placement, and one case of enterocutaneous fistula which required small bowel resection due to an unrecognized cautery injury [22, 25]. Robotic ureterolysis was unsuccessful in 7 of 40 patients (18%) and a second surgery required for persistent obstruction. Another study produced similar results with 14% requiring reintervention with ureteral reimplantation, robotic ureteroureterostomy, or laser endoureterotomy [14]. The use of intraperitonealization or omental wrapping can potentially prevent the risk of recurrent obstruction and need for additional interventions. Intraoperative ureteral stent placement may minimize the risk of postoperative obstruction or urinary leak [21].

#### Minimally invasive ureteral reimplantation

Robotic ureteral reimplantation has been shown to be safe in patients with minimal postoperative complications. Minor complications were common in a study of 16 patients where 75% had a postoperative complications. The majority included urinary tract infection, pneumonia, ileus, prolonged anastomotic healing, and prolonged abdominal pain. There was a small number of patients (13%) who required additional procedures [8]. Conversion to open approach is an uncommon intraoperative complication during robotic ureteral reimplantation or ureteroureterostomy, and was reported in two out of 16 patients (13%) in one study [26].

Anastomotic strictures following minimally invasive reimplantation was found in 10% in a study of 61 pediatric patients who underwent robotic extravesical reimplantation [27]. We use renal ultrasound as the first step in making the diagnosis, with excretory urography as confirmatory test. Placement of a ureteral stent is usually indicated to drain an obstructed system. If a stent is not possible, however, percutaneous nephrostomy tube placement may be necessary. Postoperative stricture can be managed initially conservatively with dilation, but if recurrent it may ultimately require additional surgeries to insure patient anastomosis. Transient obstruction secondary to edema is common postoperatively, and stenting for 4–6 weeks postoperatively is recommended. However, surgeons should be aware that after the stent is removed, patients may experience transient obstruction and may require stent replacement [28–30].

Urinary leak is a known postoperative complication and can be managed with maximal drainage, Foley catheter, and indwelling stent, and consideration of percutaneous drain placement. We suggest that a cystogram should be performed at the time of stent removal to confirm the absence of leak.

#### Minimally invasive ureteroureterostomy

The most common postoperative complications of robotic ureteroureterostomy include anastomotic stricture and urinary leakage. Although the published rates of postoperative complications for robotic ureteroureterostomy are low, a small series of eight patients were found to have a 25% rate of postoperative complication. All patients had radiographic and symptomatic success rates following surgery [14, 31, 32]. Obstructed retrocaval ureter have been repaired robotically by resecting diseased ureter and performing ureteroureterostomy without postoperative complications [6, 33, 34].

A significant amount of literature has shown that robotic ureteral surgery is safe for the treatment of upper urinary tract urothelial cell carcinoma. Proximal segmental ureteral surgery with ureteropelvic anastomosis and distal ureterectomy with reimplantation have both been performed for low-grade urothelial cell carcinoma without complications [35–38].

## New techniques in robotic reconstructive surgery

Complex proximal ureteral strictures can be challenging to manage. Although distal to mid-ureteral strictures can be successfully managed with ureteral reimplantation with psoas hitch or Boari flap, proximal ureteral strictures are often managed with ureteroureterostomy. However, when the afflicted ureteral segment is long, adequate mobilization to bridge the gap between healthy distal and proximal ureteral mucosa to allow for ureteroureterostomy may not be possible. Long or multifocal proximal ureteral strictures may require ileal substitution or autotransplantation of the kidney, options which are associated with significant potential morbidity from bowel and vascular complications.

The first use of oral mucosa grafts for ureteroplasty was in an animal model in 1984 [39]. Open buccal mucosa ureteroplasty has been used, but had not gained widespread use, because buccal mucosa is not often used by urologists [40–42]. However, for reconstructive urologists, buccal mucosa grafts have been a mainstay of treatment for ureteral strictures since it was first described in 1941 due to particular characteristics that make it ideal for the urinary tract [43, 44]. It has a pan-laminar vascular plexus ideal for engraftment and a thick nonkeratinized epithelium compatible with a wet environment. It is a graft material that has proven to be durable in the urinary tract without the risk of metabolic complications associated with use of bowel interposition [45].

## Indications and contraindications

Buccal ureteroplasty should be considered in patients with long or multifocal proximal ureteral strictures that are not amenable to ureteroureterostomy and that are being considered for autotransplantation or ileal ureter. Ureteral injury may be due to various etiologies such as trauma, iatrogenic injury from ureteroscopy or failed prior reconstructive surgery, or long standing nephrolithiasis. Renal scan should be performed to demonstrate obstruction, and adequate function in the affected kidney. Contraindications to buccal ureteroplasty include any oral diseases that prevent harvest of oral mucosa.

## Surgical steps

Following exposure of the ureter, we perform simultaneous ureteroscopy to allow for identification of the distal extent of the stricture. The use of dynamic ureteroscopy or intraureteral ICG can be used to confirm the extent of ureteral disease. Both the proximal and distal ends of the ureteral stricture are marked with a stay suture.

The graft site is prepared by making a ureterotomy lengthwise through the previously demarcated stricture segment until healthy-appearing normal-caliber ureter is reached proximally and distally. We have performed both anterior and posterior ureterotomies for buccal mucosa graft onlay. It has not yet been determined whether one approach is advantageous over the other.

The buccal mucosa graft (BMG) is prepared in the standard fashion and introduced into the abdomen through the assistant port and sutured onto the ureterotomy as an onlay graft (Figure 103.4). The edges are sutured in running fashion using 4-0 polyglactin suture. Dynamic ureteroscopy allows for visualization of the anastomosis from the ureteral lumen and early recognition of a misplaced of the suture to prevent improper ureter reconstruction. After the anastomosis is complete, a double-J ureteral stent is placed in retrograde fashion over a wire, and a Foley catheter is placed.

Graft survival depends on adequate apposition of the graft to its blood supply and we frequently use a flap of omentum because of its convenient location and ease of harvest. The omentum is prepared as previously described, and sutured to the omentum to maximize graft apposition to its new blood supply. If there is no omentum available, a flap of perirenal fat or the psoas muscle may be used to provide blood supply. As in previous reconstructive cases, we place a drain by the surgical site in case of urine leakage.

## Postoperative management

Patients undergoing buccal mucosa reconstruction require additional postoperative instructions. The use of antiseptic mouthwash protects the buccal mucosa harvest site, and we slowly advance the patient's diet. If a

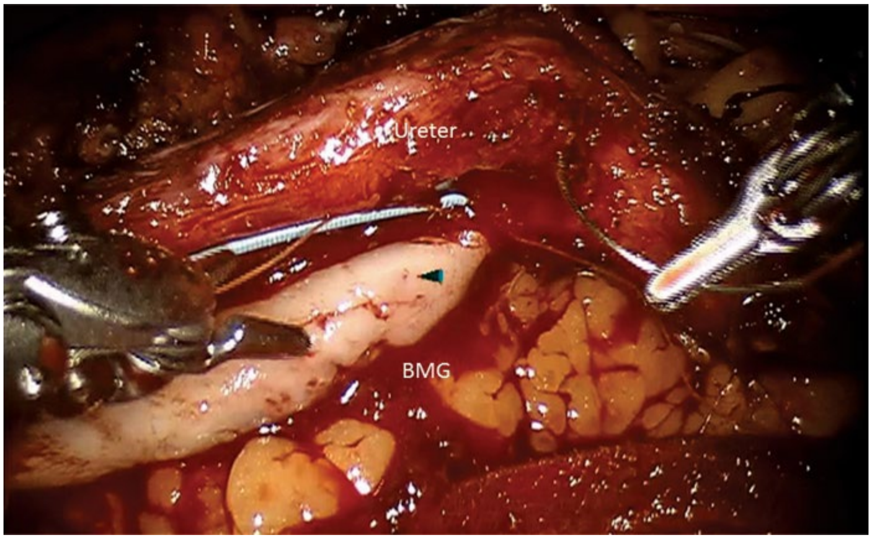

**Figure 103.4** Lengthwise ureterotomy performed, with stent visualized and graft prior to placement.

nephrostomy tube is in place, this is left in place and capped. As with all reconstructive cases, creatinine is checked prior to catheter removal and again prior to drain removal.

Six weeks after surgery, a retrograde or antegrade pyelogram is performed to confirm that there is no leak at the graft site prior to stent and nephrostomy tube removal. Subsequent surveillance includes renal ultrasound to evaluate for hydronephrosis after stent removal and diuretic renography at approximately three months to ensure the absence of obstruction.

### Follow-up

Our group has performed robotic buccal mucosal ureteroplasty on nine patients and there were no intraoperative complications noted [15]. The intraoperative techniques maneuvers to ensure a successful repair are the use of a well-vascularized tissue bolster, omental flap, or perirenal flap, to provide a vascular bed, use of intraoperative ureteroscopy to localize the stricture, ureteral instillation of ICG to identify well-vascularized ureteral tissue, and dynamic ureteroscopy during anastomosis to prevent back-walling the ureter during suture placement and to confirm a watertight anastomosis. From our early experience, we have recorded resolution of obstruction in 100% (mean 18 months). Early complications such as fever, which responded to antibiotics and antipyretics, and ileus, which was managed conservatively, have been noted [15].

## Conclusions

Robotic reconstruction has increased in popularity as surgeons are more comfortable with the robotic surgical system. Although only a small number of institutions have published their results, these studies have demonstrated the safety and efficacy of robotic ureteral reconstruction [4, 7, 8, 31]. These reports have also shown equivalent outcomes compared with open or pure laparoscopic approaches [10, 11]. The intraoperative and postoperative complications are generally low for robot-assisted ureteral reconstruction surgeries [12, 32, 35]. Inexperience with suturing is the most difficult aspect of these procedures and continues to be the challenge limiting the spread of this technology into the community. As robotic systems become more popular, and patients demand for this technology grows, robotic reconstruction will become more prominent throughout all urologic practices [3].

Unfortunately, the published reports on robotic reconstruction surgery are all retrospective case series [6, 7, 15, 31, 36, 41]. Well-powered, prospective, comparative trials are needed to assess the superiority of these techniques to traditional approaches. Another limitation of published reports is short follow-up; we need longer detailed reviews to evaluate whether radiologic and symptomatic success rates are sustained. Lastly, we need standardized definitions of complications for all institutions; this would help us to understand the actual morbidity of these surgeries and, more importantly, to create strategies to minimize complications.

See accompanying Video 103.1.

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# 104

# Laparoscopic Applications to Renal Calculus Disease

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## Introduction

The advancements in extracorporeal shock-wave lithotripsy (ESWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PCNL) have rendered open stone extraction for renal calculus disease obsolete. The use of open stone extraction has been limited, therefore, to more complex cases and only accounts for 2–5.4% of all stone cases [1, 2]. Nevertheless, open stone extraction is still indicated in complex cases with extremely large stones, renal malformations, special anatomic considerations, or in regions where ESWL, URS, or PCNL are not available [3]. The application of laparoscopic technology has allowed a minimally invasive surgical approach where open stone extraction is indicated (Table 104.1). With lower analgesia requirements, shorter hospital stay, and shorter convalescence [4, 5], laparoscopic stone extraction (LSE) is a better alternative than open stone extraction whenever expertise in laparoscopic techniques is available [6]. Utilization of laparoscopy has increased further with the adaptation of the da Vinci® robotic surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA), which offers unique advantages in maneuverability and intracorporeal suturing, allowing the surgeons to replicate nearly any open stone extraction laparoscopically. Although highly effective, LSE still remains as an alternative therapy in most cases due to its more invasiveness and higher complication risks. This chapter focuses on the applications and outcomes of LSE in renal calculus disease.

## Laparoscopic pyelolithotomy

In the modern era with the availabilities and advancements in the instruments for ESWL, URS, and PCNL, laparoscopic pyelolithotomy (LPL) is largely reserved for a complex renal anatomy, failed endourologic management, or simultaneous repair of ureteropelvic junction (UPJ) obstruction. It can also be considered in patients with very large stones and a large renal pelvis whereby whole extraction of such stones may result in higher stone-free rate (SFR) than PCNL. Furthermore, in some regions where the access to endourological instruments is limited, LSE can often be the most minimally invasive option available.

### Outcomes

Multiple studies have described both transperitoneal and retroperitoneal LPL for large renal pelvis stones ranging from 1.6 to 4 cm with high SFR (range 71–100%) (Table 104.2) [7–13]. Complication rates have been reported to range from 0% to 27% with open conversion rate up to 20%. Although earlier cases reported prolonged urinary leakage likely from pyelotomies that were not closed, later cases with intracorporeal suturing of the pyelotomy resulted in decrease in urinary leakage [8].

Initial comparison studies of both transperitoneal and retroperitoneal LPL to PCNL for a large renal pelvis stones have reported comparable SFRs (88% vs. 82%), estimated blood loss (EBL) (173 ml vs. 141 ml), complication rates (12% vs. 18%), and length of stay (LOS) (3.8 days vs. 3 days), respectively [14, 15]. The mean operative time, however, was significantly longer for LPL (142 minutes vs. 72 minutes). These results were later confirmed by a larger, randomized study [16]. In this series, no significant differences were seen on the intra- and postoperative parameters such as EBL, pain control, rate of blood transfusion, LOS, or SFR at three months (100% vs. 96%, respectively). The only difference was the mean operative time, which was significantly longer for the LPL group (130.6 minutes vs. 108.5 minutes, respectively).

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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The advancements in laparoscopic techniques, however, translated into more favorable outcomes with LPL in the more recent studies. Tefekli et al. reported a lower EBL and postoperative decrease in hemoglobin with LPL compared to the match-paired patients treated with PCNL [13]. Although not statistically significant, higher SFR (100% vs. 88.4%, respectively) was also seen with LPL. Recent randomized study and meta-analysis confirmed these results where shorter mean operative time and LOS was associated with PCNL whereas lower transfusion rates were seen with LPL [20, 22]. When compared to ESWL, LPL was also shown to have higher SFR, lower levels of postoperative pain, and a faster recuperation [23]. Some series also reported higher single-session SFR with LPL compared to ESWL and PCNL, especially with a larger stone burden [24]. Despite these more favorable contemporary series, the current combined evidences still suggest that LPL, although feasible, is only indicated under special considerations [12].

## Special consideration: renal pelvic stones with a concomitant UPJ obstruction

Renal pelvic stones with a concomitant UPJ obstruction is one of the most common situations where LPL is considered over other means of therapy. Approximately 20% of patients with UPJ obstruction harbor stone disease [25]. An extended pyelotomy, which can later be incorporated into the final pyeloplasty incision, is used to extract the pelvic stones with rigid graspers under direct laparoscopic vision [26]. A flexible endoscope (cystoscope preferred over ureteroscope) passed through one of the laparoscopic

**Table 104.1** Indications of the laparoscopic stone surgery.

| | Complex renal anatomy | Large stone burden requiring multiple endourological procedures | Failed endourological management | Lack of access to endourological instruments | Concomitant UPJ obstruction | Concomitant calyceal diverticulum | Nonfunctional renal unit due to calculus |
|---|---|---|---|---|---|---|---|
| Laparoscopic pyelolithotomy | ● | ● | ● | ● | ● | | |
| Laparoscopic anatrophic nephrolithotomy | ● | ● | ● | | | ● | |
| Laparoscopic ureterolithotomy | ● | ● | ● | ● | | | |
| Partial or simple nephrectomy | | | | | | ● | ● |
| Laparoscopy-assisted endourology | ● | | | | | | |

**Table 104.2** Comparison between the robotic and laparoscopic pyelolithotomy without concomitant pyeloplasty.

| | Laparoscopic stone surgery | Robot-assisted laparoscopic stone surgery |
|---|---|---|
| Available approach | TP and RP | TP and RP |
| Mean stone size | 2–4 cm [8, 10, 11, 13–16] | 2.9–4.2 cm [17–19] |
| Stone-free rate | 71–100% [9–11, 15, 16] | 93–100% [17–19] |
| Mean operative time | 80–149 min [8, 10, 15, 16, 20] | 96–158 min [18, 19] |
| Mean EBL | 53–173 ml [10, 11, 14–16] | 19–100 ml [17–19] |
| Conversion rate | 20–27% [8, 9] | 0% [17–19] |
| Complication rate | 10–12% [8, 16] | 0–7.1% [19, 21] |
| Mean length of stay | 3.6–6.5 days [8, 13–16] | 2–3.8 days [17–19] |

TP, transperitoneal; RP, retroperitoneal; EBL, estimated blood loss.

ports, then through the pyelotomy, and into the renal collecting system can then be used to inspect and clear the calyces of remaining stones. In many series, SFRs of 75–90% can be achieved with up to 90% of patients showing no evidence of obstruction on follow-up diuretic renal scan [26, 27]. In a comparative study by Stein et al., concomitant LPL, compared to the laparoscopic pyeloplasty alone, was also shown to be both effective and safe with high SFR of 80% and comparable success rates of UPJ obstruction (93% vs. 100%, respectively) without a significant increase in morbidity or operative time (174 minutes vs. 170 minutes, respectively) [25]. Other intra- and post-operative parameters such as EBL, number of ports, and LOS were also similar between the two groups.

The application of robotics, especially with concurrent reconstruction, have also been reported, with advantages in improved maneuverability and visualization. Studies have reported additional mean operative time of 61.7 minutes for concomitant stone extraction without added complications or LOS during robot-assisted pyeloplasty (RAP) [21, 28]. One of the main concerns for any robotic application, however, is its added cost. These cost increases are mainly from the equipment depreciation, maintenance, and replacements, as well as longer operative time. Studies have shown that RAP may cost 1.7–2.7 times more than laparoscopic pyeloplasty [29, 30]. Its cost, however, can be mitigated by its shorter mean operative time (140 minutes for RAP vs. 235 minutes for laparoscopic pyeloplasty in one series) as well as lessened depreciation impact of the equipment in high-volume centers [30].

## Procedure

A preoperative evaluation with computed tomography (CT) should provide sufficient data regarding stone size, location of stone, and pertinent anatomy. A CT with contrast and delayed imaging may be of benefit when vascular abnormalities or other anatomic aberrancies exist (e.g. malrotated kidney). If a CT is not available, an intravenous pyelogram (IVP) can be considered.

Both transperitoneal and retroperitoneal approaches are feasible for LPL. The author's preference is the transperitoneal approach. After positioning the patient in the modified contralateral decubitus position with all pressure points well padded and the patient appropriately secured to the bed, the patient's abdomen and genitalia are prepped and draped in the usual sterile manner. A Foley catheter is then placed. Pneumoperitoneum is achieved with the surgeon's preferred method. A Veress needle or Hasson technique is utilized to establish pneumoperitoneum at either umbilical or left upper quadrant (Palmer's point) areas. Once pneumoperitoneum is established with 15 mmHg of $CO_2$ pressure, three ports are placed in a triangular configuration, with a 12 mm port at the umbilicus, a 12 mm port in the ipsilateral lower quadrant and a subxiphoid 5 mm port (may be upsized to a 12 mm port) (Figure 104.1). An additional 5 mm incision with or without port under the xyphoid process can be utilized for a self-locking grasper for liver retraction during the right-sided procedure if necessary. For an obese patient, the ports are displaced laterally and cephalad.

Once ports are placed, the table is rotated toward the contralateral direction such that the camera port is flat to the horizon. Using a 30° down scope, the abdominal contents are inspected and the white line of Toldt is incised to allow for medial reflection of the colon. The ureter is then identified over the psoas muscle (running parallel to the gonadal vessels) and traced up to the renal pelvis. Stones in renal pelvis are generally easily identified due to their bulge. If the identification is difficult due to surrounding inflammation and/or adhesions, more thorough dissection to expose the renal pelvis may be necessary. Care must be taken to avoid inadvertent injury to the ureter or renal pelvis in case of tissue friability which is often present. Laparoscopic ultrasound or on-table fluoroscopy can be utilized to locate the stone in the pelvis or any fragments in the calyces.

A pre-positioned ureteral catheter may facilitate identification of the ureter and renal pelvis. This can also serve to test for watertight closure of pelvis and to place a ureteral stent in a retrograde manner toward the end of the case. Placement of ureteral catheter should be performed at the beginning of the case, either before the laparoscopic portion or, alternatively, during, with a flexible cystoscope by the assistant surgeon while the patient is in the modified flank position and undergoing the laparoscopic portion of the case. Alternatively a ureteral

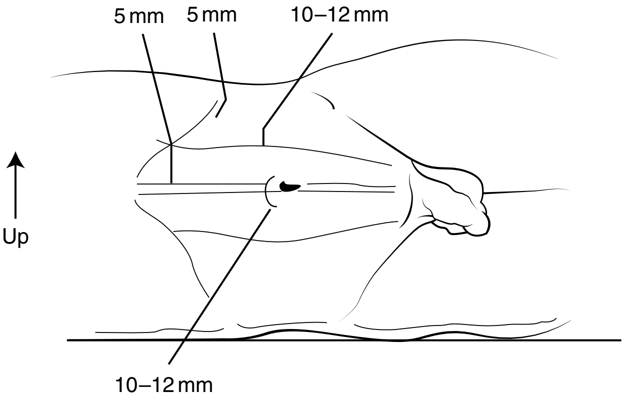

**Figure 104.1** Port placement for laparoscopic pyelolithotomy via transperitoneal approach. *Source:* Gandhi HR, Thomas A, Nair B et al. Laparoscopic pyelolithotomy: an emerging tool for complex staghorn nephrolithiasis in high-risk patients. *Arab J Urol* 2015;13(2):139–145. Reproduced with permission of Elsevier.

stent can be passed in the antegrade fashion before closure of the pyelotomy.

Pyelotomy should be made and extended with laparoscopic scissors in a longitudinal fashion using a curvilinear incision (Figure 104.2a). The surgeon must plan the size and direction of the pyelotomy based on the size and location of the stone, the renal pelvis anatomy, and whether or not it will be incorporated into a pyeloplasty. A flexible cystoscope, and if necessary a flexible ureteroscope, may be passed through one of the 12 mm ports into the pyelotomy to inspect the renal pelvis and all calyces for stone (Figure 104.3). Stone basket extraction may be performed when necessary. Pressure irrigation to 300 mmHg with normal saline is used to create a turbulent flow inside the pelvis for adequate hydrodistention for exploration. The mucosal adhesions to the stones can be dissected off using a right-angle dissector [31]. An endoscopic retrieval bag may be used to minimize the risk of intra-abdominal stone loss and to facilitate the extraction of multiple and/or small stones (Figure 104.2b). A double pigtail ureteral stent is left in place; either placed over a wire inserted through the previously placed ureteral catheter or introduced over a wire in the antegrade direction through the pyelotomy (Figure 104.2c). The pyelotomy is then closed with a 3-0 absorbable suture (e.g. polyglactin) (Figure 104.2d). A closed suction drain is placed in proximity to the pyelotomy. The abdominal fascia on the 12 mm port sites are closed with figure-of-eight 2-0 polyglactin sutures, and the skin is closed either with running subcuticular closure or staples.

In the retroperitoneal LPL, the patient is placed in the full-flank position and secured to the bed with all pressure points well padded. A 2 cm incision is made below the tip of the 12th rib on the posterior axillary line. The retroperitoneal space is then bluntly dilated with the index finger. A 12 mm balloon trocar system is then used to further develop the retroperitoneal cavity. Pneumoretroperitoneum is created with insufflation pressure of 15 mmHg. Under direct visualization, the working trocars (12 mm and 5 mm) are placed four fingerbreadths away from the camera port directly above (12 mm port) and below (5 mm port) it. In an obese or tall patient, the trocar placements should be displaced superiorly for optimal working environment. A fourth trocar can be placed after further reflection of the peritoneum anteriorly if needed. The renal pelvis should be visualized first in the hilum. The rest of the procedure is carried out similar to the transperitoneal LPL.

The retroperitoneal approach has several theoretical advantages over the transperitoneal approach. It is thought to have decreased risks of visceral injury from the trocar placement as well as from manipulation during the procedure. Less irritation of the intestine and peritoneum from urine in the retroperitoneal space is another theoretical advantage. The transperitoneal approach, however, provides more familiar anatomy to most surgeons with larger working space. Balloon dissection to create the retroperitoneal space is also not necessary in this approach. As discussed above, both approaches are considered safe and effective during LPL, and it is the surgeon's preference and comfort level that should dictate the method of choice.

## Laparoscopic anatrophic nephrolithotomy

Laparoscopic anatrophic nephrolithotomy (LAN) is mostly reserved for large staghorn calculi that have failed or may require multiple endourological treatments with PCNL and/or ESWL [32]. SFR is particularly important in staghorn stones, with attendant high risks of renal function deterioration and recurrence rates [33]. Anatrophic nephrolithotomy can be advantageous in achieving high SFR with less cost over multiple endourological procedures required to attain a similar, if not less successful, result [34]. Esen et al. compared open anatrophic nephrolithotomy (OAN) with ESWL monotherapy and ESWL with PCNL combined therapy in patients with staghorn calculi [35]. SFRs of 80%, 32%, and 50% were achieved with OAN, ESWL monotherapy, and ESWL–PCNL combination therapy, respectively. Although higher EBL was noted with OAN, the benefits of OAN with SFR was substantial.

### Outcomes

LAN is a minimally invasive alternative to OAN. In 2003, Kaouk et al. were the first to describe LAN in a porcine model [36]. This study, which utilized the techniques of OAN with a mean warm ischemia time of 30 minutes, showed the feasibility of laparoscopic application for a large staghorn stones. This was quickly followed by Deger et al. describing the first LAN in patients with complete staghorn stone via transperitoneal approach [37]. Cold ischemia with ice slush was used, with mean ischemia time of 45 minutes. The collecting system was closed with an absorbable running suture. No complications were reported, and the patient's follow-up IVP and renal scan showed resolution of obstruction and improvement in renal function, respectively. Since then, more contemporary series utilizing warm ischemia have reported similar efficacy and safety of both transperitoneal and retroperitoneal LAN in treating staghorn stones [38–40]. In over 40 patients with mean stone sizes ranging from 4.5 to 6.5 cm, warm ischemia time and operative time ranged from 29 to 35 minutes and 120 to

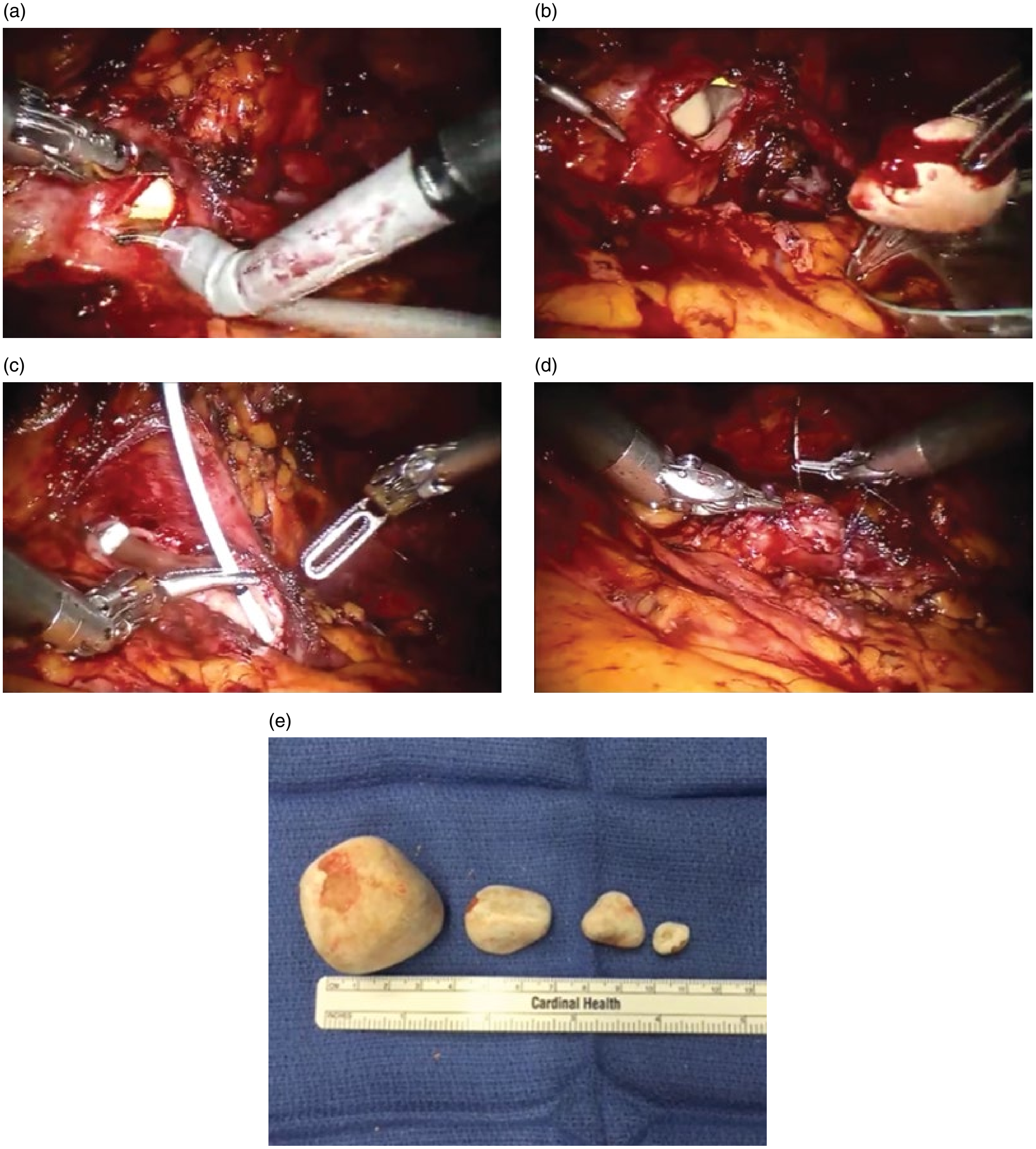

**Figure 104.2** Robot-assisted laparoscopic pyelolithotomy. (a) Pyelotomy for stone retrieval. (b) Stone retrieval with endoscopic retrieval bag. (c) Antegrade ureteral double pigtail ureteral stent placement. (d) Closure of pyelotomy with running suture. (e) Retrieved renal stones.

225 minutes, respectively. The reported SFRs ranged from 88 to 91% with the majority of residual stones successfully managed with postoperative ESWL. Postoperative IVP confirmed significant improvements in obstruction and functional corresponding renal unit in all studies. Mean LOS of 3.5 days with minimal changes on serum creatinine values were also reported [41]. Despite its effectiveness, LAN is still considered an invasive procedure with one of the series reporting a rather high transfusion rate of 24% with 20% rate of Clavien

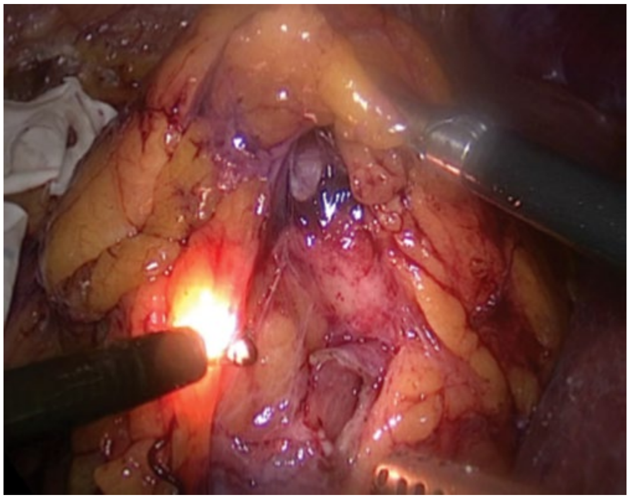

**Figure 104.3** Use of flexible endoscope for stone exploration during laparoscopic pyelolithotomy. *Source:* Gandhi HR, Thomas A, Nair B et al. Laparoscopic pyelolithotomy: an emerging tool for complex staghorn nephrolithiasis in high-risk patients. *Arab J Urol* 2015;13(2):141. Reproduced with permission of Elsevier.

grade III or higher complications including nephrectomy [39]. LAN should, therefore, be limited to expert laparoscopic surgeons.

Another concern during LAN is the inevitable ischemia with no known long-term functional outcome following LAN. The proficiency of laparoscopic suturing technique as well as patient selection are, therefore, crucial in the success of LAN. Extrapolating results from partial nephrectomy, the reported warm ischemia times for LAN are acceptable for long-term preservation of renal function [42]. Those with multiple particles in different calyces, rather than a single large staghorn stone, may have increased warm ischemia times making them less suitable for LAN. Robotic applications for LAN have also been reported with cold and warm ischemia times, SFRs, and mean operative times comparable to those for nonrobotic LAN [43, 44].

## Special consideration: calyceal diverticular stone

Laparoscopic diverticulectomy with simultaneous stone removal is another relative indication for a laparoscopic nephrolithotomy (LNL). Although rarely indicated or performed, the laparoscopic approach is a suitable option for a previously failed endourological intervention, anteriorly located diverticula which are usually difficult to access percutaneously, or large stone burden with narrow diverticular neck which precludes management with ESWL or URS [45]. The incidence of calculi within calyceal diverticula has been reported to be between 10% and 50% [46]. Multiple series with laparoscopic applications for calyceal diverticula with concomitant stones have been reported with high efficacy and safety (Table 104.3) [47–52]. Stone localization is usually achieved without much difficulty as the overlying cortex in such cases is generally thin and is either bulging with the stone or depressed because of scarring. Palpation with instrument, aspiration, indigo carmine injection, fluoroscopy, or ultrasonography have been utilized for locating the stone-filled diverticula. A "cut to the light" technique is also useful where endoscopic light from the flexible ureteroscope introduced at the obstructed calyx localizes the location of the diverticula (Figure 104.4a) [53].

**Table 104.3** Laparoscopic calyceal diverticulectomy with simultaneous stone removal.

| | |
|---|---|
| Stone size | 3–45 mm [48–52] |
| Diverticulum size | 1.3–4.5 cm [48–52] |
| Stone-free rate | 100% [48–52] |
| Diverticulum recurrence rate | 8.3% [48–52] |
| Mean operative time | 80–215 min [48–52] |
| Estimated blood loss | 0–150 ml [48, 49] |
| Conversion rate | 0% [48–52] |
| Complication rate | 8.3% [48–52] |
| Mean length of drain | 1–4 days [48–51] |
| Mean length of stay | 1–4 days [48–52] |

Once the stone is removed, diverticula are generally managed with fulguration [11], argon beam coagulator [52], closure of the cavity with perirenal fat [49] or synthetic glue [50], or suturing of the diverticular neck [48]. The presence of diverticula with a thick rim of renal parenchyma, however, is a relative contraindication for the laparoscopic approach. In such cases, difficulties with the localization of diverticula as well as the control of bleeding from the nephrolithotomy incision are expected. LNL in such cases is still feasible but the technique would then resemble a partial nephrectomy for an endophytic tumor rather than a stone extraction. Although ultrasonography with color Doppler may aid in localization of the diverticula while avoiding major vessels [52], Gerota's fascia is opened, making spontaneous compression unlikely for hemostasis (unlike the percutaneous procedures). Preoperative review of imaging studies is, therefore, paramount as these patients may need to be counseled for renorrhaphy following diverticulectomy and stone removal.

## Procedure

Patient positioning and port placement are similar to those used for transperitoneal approach described above. The renal hilum is skeletonized and the kidney is mobilized completely. A laparoscopic ultrasound is performed

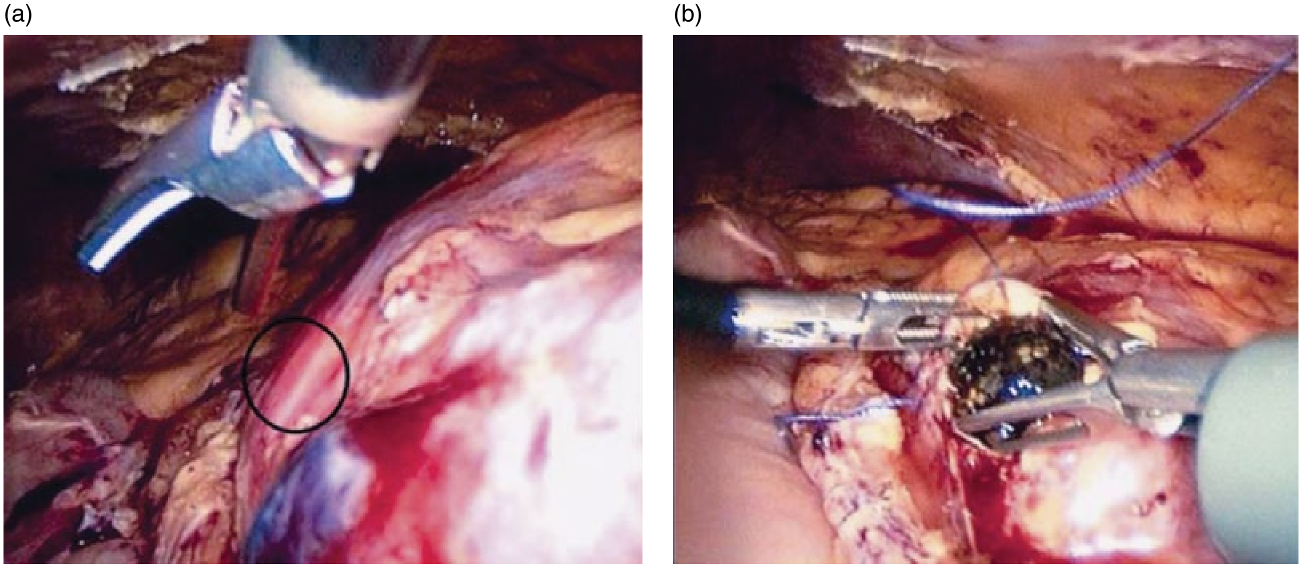

**Figure 104.4** Laparoscopic management of calyceal diverticular stone. (a) Endoscopic light transilluminates the location of the obstructed upper pole calyx (area inside circle). (b) The kidney is incised over the lighted parenchyma and the stone removed laparoscopically. *Source:* Nadu A, Schatloff O, Morag R et al. Laparoscopic surgery for renal stones: is it indicated in the modern endourology era. *Int Braz J Urol* 2009;35(1):9–17. Reproduced with permission of Oscar Schatloff.

to assess location of stone burden. Laparoscopic bulldog clamps are applied to the renal hilum. The author prefers two bulldogs placed on the renal artery and one bulldog on the renal vein (Figure 104.5a). A longitudinal incision through the renal parenchyma at Brodel's line is created (Figure 104.5b). This is the theoretically avascular line separating the anterior and posterior segmental arterial distribution and is typically located at one-third of thickness from the anterior aspect. Incision is continued with laparoscopic scissors until calyces are entered and stone is identified. A laparoscopic scissor or scalpel can be used to extend the incision into the collecting system to allow for full identification and extraction of the stone. Once all stone is evacuated and placed into the endoscopic retrieval bag, the collecting system is reapproximated utilizing a running 3-0 polyglactin suture and a capsular renorrhaphy is performed using 2-0 polyglactin or V-Loc™ (Covidien/Medtronic, Minneapolis, MN, USA) suture (typically with a sliding Hem-o-lok® (Teleflex Medical, Research Triangle Park, NC, USA) technique) (Figure 104.5c). Next, the bulldog clamps are removed, the kidney is assessed for reperfusion and hemostasis, and a drain is placed. The endoscopic retrieval bag is extracted and port sites are closed.

## Laparoscopic ureterolithotomy

Laparoscopic ureterolithotomy (LUL) is an alternative option for a large impacted ureteral stone, following a failure of ESWL or URS therapies, for a socioeconomic necessity where stone clearance with a single treatment session is required, or where appropriate technological instruments are lacking. Since the first description of LUL by Wickham in 1979 [54], multiple studies have reported its efficacy and safety [8, 55–60].

### Outcomes

LUL duplicates open ureterolithotomy with the advantage that it is minimally invasive. Both transperitoneal and retroperitoneal LUL were compared with open ureterolithotomy, and lower analgesia requirements, shorter LOS (3–3.3 days vs. 4.8–8 days), and shorter convalescence (1.8 weeks vs. 3.1 weeks) were reported with LUL [55, 56]. No significant differences were seen in the mean operative time (108.8 minutes vs. 98.8 minutes, respectively) and EBL (58.5 ml vs. 50.5 ml, respectively). One study reported 12% conversions due to stone migration into the kidney, inability to locate the stones due to extensive periureteric fibrosis, or vascular injury [56]. These conversions, however, occurred early in the series with no conversions reported in their later cases. Although this may raise a concern for a steep learning curve, Fan et al. reported that such curve is rather shallow with improved complication rates and operative time after first 20 cases [57].

The SFRs in most series with both transperitoneal and retroperitoneal LUL approached 100% with low conversion rates [8, 55–60]. In the largest LUL series by Simforoosh et al. with 123 patients, an SFR of 96.7% was reported with calculi ranging from 1 to 5.6 cm. The mean

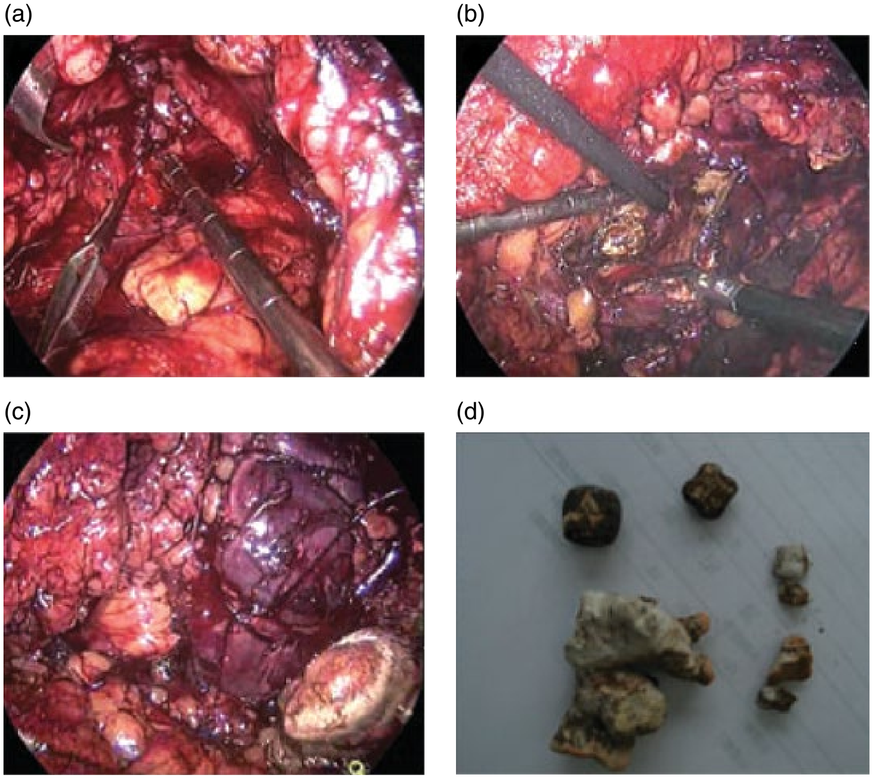

**Figure 104.5** Laparoscopic anatrophic nephrolithotomy. (a) Renal artery clamped temporarily with a bulldog clamp. (b) Nephrotomy incision. (c) Nephrotomy closure with running sutures. (d) The staghorn stones extracted. *Source:* Zhou L, Zuan, Q, Wu B et al. Retroperitoneal laparoscopic anatrophic nephrolithotomy for large staghorn calculi. *Int J Urol* 2010. Reproduced with permission of John Wiley & Sons.

operative time was 143.2 minutes [58]. A minor complication rate of 11.4% was reported, including an open conversion due to migration of the calculus. Interestingly, multiple studies reported a significant difference in the mean operative time between the transperitoneal and retroperitoneal approaches (137.3 minutes vs. 171.3 minutes in one study, respectively) without significant differences in EBL and transfusion requirements [58, 60]. In a recent prospective study, a significantly lower SFR (72% vs. 100%) with retroperitoneal approach was also reported [61]. Although the retroperitoneal approach was associated with shorter time to oral intake (15 vs. 21 hours), longer mean operative times with higher open conversion rates (27.3% vs. 0%) were reported as well. Although no randomized studies are available comparing the two approaches, these data suggest that surgeons still early in their learning curve in LSE should perform LUL using a transperitoneal approach. The application of robotics in LUL has also been reported with high SFRs and decreased operative times, likely due to its improved control, dexterity, and precision [62, 63].

The comparison studies of LUL with URS, PCNL, or ESWL for ureteral stones have shown favorable SFRs for LUL, reaching up to 100% [64–66]. Although longer mean operative times and LOS were observed with LUL when compared to URS (with no increased risk of complication), comparable mean operative times, EBL, urinary leakage rates, and LOS were seen compared to PCNL. LUL, however, has significantly higher SFRs compared to ESWL (93.3% vs. 35.7% in one study). Although these recent reports showing higher SFRs with LUL could represent advancements in laparoscopic skills, flexible ureteroscopes which could aid in stone clearance with stone migration into the renal pelvis were not utilized in some of the studies. The stone up-migration is usually significantly higher with URS.

In LUL, the most common early postoperative complication is urine leak (0–20%) followed by stricture formation (1.4–5.2% risks) [8, 56, 57, 65, 67–70]. Controversy about whether to close the ureterotomy and whether to place a ureteral stent, therefore, still exists. No significant differences have been reported between closing the ureterotomy [8, 69] and leaving it open [67, 68], as well as stenting and no-stenting after LUL [71]. The duration of urine leakage is probably longer, however, if the ureterotomy is neither closed nor stented [70]. The most serious late complication of LUL is ureteral stricture formation, which occurs at an incidence of up to 20% [12]. The common etiologies for stricture development are periureteritis, urinary leak, use of diathermy to incise the ureter, and stone impaction.

One potential application of LUL is in cases where there has been prolonged impaction of a large stone within the ureter associated with significant periureteral fibrosis and adherence of stone to the ureteral mucosa. In such cases, endoscopic management may result in high ureteral stricture rates [71, 72] and it may be best to perform a laparoscopic or robotic segmental ureterectomy with primary uretero-ureterostomy, if the defect is not prohibitively long.

### Procedure

Preoperative evaluation, patient positioning, peritoneal access, and port placements are similar to those of LPL and LAN. The ureter is located on top of the psoas muscle after the mobilization of colon. The stone is then identified either with palpation or visual contact. Laparoscopic ultrasound or on-table fluoroscopy can aid in its localization as well. Once the stone is localized, the ureter is occluded both proximal and distal to the stone with the vessel loops to minimize the risk of stone migration. A longitudinal incision is made over the stone with a laparoscopic scissor to remove the stone with the stone grasper. Care should be taken not to use any thermal energy on the ureter to minimize the risk of ureteral stricture disease. An endoscopic retrieval bag is used to remove the stone from the abdomen. Different methods have been described for the ureterotomy management. It is perhaps best to both close the ureterotomy with 4-0 polyglactin interrupted sutures and place the double-J ureteral stent to minimize the risk and duration of urine leak. However, if the ureter is chronically inflamed, edematous, and friable due to infection or prolonged impaction, the ureter should only be stented and not sutured to decrease the risk of prolonged leakage [70]. A drain is placed as well and removed in postoperative day 1 if urine leak is not suspected. The ureteral stent is removed in one to two weeks in the office.

The retroperitoneal approach is also feasible for proximal and midureteral stones. The port placements and retroperitoneal access are similar to those of LPL or LAN. The distal ureteral stones, however, are difficult to reach retroperitoneally, and transperitoneal approach is recommended. The fascia and skin are closed in a similar fashion as in LPL or LAN.

## Laparoscopic partial or simple nephrectomy

Laparoscopic partial or simple nephrectomies are considered when the function of the entire kidney or a renal moiety in a duplex system is lost due to renal calculus diseases [10, 11, 70, 73–76]. Overall SFRs approach 86–100%, but the prolonged inflammation and/or infection in the renal or the perirenal tissues usually associated with these conditions make the procedures more difficult, with reported open conversion rates up to 14%. A history of multiple prior endourological interventions is also often encountered in these patients, further obscuring the tissue planes. If excess adhesions are suspected or encountered, the hilum should first be approached outside of Gerota's fascia, which leads to safe dissection with minimal bleeding [10]. The procedural basics of laparoscopic partial and simple nephrectomies largely duplicate those of the laparoscopic oncologic counterparts and are discussed in detail elsewhere in the text.

## Anatomic anomaly and laparoscopically assisted endourology

Renal anomalies such as horseshoe kidney, ectopic kidney (most commonly in the pelvis), crossed fused ectopic kidney, transplant kidney, or urinary diversions introduce challenges to the urologist due to less effective endourological interventions compared to those without the anomalies and increased risk of complications associated with the interventions. These patients are also at increased risk of stone disease from relative urinary stasis. Although PCNL, unlike URS and ESWL, has been shown to be as effective in patients with renal anomalies as in those with normal anatomy with stones [77–81], difficulties in gaining access due to increased skin-to-stone distance and/or abnormal location raises concern for suboptimal access or complications including bowel or vascular injuries. Puncture through suboptimal structures (e.g. greater sciatic foramen, transhepatic, and transiliac) have been described in the past [82–84]. Laparoscopic application in renal anomalies, therefore, could be considered with its advantages of direct visualization and high SFRs.

The evidence relating to LSE in renal anomaly is scant, but excellent outcomes have been reported in small series. The reported SFR ranges from 91% to 100%, with mean operative time, EBL, and LOS comparable to those with normal anatomy [85–87]. Due to anatomic variances associated with renal anomaly, preoperative ureteral catheter or stent placement may aid in localization and repair in these cases.

As flexible endoscopes are utilized during LSE for stone fragment localization and/or retrieval, laparoscopy can be combined with endourological procedures, especially with PCNL, to aid in safe and successful access in the patients with renal anomalies. Multiple studies have reported high SFRs and low complications [88–91]. Patients are usually positioned in the Trendelenburg position to move the bowel away from the area of interest, and the kidney is punctured under direct visualization with continued displacements of bowel or the adjacent structures to avoid injury. Both transperitoneal and extraperitoneal approaches have been described with SFRs up to 100% and operative times and complication rates comparable to those of standard PCNL [90, 91]. Suturing of the nephrostomy site with ureteral stent placement under laparoscopic guidance, which eliminated the need for a nephrostomy tube, has also been described [91].

### Common limitations

One of the challenges of LSE is locating the original stone, especially in the ureter, as well as the small residual stones/fragments. Although the large stone burden prompting LSE often causes enough of a bulge or depression of the overlying tissue aiding in its identification, inflammation of the surrounding tissue can make it difficult during laparoscopy where tactile feedback is suboptimal. Lost stone in the abdomen during LSE is another challenge which may prompt open conversion if the stone is too large, too numerous, or infected. Fluoroscopy can aid in this process if it is available during LSE. Introduction of a C arm, however, is cumbersome during LSE. The image quality is also suboptimal due to the insufflation and free fluids in the abdomen during LSE. Intraoperative ultrasound has been utilized, but the difficulty still remains in locating the small residual stones.

Combining the flexible cystoscope with LSE is also challenging due to the crowded operative field with the instruments and limited ability to achieve enough irrigation pressure when the incision is made in the urinary system. The urine and free fluid introduced into the abdomen from the irrigation fluid are also a concern, as these may irritate the bowel, causing ileus. A retroperitoneal approach can theoretically minimize this problem if the surgeon is familiar with the anatomy. Efforts should be made to aspirate as much free fluid as possible at the end of the case by placing the patient in a Trendelenburg position to allow the fluid to accumulate under the diaphragm for easier aspiration during laparoscopy. Furthermore, many of the procedures described above for LSE require significant mobilization of the kidney within Gerota's fascia which may reduce the ability of this layer to provide protection against urinary leakage and hemorrhage.

## Conclusions

Although LSE is a less invasive alternative to open stone extraction with favorable safety and efficacy, the classical endourologic procedures should still remain the gold standard in the treatment of renal stone diseases. LSE is a good treatment modality, however, that is available to the urologist when other endourological options are suboptimal or have failed.

See accompanying Video 104.1.

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## 105

# Laparoscopic Treatment of Renal Cysts and Diverticula

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## Laparoscopic treatment of renal cysts

### Introduction

Renal cysts are localized fluid-containing formations separated from the renal parenchyma by a pseudocapsule and are considered the most common incidental findings of the kidney. Approximately 70–80% are solitary, unilateral, and cortical, but they can potentially develop in every part of the kidney and appear as multiple or bilateral cysts, with a variable dimension from few millimeters to more than 10 cm. In about a quarter of total cases, mostly in young patients, they grow bigger over time. A specific rate of growth has never been clarified, but in general they develop through as much as space as they can find. Cysts never communicate directly with the urinary excretory system and their internal surface is never covered by urothelium [1–4].

Renal cysts are common findings in routine imaging examinations and their incidence increases with patients' age. Between birth and 20 years old, the occurrence of new cysts is very rare, but thereafter it begins to increase in incidence, with a male-to-female ratio of about 2:1 in some series. About one-third of the population over the age of 50 has an asymptomatic renal cyst.

Occasionally they can become symptomatic, mainly due to compression of renal sinus or of the ureter, which can cause acute pain manifesting as renal colic, infection, or urinary obstruction due to urinary stasis. In addition, hemorrhagic or malignant degeneration of the cyst is also possible [5, 6].

Some congenital diseases, such as autosomal dominant polycystic kidney disease (ADPKD), von Hippel–Lindau (VHL) syndrome, and tuberous sclerosis disease, are commonly associated with the presence of multiple characteristic cysts, often with a tendency toward malignant degeneration [7].

The application of laparoscopic surgery in renal cyst management sometimes has a proper rationale. This chapter covers the role of laparoscopy in simple renal cyst exploration and decortication. Complex cyst management is discussed elsewhere.

### Radiologic findings

Simple cysts are classically cortical with an exophytic growth pattern and can alter the renal profile. They can present with a circular or oval shape and are filled with a homogeneous fluid with a radiodensity comparable to water, usually ranging from −10 to 20 Hounsfield units (HU) on computed tomography (CT) imaging. Nearly 6% of simple cysts are complicated by hemorrhage. A hemorrhagic cyst may progress from blood liquefaction subsequent to a local trauma involving the kidney parenchyma, or a hemorrhage may be a complication of a simple cyst developing due to expansion or bleeding diathesis. The CT attenuation value of an acute hemorrhagic cyst ranges from 70 to 90 HU, but it falls as blood liquefies and organizes. The evolution of a hemorrhagic cyst includes development of calcification in a central or peripheral configuration with subsequent thickening and alteration of morphology, becoming multilocular as consequence of septae expansion, acquiring some features of a complex cyst. Infection is an additional potential complication of simple cysts. The walls of infected cysts are often markedly thickened with an increased HU attenuation, without contrast enhancement.

In patients with history of ADPKD, VHL, or tuberous sclerosis, specific radiologic screening is compulsory because of the high risk of cyst development and malignant degeneration.

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Companion website: www.wiley.com/go/smith/textbookofendourology

Renal cysts are generally categorized using the radiological system formulated by Bosniak [8], who classified them based on their morphological appearance and contrast enhancement on CT abdominal scan. Type I cysts have a flat muscle wall, and are filled with clear amber liquid; type II cysts, also benign, have minimal septation and small amount of calcification; type III cysts have a large number of septae with thick cyst walls; type IV cysts have irregular walls, with calcifications or hemorrhagic areas and sometimes a clear solid mass inside the cyst, suggesting a carcinoma [9].

Although the original Bosniak classification of a stage I renal cyst does not include their dimensions, an update published in 2005 notes a diameter of ≥3 cm as requiring follow-up and employs this size among the main variables used to discriminate between a stage II or IIF cyst [10].

Another revision of this classification system was suggested in 2004 by Israel et al., with a direct comparison between CT and magnetic resonance imaging (MRI) findings [11]. Analyzing a cohort of 59 patients with an overall number of 69 renal masses, they validated Bosniak classification using MRI images and demonstrated that MRI is better than CT in determining cyst morphology, septations, calcifications, or contrast enhancement. These findings suggest that MRI imaging may be an alternative imaging technique to CT, especially for younger patients who will undergo repeated examinations. Moreover, clinicians should select the same imaging methodology for each patient, as a switch from CT to MRI imaging could give the erroneous appearance of cyst evolution.

A full classification of renal cysts according to Bosniak criteria is presented in Table 105.1.

## Indications and contraindications to laparoscopic treatment

### Simple renal cysts (Bosniak I and II)

Most simple cysts are totally asymptomatic and will never demand active treatment.

Although surgical treatment of Bosniak I and IIF renal cysts is not normally needed, patients may present with important symptoms such as pain, infection, and urinary obstruction. In fact, simple cysts can in some cases grow enough to result in compression or rupture of collecting systems, likely related to a trauma [12]. Moreover, cystic fluid can become infected, needing surgical treatment. As a simple cyst grows, it may rarely result in systemic hypertension or impairment of renal function by causing tubular obstruction or local ischemia [13].

Nowadays, percutaneous drainage and sclerotherapy are the most frequent first-line treatments for symptomatic simple renal cysts [14]. Laparoscopic treatment is accomplished for patients in whom conservative procedures have failed or are contraindicated (obese patients, bleeding disorders, complex location of the cyst, etc.). Another indication for first-line laparoscopic treatment is the presence of concomitant pathologies of the ipsilateral kidney or upper urinary tract which necessitate surgical treatment (i.e. pielolithotomy, pyeloplasty, simple tumor enucleation, or partial nephrectomy) [15].

Marsupialization, decortication, and unroofing are the three main techniques described for simple renal cyst laparoscopic treatment. The patient should be preoperatively informed that if malignancy is suspected intraoperatively, the treatment can vary toward a more radical surgical excision [16].

### Complex renal cysts (Bosniak III and IV)

Diagnosis of simple cysts is often incidental in the absence of specific symptoms. A specific meta-analysis found that Bosniak class II, III, and IV cysts are associated with the risk of 24, 41, and 90% of malignancy, respectively [17].

Some authors have described the possibility of cyst aspiration to rule out the presence of malignant cells, even if this practice is strongly not recommended because of the high risk of tumor seeding and the possibility of a false-negative result [18]. Conservative management is never recommended for lesions Bosniak III–IV because of the high suspicion of cancer and, as for percutaneous aspiration, preoperative biopsy is not indicated.

Finally, in view of the findings that approximately 40–60% of class III and 85–100% of class IV cysts prove to be malignant, laparoscopic simple enucleation, partial or radical nephrectomy is always demanded [1, 2].

The main limit for the laparoscopic approach is represented by intraparenchymal cysts, treatment of which can be difficult because of the risk of significant bleeding and injury to the collecting system. In these situations, an open surgical approach should be considered.

## Laparoscopic treatment

Laparoscopic treatment of simple renal cysts represents an ideal approach as it minimizes surgical morbidity potentially related to lombotomic incision performed for conventional open procedure. Before deciding on laparoscopic treatment for a patient with a simple renal cyst, percutaneous puncture could be performed under ultrasound guidance with aspiration of cystic liquid. This would demonstrate a cause-and-effect relationship between the cyst itself and symptoms reported by the patient [19].

### Preoperative evaluation and patient preparation

Even if standard abdominal ultrasound study is used to diagnose simple renal cysts, a detailed preoperative

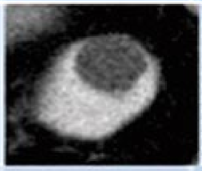
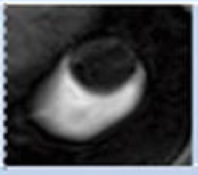
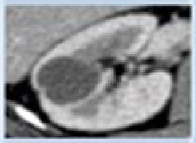
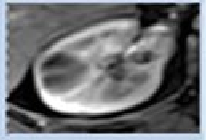
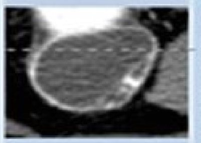
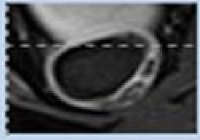
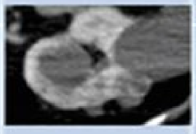
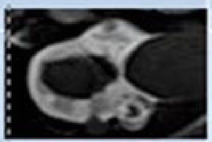
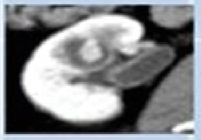
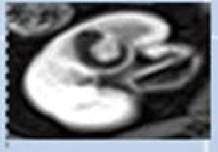
| Renal cysts<br>Bosniak categories | CT | MRI | CT management |
|---|---|---|---|
| **Bosniak grade 1**<br>Simple cyst imperceptible wall, rounded<br>Percentage malignant: ~0% |  |  | None |
| **Bosniak grade 2**<br>Minimally complex a few thin <1 mm septa or thin calcifications; non-enhancing high-attenuation (due to proteinaceous or haemorrhagic contents) and generally well marginated.<br>Percentage malignant: ~0% |  |  | None |
| **Bosniak 2F**<br>Minimally complex increased number of septa, minimally thickened with nodular or thick calcifications there may be perceived enhancement of hairline-thin smooth septa. Cyst diameter of ≥3 cm.<br>Percentage malignant: ~5%[1] |  |  | Follow-up: needs ultrasound/CT follow up - no strict rules on the time frame but reasonable at 6 months |
| **Bosniak grade 3**<br>Indeterminate thick, nodular multiple septa or wall with measurable enhancement, hyperdense on CT (see 2F)<br>Percentage malignant: ~55%[1] |  |  | Treatment/work-up: partial nephrectomy or radiofrequency ablation in elderly or poor surgical candidates |
| **Bosniak grade 4**<br>Clearly malignant solid mass with a large cystic or a necrotic component<br>Percentage malignant: ~100% |  |  | Treatment: partial or total nephrectomy |

**Table 105.1** Bosniak classification of renal cysts. Comparison between CT and MRI imaging findings.

radiological evaluation is required to plan the surgical strategy and to avoid potential complications. Three-phase renal CT with precontrast, nephrogram, and delayed images is the gold standard among imaging modalities. It gives crucial information about the number, size, location, exophytic/endophytic growth of the renal cyst, and its relation to renal hilum, the pyelocalyceal system, and proximal ureter. Moreover, it allows the relation with contiguous structures such as bowel, liver, or spleen and Bosniak classification to be identified. Finally, this study can guide surgeons on the decision as to what surgical approach to use. In general, a transperitoneal approach is indicated for cysts located in the anterior renal face or parapelvic or when concomitant diseases have to be treated, such as stones affecting the ipsilateral kidney [15]. The retroperitoneal approach is more appropriate for posteriorly located or inferior pole cysts.

In patients where CT is contraindicated (i.e. chronic kidney disease or previous contrast medium reactions), abdominal MRI is a valid alternative. Previous surgical history, body mass index (BMI), and patient comorbidities should be ruled out in order to choose the most suitable therapeutic approach.

Patient preparation includes a complete evaluation of previous abdominal surgical procedures or diseases in order to exclude situations which may impair laparoscopic treatment (i.e. previous transperitoneal procedures, open surgery procedures, hepatosplenomegaly, chronic obstructive pulmonary disease, kyphoscoliosis, or coagulation disorders) [20].

An adequate preoperative bowel preparation regime is required for the transperitoneal approach, but is not useful for the retroperitoneal one. Trichotomy of the surgical access point is necessary and the surgical site should be marked before access to the operating room. A detailed informed consent including surgical procedure and potential complications should be obtained from the patient. Prophylactic antibiotic is given at the time of general anesthesia induction and a Foley urethral catheter is placed before patient positioning. An orogastric tube is only required for transperitoneal procedures.

### Operating room configuration and patient positioning

Once general anesthesia has been administered, patient positioning maneuvers can begin, according to the type of approach being used. The operating room configuration is independent of the type of approach selected. All members of the operating room team can visualize the procedure from a principal monitor placed on the opposite side from the surgeon. The primary tower with insufflator, light source, and camera box has to be visualized by the surgeons in order to be able to modify the setting during the procedure. For transperitoneal approach, the surgeon and assistant are on the contralateral side of the renal cyst, facing the patient's abdomen (Figure 105.1); for retroperitoneal approach, the surgeons stay behind the patient's back (Figure 105.2).

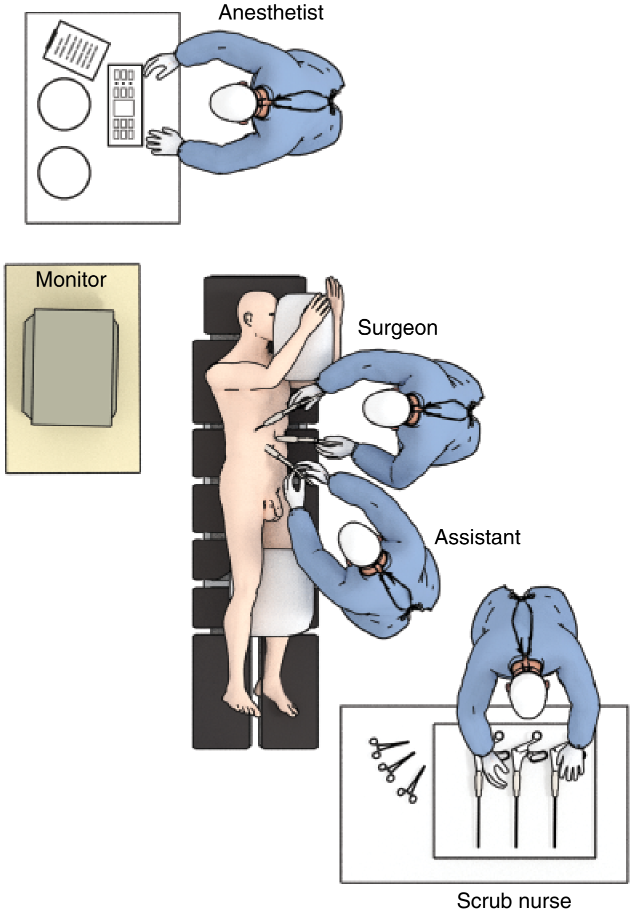


**Figure 105.1** Operating room configuration for transperitoneal right renal cyst decortication.

The table is slightly split in order to have tension on the interested flank. This position is also achieved by using light Trendelenburg placement and by putting a raising towel under the contralateral flank. For the transperitoneal procedure the patient is placed in a modified flank position with a 45° of patient angulations to the operating table. For the retroperitoneal approach, the patient is placed in a full flank position. Moreover, the working space is increased by splitting the operating table at the lumbar level in order to achieve a wide space between the iliac crest and the 12th rib.

All pressure points (including contralateral elbow, legs, and ankles) are properly padded to avoid decubitus lesions. An axillary roll is preferred to protect the contralateral brachial plexus. The lower leg is flexed and the upper one is kept extended and some pillows are positioned between them in order to avoid direct pressure

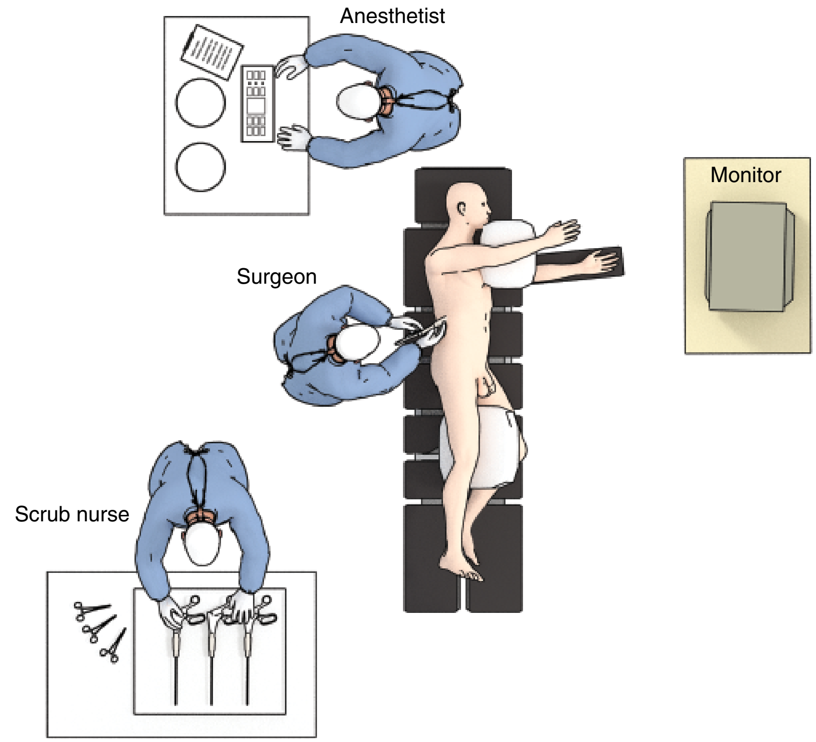


**Figure 105.2** Operating room configuration for retroperitoneal right renal cyst decortication.

contact. The umbilicus is at the level of the operating table break. The patient is secured to the operating table with wide tape at the level of axilla, hips, and legs. The surgical field is prepared and painted with povidone–iodine (Betadine®) from the nipples to pubis level and from the contralateral pararectal space up to the level of the spine.

Laparoscopic access can be achieved using different techniques, depending on surgeon personal experience and patient characteristics [21].

### Trocar positioning – transperitoneal procedure

For laparoscopic transperitoneal access we prefer to adopt a linear port configuration, rather than the triangulation rule as classically depicted. As described by Harper et al., three 5 mm trocars are positioned on the ipsilateral pararectal line [22]. The camera trocar, cranial, with a 30° lens, is positioned two fingerbreadths below the costal margin on the site where the Veress needle was previously placed in order to achieve a 15 mmHg pneumoperitoneum. The other ports are then positioned with a distance of four fingerbreadths between them under direct vision. This trocar positioning avoids interference between surgeon and camera assistant and improves the ergonomics (Figure 105.3) [15]. In the case of obese patients, all ports can be positioned more laterally, according to patient habitus. A low transverse incision such as Pfannenstiel is performed if needed for extraction of surgical specimen.

### Trocar positioning – retroperitoneal procedure

As the retroperitoneal approach gives a smaller working field and a limited area for port positioning, particular maneuvers are needed in order to achieve ideal access. The patient is placed in a fully flank position without any angulation, in order to displace the posterior peritoneum as far as possible. The first 5 mm trocar is placed under direct vision along the posterior axillary line halfway between the iliac crest and the tip of the 12th rib, in the area called Petit's triangle. By mechanical blunt dissection, the retroperitoneal working space is progressively developed at the same time as $CO_2$ insufflation. Some authors suggest the use of a mechanical balloon dilator, progressively insufflated with 800–1000 ml [23].

The peritoneum is then medialized and two additional 5 mm trocars are positioned along the middle and anterior axillary line at the level of the first trocar site under direct vision. A 5 mm port is used for the optic and the others are the working ports for the surgeon, allowing a good balance between vision and ergonomics [24, 25] (Figure 105.4).

As described, three trocars are usually needed for this approach. A useful alternative is the application of laparoendoscopic single-site (LESS) surgery. After the application of the 5 mm single port at the level of Petit triangle, the intervention is performed without the need for further cutaneous incisions. Modern 5 mm flexible tip laparoscopes aid laparoscopic skilled surgeons to

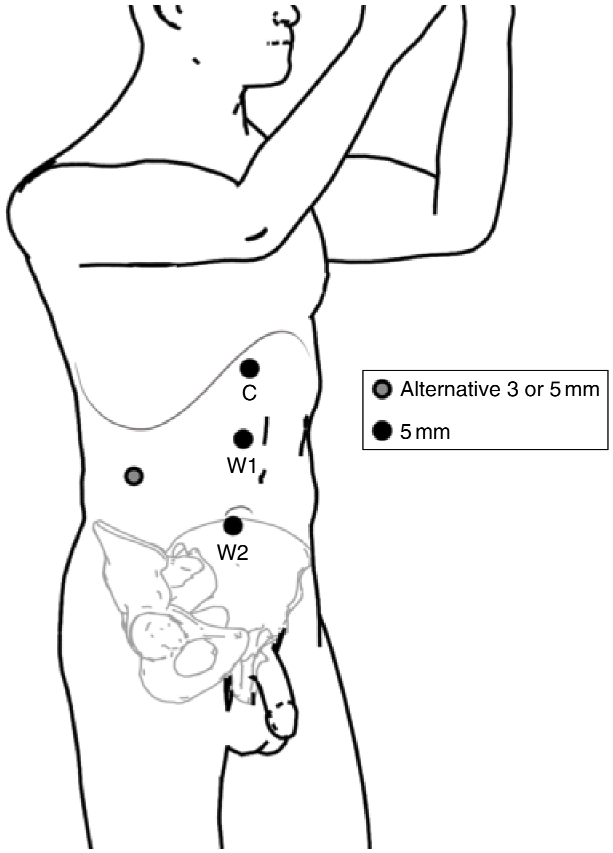


**Figure 105.3** Port placement for transperitoneal right renal cyst decortication. Three 5 mm trocars are positioned on the ipsilateral pararectal line. C, camera port for the assistant; W1, W2, working ports for the surgeon.

make this intervention an effective and feasible alternative to conventional laparoscopy [26] (Figure 105.5).

### Surgical technique – transperitoneal procedure

The first passage consists in kidney exposition. After trocar placement, the parietal peritoneum is excised along the white line of Toldt laterally to the whole extent of descending colon on the left side and of ascending on the right side. On the left, phrenocolic, lienorenal, and splenocolic ligaments should be divided. On the right, liver retraction is useful to fully expose the upper pole of the kidney, and the renal hilum is exposed by means of full medialization of the colon and duodenum. For medially located cysts, a Kocher maneuver is needed to provide full exposition. For a large cyst there is normally no doubt about cyst location as it is fully evident, usually displacing perirenal adipose tissue and adjacent organs. The cyst is then opened with laparoscopic scissors and the cystic liquid aspirated and sent for cytological exam if neoplasia is suspected. The cyst wall is then fully excised with laparoscopic scissors (Figure 105.6), extracted with an Endo Catch® bag and sent for pathological evaluation. Usually some biopsies of renal parenchyma at the base of the cyst are taken. The base of the cyst is then fulgurated with bipolar or monopolar coagulator to achieve perfect control of hemostasis, usually further improved by apposition of local hemostatic agents such as oxide cellulose sponge. If an inadvertent lesion of the collecting system has occurred, immediate repair is performed with continuous suturing. Final inspection is mandatory for hemostasis and absence of urinary leakage. A drain is usually placed from one of the ports. The abdomen is desufflated, peritoneal cavity exited, and port entry sites closed. If a collecting system lesion is noticed, the open-ended ureteral catheter can be substituted with a double-J ureteral stent, which is usually left in place for one month and removed in ambulatory regimen.

In the case of parapelvic or suspected complex cysts, intraoperative ultrasound is needed to define their nature and location. Moreover, for parapelvic cysts, a ureteral catheter should be placed at the beginning of the procedure with two aims: first, to permit the execution of a retrograde pyelography, which will help the surgeons to clarify the relation between the cyst and collecting systems; and second, to allow confirmation of the absence of communication between the cyst and collecting

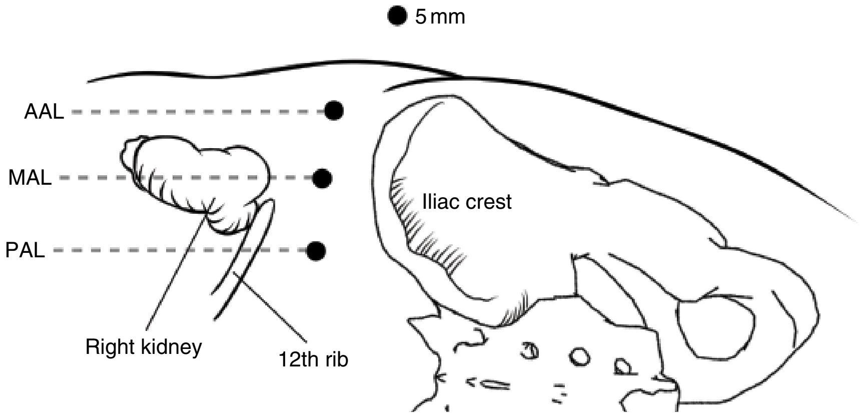


**Figure 105.4** Port placement for retroperitoneal right renal cyst decortication. The first 5 mm trocar is positioned along the posterior axillary line (PAL), halfway between the iliac crest and the tip of the 12th rib. The two other trocars are positioned on the same line as the first, respectively along the medial axillary line (MAL) and the anterior axillary line (AAL).

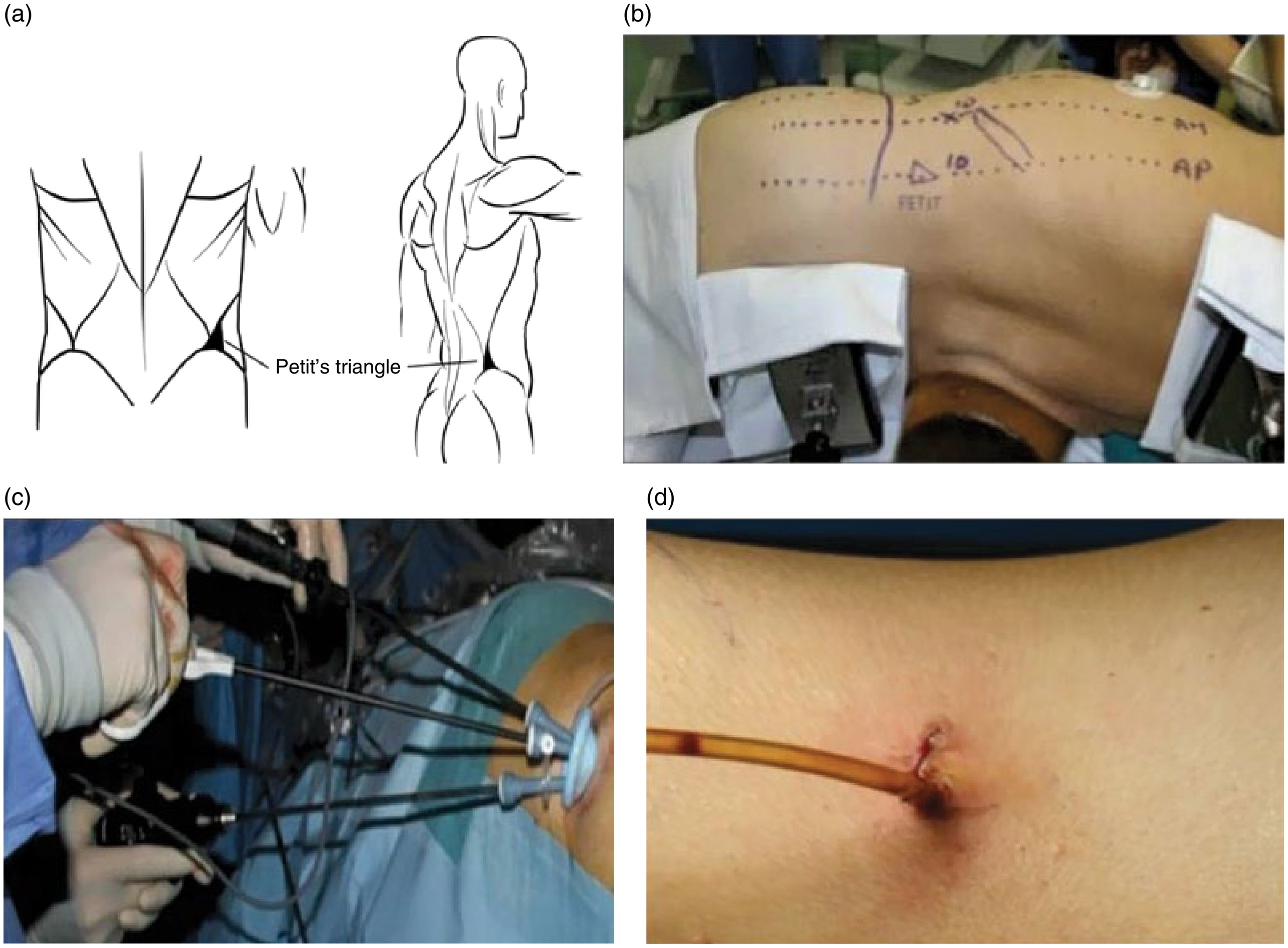


**Figure 105.5** Laparoendoscopic single-site (LESS) surgery summary. (a,b) Anatomical landmarks of Petit's triangle, preferred entry point for retroperitoneoscopic LESS surgery. (c) Instrument positions during the surgical procedure. (d) Final surgical scar.

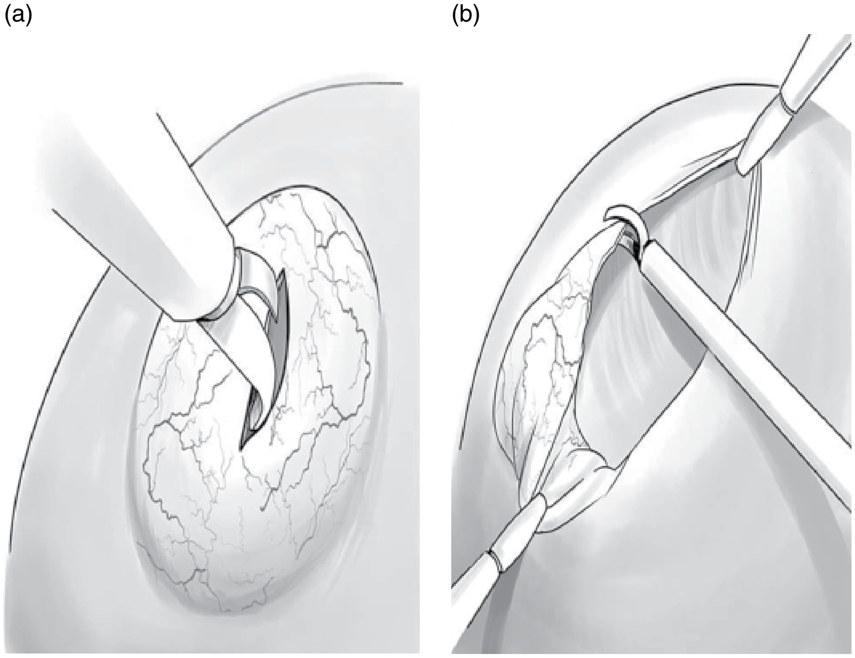


**Figure 105.6** Schematic drawing of the renal cyst decortication procedure. (a) First incision of the cystic mass. (b) Cyst excision from the underlying renal parenchyma.

systems. If an intraoperative lesion is suspected, indigo carmine can be injected via the ureteral catheter: if blue liquid is aspirated from the cyst it must be due to a communication with the urinary system.

### Surgical technique – retroperitoneal procedure

Once retroperitoneal access is obtained, the cyst is usually suddenly recognizable as it dislocates the parietal peritoneum medially and its landmarks are clearly distinguishable from the main muscles of the lateral lumbar region, psoas major, and quadratus lomborum. Medially to psoas muscle, the ureter can be identified and followed up to renal hilum. After identification of the cyst, the surgical technique of removal is the same described for transperitoneal approach.

Retroperitoneoscopy is commonly advised for posteriorly located and lower pole cysts; however, some authors utilize this technique for any kind of renal cysts. Moreover, retroperitoneal access can potentially avoid intraperitoneal tumor seeding in case a malignant cyst is detected [27]. A recent multicentric retrospective study by Ozcan et al. investigated a cohort of 40 patients who underwent laparoscopic transperitoneal or retroperitoneal approach for simple renal cyst decortication. The results of this comparison were slightly in favor of the retroperitoneal approach as it was associated with a relative but significant reduction in operative time and postoperative pain [28].

## Robotic surgery applications

To the best of our knowledge, robot-assisted treatment is not indicated for simple renal cysts. We believe that this kind of surgery is perfectly managed with laparoscopy and that robot-assisted surgery should be reserved for more complex pathologies. Akca et al. recently described a comparison between cystic and solid renal neoplasms treated with a robot-assisted partial nephrectomy. They concluded that surgical outcomes in terms of oncologic radicality and preservation of renal function are equal when treating a suspicious cystic or solid renal neoplasm. Nephron-sparing surgery can therefore be safely proposed for those patients [29, 30].

## Single-site surgery

LESS surgery has been developed in an attempt to further reduce the invasiveness and reduce the cosmetic impact associated with conventional laparoscopic surgery [31]. Many clinical series have demonstrated that LESS surgery is feasible for a broad range of retroperitoneoscopic urologic procedures [26].

The main limitations to the widespread application of this technique are technical problems, such as clashing of instruments and loss of triangulation, which have limited LESS surgery to just a few highly qualified centers. To overcome these problems, robotic technology has been applied to single-site surgery and some patient series have started to appear in the literature, demonstrating the benefits and applicability of this technique [32, 33].

An interesting report by Haber et al. described the clinical application of an innovative device (SPIDER surgical system, TransEnterix, Morrisville, NC, USA) that facilitates LESS procedures, restoring the ergonomics of laparoscopic triangulation and avoiding instruments clashing. The first case reported was decortication of a Bosniak II left renal cyst. The SPIDER system was introduced through a GelPOINT and vision was through a 5 mm flexible-tip laparoscope (EndoEYE, Olympus, Orangeburg, NY, USA) inserted through a static channel of the SPIDER platform [34].

An example of retroperitoneoscopic LESS surgery application is presented in Video 105.1, where we show the decortication of a 10 cm renal cyst. At preoperative CT scan evaluation, three months before surgery, the appearance was of a simple Bosniak I renal cyst. Intraoperatively, we discovered it was hemorrhagic. An intraoperative frozen section confirmed that the lesion was benign and we easily completed cystic wall excision. Postoperative follow-up was negative for recurrences or complications. This case demonstrates how even a simple cyst can become complicated (i.e. for a traumatic event) and may modify its appearance in a short period of time.

## Postoperative management and follow-up

Patients are fully mobilized from the day after surgery. The bladder catheter is removed when drain output is minimal or when drainage creatinine levels are comparable to those in serum, usually few days after surgery. If the output remains absent, the drain is removed the day after bladder catheter removal. Patients are usually dismissed on day 1–3 after surgery, depending on cyst complexity.

An ambulatory sonography is usually performed 2–3 months after surgery and no other follow-up indications are subsequently necessary.

## Complications

Hemorrhagic lesions or urinary leakage are the most frequent reported complications. Even if they delay patient recovery, their resolution is usually conservative. Other reported complications are linked to chemical peritonitis, which mainly occurs after decortication of cysts in patients with polycystic kidney disease. This may lead to fever, prolonged paralytic ileum, or local pain that can be managed with conservative measures (parenteral antibiotics, hydration, parenteral nutrition) and with prolonged hospitalization [16].

## Laparoscopic treatment of calyceal diverticula

### Introduction

Calyceal diverticula are classically depicted as intraparenchymal outpouchings of renal collecting systems, covered by urothelial epithelium, interconnecting with them by a narrow neck, without a proper draining papilla, resulting in reduced passage of urine [35]. A recent review [36] reports that they are found in 0.21–0.6% of intravenous urographies, with similar prevalence in adults and pediatric populations, and are slightly more common in women than in men (63% vs. 37%). They are more common in the upper pole calyces, with a frequency of 48.9%, versus 29.7% and 21.4% in the middle and lower poles respectively.

Pathological conditions are mostly related to development of stones due to urinary stasis, which is reported in 9–50% of cases. This can be the leading cause of chronic or acute flank pain, hematuria, or recurrent urinary tract infections. In some cases, these events can determine impairment to renal function or parenchymal damage [37].

Even only from case report series, upper urinary tract urothelial carcinoma has been reported as an additional possible disease with a high potential of invasion of the renal parenchyma [38, 39]. Because of the rareness of this finding, our knowledge derives mostly from small patient series or case reports and there is lack of studies that compare different treatment modalities.

Calyceal diverticula pathophysiology is still uncertain. Many authors suggest a congenital origin, during the development of the ureteric bud, even if a clear etiology has never been demonstrated [40, 41]. Other authors have suggested potential acquired causes, such as fibrosis of a calyceal infundibulum, obstruction, neuromuscular or traumatic pathogenesis. Obstruction can be secondary to stone formation or to an infective focus (i.e. an abscess); another factor is the possible development of smooth muscle or autonomic deficiency that creates a sphincter achalasia, with progressive collecting system dilatation, finally resulting in a diverticulum [42].

A morphologic classification divides calyceal diverticula into two types: type I diverticula are smaller and drain into minor calyces; type II are larger and drain into major calyces [43]. An alternative classification of calyceal diverticula was proposed in order to help the management of the related stone disease: type I with open mouth and short neck, more suitable for extracorporeal shock-wave lithotripsy (ESWL); type II with closed mouth and short neck, with more indication for ureteroscopy (URS); types III and IV with closed mouth and long or obliterated neck, passable only by percutaneous nephrolithotomy (PCNL) [44].

### Radiologic findings

The sonographic appearance of calyceal diverticula is similar to that of simple renal cysts, except that they frequently contain mobile stones [45]. CT, urography, or pyelography are essential to clarify the communication with collecting systems. CT is normally sufficient to clarify the diagnosis (Figure 105.7).

A recent report concluded that multiphasic contrast-enhanced CT should be performed in cases of calyceal

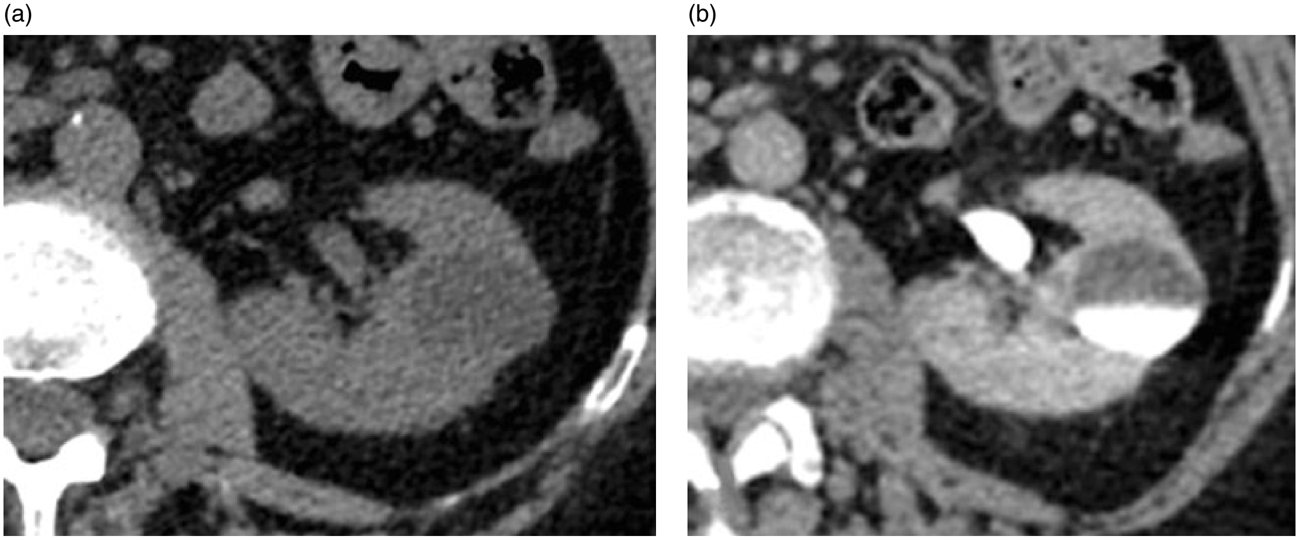


**Figure 105.7** Calyceal diverticulum. CT scan before (a) and after (b) intravenous administration of contrast material in excretory phase. *Source:* Perugia University, Perugia, Italy. Reproduced with permission of Michele Scialpi.

diverticula to rule out the presence of complex atypical Bosniak renal cysts [46].

Other differential diagnoses on imaging can be hydrocalyces, parapelvic cysts, or upper urothelial tumors. Radiologists should be aware of infundibular obstruction to rule out hydrocalycosis, connection with the pelvicalyceal system to exclude cystic disease, or irregular contrast opacification of the cavity for suspicion of neoplasms.

## Indications to surgical treatment

Calyceal diverticula are mostly incidental findings and patients are asymptomatic. Indications to active management are acute or chronic pain, macroscopic hematuria, recurring infections, or parenchymal damage leading to impairment of renal function [47]. Stone-bearing calyceal diverticula are often symptomatic and active management is frequently recommended. As the incidence of this disease is rare, there are no clear therapeutic guidelines. Main options include ESWL or endourological treatments such as URS and PCNL [48, 49].

Because it is the most invasive treatment for this pathology, laparoscopic surgery is indicated in cases of large size stones where previous treatments have failed or for particular anatomic situations such as anteriorly located calyceal diverticula or diverticula with thin overlying parenchyma, where PCNL is not indicated [50]. The goal of laparoscopic intervention is to achieve complete stone clearance and contemporary obliteration of infundibular neck and diverticular cavity.

## Laparoscopic treatment

Both transperitoneal and retroperitoneal approaches have been described; as the incidence of the disease is low, we cannot make a direct comparison between these two techniques. However, the location of the diverticulum, a previous history of major abdominal surgery, and surgeon personal experience should be evaluated before selecting the surgical approach.

First reports were from Gluckman et al. in 1993 [51], who reported a case treated with a five-port transperitoneal access, where the calyx was identified by retrograde methylene blue injection and unroofed, removing the stones and ablating the diverticulum with argon. Hoznek et al. [52] reported in 1998 a series of three patients who underwent renal diverticulum deroofing for intradiverticular lithiasis by a retroperitoneoscopic approach, two with previous failed ESWL and one with an infective complication. After the complete removal of the diverticulum and stones, the authors used a gelatin resorcinol formaldehyde glue on the resection plane. No complications were reported and the early follow-up was negative for recurrences. More recently, Miller et al. [53] reported a series of five patients managed with a retroperitoneoscopic approach in which the diverticulum was identified alternatively by injection of indigo carmine, fluoroscopy, and/or laparoscopic ultrasound. They performed calyceal diverticulectomy, achieving in all cases a complete stone-free rate with fast recovery and without complications. A recent study by Taylor and Thiel [54] compared six cases of minimally invasive calyceal diverticulectomy (four approached laparoscopically and two with a robot-assisted technique). All had history of urinary tract infection and five had associated stone disease. Although the case series is limited, the robotic approach appeared to be feasible and effective, capable of giving results similar to those achieved using traditional laparoscopic surgery. Some authors [55, 56] have also described a combined technique for urolithiasis associated with calyceal diverticula in which, after transperitoneal isolation of the kidney and diverticulum, a transperitoneal PCNL was performed by a nephroscope inserted through an additional 12 mm trocar. This technique minimized bowel lesions and targeted the puncture to the affected diverticulum, improving the stone-free rate and minimizing complications.

Although all these studies have limited series, it is suggested that the laparoscopic approach may have validity for highly selected cases. Despite its invasiveness compared to ESWL and other endourological approaches, perioperative outcomes and long-term follow-up are optimal, without recurrence or late complications reported. Larger studies are still needed in the literature to confirm these statements.

### Operating room configuration, patient and trocar positioning

The operating room is configured in order to give all staff a good view of the procedure, as already observed for renal cyst decortication (Figures 105.1 and 105.2). Monitors are placed on the opposite side from the surgeons. Normally, the first step of the procedure is the retrograde placement of a ureteral catheter in order to perform retrograde pyelography and have an intraoperative marker for the ureter. Thus the patient is initially placed in dorsal lithotomy position. Intraoperative radiological control is needed in order to ensure precise positioning of the ureteral catheter.

After this passage, the patient is positioned for laparoscopic access. As explained for renal cyst ablation, the position varies in order to accomplish the desired surgical approach. The choice of treatment modality is guided by consideration of the patient's habitus and medical conditions and by radiographic evaluation. For an anterior diverticulectomy, the lateral oblique position with

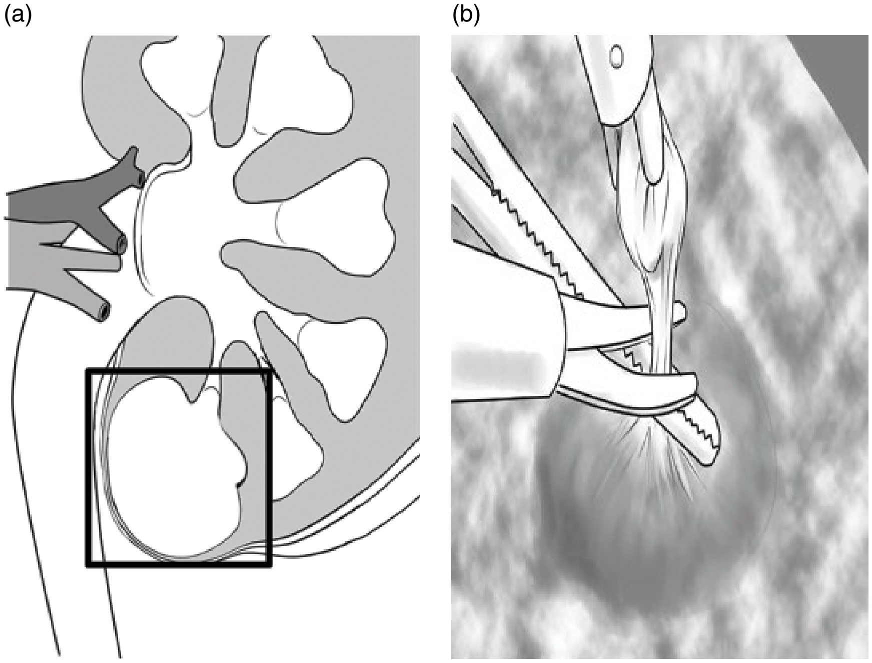


**Figure 105.8** Schematic drawing of a calyceal diverticulum. (a) Coronal morphological view. (b) Diverticular excision after complete isolation of its neck from the sac and the underlying renal calyx.

the torso inclined at 45° is preferred, as for the usual transperitoneal approach to the kidney. If the diverticulum is located posteriorly, a retroperitoneal approach is advisable and the patient is placed in flank position. Consequently, port placement is the same as the one described for laparoscopic renal cyst excision or nephrectomy [57].

**Surgical technique**

The first passage consists of kidney isolation and identification of the diverticulum. Some authors describe the use of intraoperative ultrasound to find the precise position of the diverticulum, and in order to selectively dissect the overlying portion of Gerota's fascia and perirenal fat. It may also help to use insufflation of saline solution via a ureteral catheter in order to distend the wall of the diverticulum. Complete examination of the kidney surface is subsequently performed via laparoscopy. In cases with thick renal parenchyma overlying the diverticulum, intraoperative ultrasound may help the identification of the correct site. A longitudinal nephrotomy is performed with electrocautery scissors on renal parenchyma at the level of diverticulum, in order to gain full exposure of this structure until its infundibulum. Next, the diverticulum is excised as shown in Figure 105.8. Any calculi inside can be grasped with forceps or trapped in an endoscopic retrieval bag or finger glove. Alternatively laser ablation can be used if a combined procedure with a rigid/flexible nephroscope is planned [58]. As the diverticular cavity is excised, deep coagulation is required to ablate the remaining epithelium of the diverticulum and to achieve complete parenchymal hemostasis. The diverticular neck can be dilated for entering the collecting system if a further exploration is demanded (i.e. multiple lithiasis). Otherwise, it is closed with simple interrupted figure-of-eight Monocryl sutures. At this point, further hemostatic materials can be applied locally or injected in order to ensure perfect closure of pyelocalyceal system. A perirenal drain is then positioned through one of the trocars. Ports are then closed and the ureteral catheter is usually left in place for about two days.

**Postoperative management and follow-up**

Patients are fully mobilized from the first day after the procedure. Bladder and ureteral catheters are normally removed on the second postoperative day if the drainage output is minimal. We usually check drainage creatinine levels on the first postoperative day in order to exclude urinary fistulas. If its value is consistent with serum creatinine, leakage can reasonably be excluded.

If there is any suspicion of urinary spilling, the drain and ureteral catheter are left in place until the anastomosis is sealed. Antibiotics are usually administered only at the moment of surgery and suspended if there are no signs of urinary tract infection. A CT is usually performed about one month after the intervention to rule out recurrences, fluid collections, or contrast medium extravasations.

Even with the limited availability of data due to the relatively rare occurrence of this pathology, perioperative outcomes of laparoscopic surgery for calyceal diverticulectomy are encouraging, with optimal long-term results without reports of recurrences.

### Complications

Reports of surgical-related complications in the literature are scarce. Postoperative bleeding requiring blood transfusions, port-site drainage, and subcutaneous crepitance due to pneumoperitoneum are only reported in sporadic cases. All these complications were successfully resolved without the need for invasive treatments. All possible general complications of laparoscopic surgery must be taken into account and explained to the patient before the surgical informed consent is signed.

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# 106

# Laparoscopic and Robotic Techniques for Management of Pelvic Organ Prolapse

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## Introduction

Pelvic organ prolapse (POP) remains a common problem for many women. It is estimated that 50% of women will be affected by POP in their lifetime and the risk for them to receive surgery for POP or stress urinary incontinence (SUI) is 11% [1]. This is particularly relevant given the increasing life expectancy rates, the increased rates of POP in the elderly, and the effect that POP has on quality of life [2]. Some have forecast that the incidence of POP will increase from 3.3 million in 2010 to 4.9 million in 2050, an overall increase of 46% [3]. Definitive therapy for POP is surgical and can be approached primarily through a vaginal or an abdominal approach. In general, vaginal correction is done through a uterosacral ligament suspension or sacrospinous ligament fixation, while abdominal surgery relies on sacrocolpopexy with the use of mesh. A Cochrane meta-analysis demonstrated that the abdominal approach led to decreased rates of recurrent vault prolapse and dyspareunia when compared to the vaginal approach [4]. Even though abdominal sacrocolpopexy has been shown to have greater long-term success, it remains decidedly more invasive, requires longer recovery time, and has a higher complication rate.

The advent of laparoscopy and robotics has led to widespread adoption of these techniques for abdominal sacrocolpopexy (ASC) without evidence demonstrating improved outcomes. Nezhat et al. published the first experience with laparoscopic abdominal sacrocolopopexy in 1994. In this initial technique, the authors advocated using a single piece of Gore-Tex® mesh attached to the posterior vaginal apex with sutures or staples to the sacral promontory [5]. There have been several modifications to this original technique, to reduce operating time, decrease complications, and improve outcomes. For women wanting a uterine-sparing procedure, the laparoscopic sacrohysteropexy has been developed. Some techniques use a single arm of posterior mesh or a combination of Y-shaped anterior mesh with posterior arm of mesh. As volume and experience grew, studies were able to show that although laparoscopic ASC was a longer procedure, it was associated with decreased intraoperative blood loss, shorter hospital stay, and reduced rates of ileus and small bowel obstruction [6]. With the introduction of the da Vinci® Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) surgeons were afforded increased ergonomic capability, more degrees of freedom, and 3D vision. The robotic system gave increased ease of surgery with similar outcomes, albeit at a higher cost [7].

In this chapter, we review the laparoscopic and robotic sacrocolpopexy approaches to the management of POP. We will cover evaluation, technique, complications, and outcomes.

## Evaluation and workup

The primary indication for robotic ASC is the presence of symptomatic apical or uterine POP. The most common symptom is a vaginal bulge or pressure, but this can be accompanied by a considerable number of other urinary, bowel, or sexual complaints [8]. These symptoms can be significantly varied based upon the patient's degree of underlying prolapse. Patients may experience SUI, obstructive urinary symptoms, or even present without any urinary issues but an occult SUI may be unmasked after a prolapse repair. Similarly, contradictory bowel symptoms may also be encountered. Patients may need to excessively strain or use perineal/vaginal pressure to defecate, while others may experience fecal incontinence. The common indications for robotic ASC

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include uterine prolapse, post-hysterectomy vaginal vault prolapse, recurrent apical prolapse, and failed previous vaginal repairs. Some factors to keep in mind during the patient selection process include the patient's pulmonary status, ability to tolerate steep Trendelenburg, and any previous abdominal or pelvic surgery which would give rise to concern for postsurgical adhesions.

Patients should undergo a thorough history and physical examination. They should also complete a preoperative voiding diary, in addition to a quality-of-life (QOL) questionnaire. The presence of a uterus should be accounted for and patients should be counseled regarding concomitant hysterectomy or consideration for a sacrohysteropexy. Specific questioning regarding Papanicolaou smear testing history, gynecologic neoplasia, pelvic sonography, and abnormal or postmenopausal uterine bleeding should be pursued.

Physical examination should be thorough, with the use of bimanual examination and both bivalve and univalve speculum examination. This will allow for assessment of all compartments and appropriate staging with the pelvic organ prolapse quantification (POP-Q) system [9]. The estrogen status of the patient should also be noted at this time. The exam should also include a cough stress test to assess for possible SUI though it should be noted that a significant number of patients may have occult SUI that may only be unmasked when the prolapse repair is performed and the urethra is unkinked [8]. Urodynamics may be used in complex cases, but determination of the need for urodynamics should be made on an individual case basis.

In 2006, the Colpopexy and Urinary Reduction (CARE) trial demonstrated that the addition of a Burch colposuspension in women without preoperative SUI who underwent an ASC had significantly lower rates of postoperative SUI (23.8% vs. 44% in the control group) [10]. The long-term outcomes from the CARE trial were published in 2013 and showed that at 7 years, women who underwent concomitant Burch colposuspension at the time of ASC had a longer time to recurrence of SUI compared to those women who did not have an anti-incontinence procedure [11]. Inevitably, there have been those who have used these data to justify prophylactic anti-incontinence procedures to be done concomitantly with prolapse surgery. A more contemporary trial that has echoed this stance has been the Outcomes Following Vaginal Prolapse Repair and Midurethral Sling (OPUS) trial. The OPUS trial concluded that a prophylactic midurethral sling placed during vaginal prolapse surgery resulted in a lower rate of SUI at 12 months postoperatively, albeit at the cost of a higher rate of adverse events [12]. Even though these results seemingly reinforced the CARE trial findings, these were vaginal procedures and cannot be used to directly extrapolate to similar outcomes in ASC, laparoscopic sacrocolpopexy (LSC), or robotic ASC. Our practice is to counsel patients regarding this risk and generally recommend the placement of a midurethral sling concomitantly with the ASC if SUI is experienced clinically or demonstrated during the workup.

## Surgical approach

### Laparoscopic sacrocolpopexy

**Step 1: Preparation**

After induction of general endotracheal anesthesia, the patient is placed in low lithotomy position with the use of Yellowfin stirrups. The patient needs to be secured in order to allow for steep Trendelenburg position and the arms should be tucked in. All pressure points are padded. Both the abdomen and the vagina/perineum should be prepped and a split drape should be employed to allow one assistant to manipulate the vagina while the other assists in the abdomen. A Foley catheter is placed in a sterile manner after draping to allow for further manipulation. A nasogastric tube may also be inserted at this time per surgeon preference.

**Step 2: Abdominal access**

The abdomen is insufflated with either a Veress needle or Hassan trocar in the periumbilical or supraumbilical region. At our institution, we prefer the use of a periumbilical Veress needle, unless there is concern for significant adhesions or chance of bowel injury. If that is the case, Veress needle access can be attempted two fingerbreadths below the costal margin at the level of the midclavicular line. Abdominal pressures should be monitored closely. If the intra-abdominal pressure exceeds 8 mmHg, the needle should be repositioned to ensure it is not in any abdominal structures, adherent to bowel or omentum, or outside the peritoneal cavity. After adequate insufflation, the trocar sites are marked out appropriately (Figure 106.1). Based on surgeon preference, 4 or 5 ports may be used in total. Local anesthesia is administered at each trocar site for preemptive analgesia. A 10–12 mm camera port is then placed at the umbilical edge or slightly cranial to the umbilicus. Two additional 10–12 mm ports are placed lateral to the rectus muscle. One or two additional ports are placed 2–3 cm cephalad and 2–3 mm medial to the anterior superior iliac spines. The sigmoid is retracted to the left and cephalad by using the left lower port.

**Step 3: Posterior peritoneal dissection**

Once the sigmoid colon is retracted, attention is drawn to the sacral promontory. Of note, this left lower port may be obviated by the use of suture retraction.

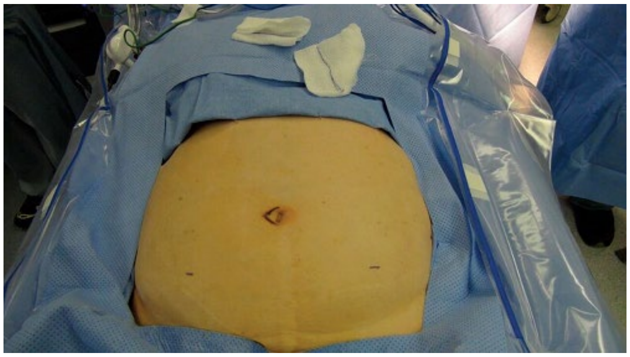

**Figure 106.1** The trocar sites. Typically anywhere from 4 to 5 ports are used, based on surgeon preference. *Source:* Wesley White. Reproduced with permission of Wesley White.

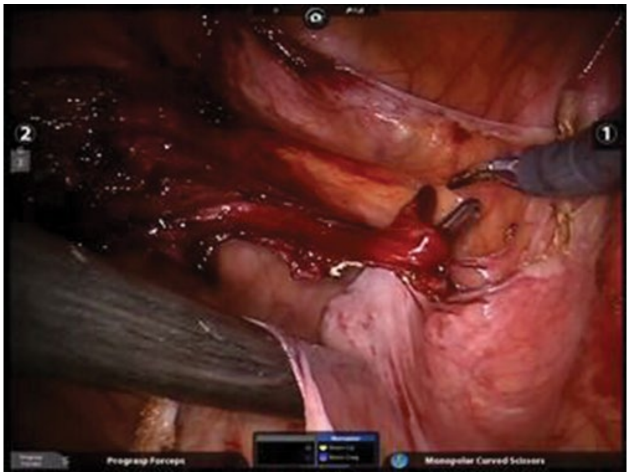

**Figure 106.2** The posterior peritoneum over the sacral promontory has been incised longitudinally to the level of the vaginal apex. *Source:* Wesley White. Reproduced with permission of Wesley White.

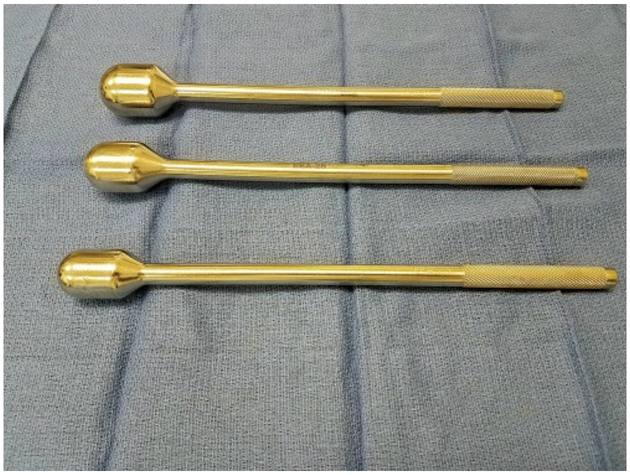

**Figure 106.3** Various sizes of reusable vaginal manipulator are available. The assistant seated at the perineum places the vaginal manipulator, such as the EEA Reusable Sizer (Medtronic, Inc, Minneapolis, MN, USA), inside the vaginal vault. *Source:* Wesley White. Reproduced with permission of Wesley White.

A 1-0 nonabsorbable suture on a large needle (CT-X) can be passed through the left lower quadrant under visualization, placed through an epiploic appendage of the sigmoid colon, and back through the left lower abdomen and clamped to the skin where retraction is desired. Once the retraction of the sigmoid colon is achieved, the sacral promontory, right iliac vessels, and right ureter are identified. The posterior peritoneum over the sacral promontory is incised longitudinally to the level of the vaginal apex (Figure 106.2).

### Step 4: Anterior vaginal dissection

The assistant seated at the perineum will place the vaginal manipulator, such as the EEA Reusable Sizer (Medtronic, Inc, Minneapolis, MN, USA), inside the vaginal vault (Figure 106.3). In general, a larger size such as the 31 or 34 mm is preferred as it distends the vagina more and allows for better vaginal support to aid in dissection. It is imperative that the assistant place the manipulator at the middle of the apex or cervical cuff in order to allow for equal distention of the vagina and prevent redundant tissue being presented. The assistant should place the vagina at a slight downward tilt in order to better expose the anterior vaginal wall to the surgeon. A grasper is used to lift the peritoneum at the vaginal apex following a hysterectomy or the cervical cuff following a supracervical hysterectomy. If the patient is post-hysterectomy, the midline of the vaginal cuff is identified. The peritoneum is incised and the avascular areolar plane between the anterior wall of the vagina and the posterior wall of the bladder is developed. Much of this space can be bluntly dissected with minimal use of cautery for hemostasis. The dissection is carried distally to the level of the bladder neck and laterally to the lateral walls of the vagina. The bladder neck is identified by the location of the Foley balloon. Excessive bleeding or difficulty dissecting the plane can be indicative of entrance into the wrong plane. If the dissection plane is difficult to identify, retrograde filling of the bladder may help further define the anatomy and identify any inadvertent bladder injuries made during the dissection. A cystoscope may also be introduced and its light may be used as a guide. If a bladder injury or vaginal wall injury is made during the dissection, it should be closed in multiple layers with absorbable suture and care must be taken not to place mesh directly on the suture line of the original injury.

### Step 5: Posterior vaginal dissection

The posterior peritoneum is incised at the level of the cervical cuff or vaginal apex. The assistant at this point should shift the vaginal manipulator superiorly in order to allow for better exposure of the posterior vaginal wall. Once again, an avascular areolar plane is encountered and should be approached in a manner similar to that used for the anterior plane. It should be noted that the rectovaginal space tends to be more areolar and may require more sharp dissection than the vesicovaginal plane. The lateral limits of dissection are defined by the uterosacral ligaments and the distal limits are either the peritoneal reflection or preferably down to the level of the peritoneal body.

#### Step 6: Identifying and developing the sacral promontory

In general, the sacral promontory is easily palpated once adequate retraction has been placed on the sigmoid colon and mesentery. The sacral promontory at the level of S1 will be moderately flat and then starts to curve inferiorly at the level of S2. The posterior peritoneum should be incised at the sacral promontory approximately 2 cm proximal to the palpable inferior curve. This peritoneal incision is carried distally and is connected to the posterior wall incision. Take care to stay medial to the ureter and lateral to the sigmoid mesentery throughout this maneuver. If bleeding is encountered in the presacral space, insufflation may be increased in order to tamponade bleeding before placing lap pads to apply direct pressure. Sutures, surgical clips, and hemostatic agents may be used to stave off persistent bleeding.

#### Step 7: Distal placement of mesh

Either a prefashioned Y-shaped polypropylene mesh or two single arms of mesh are trimmed to the anatomic specifications of the patient (typical size variation: 2–4 cm × 12–15 cm). The mesh is rolled and introduced into the abdomen. One arm is unrolled and placed upon the anterior aspect of the vagina and attached via multiple 2-0 Gore-Tex sutures, typically three rows of two sutures. If full-thickness passes are made, they do not need to be removed as they will eventually granulate over. However, full-thickness passes may cause bunching and scalloping of the vagina and are best avoided. The same is repeated on the posterior portion with the second arm of the mesh.

#### Step 8: Fixation of the proximal mesh/coverage of mesh

The tail of the mesh should then be placed over the peritoneal incision. The assistant at this point should be placing pressure with the vaginal manipulator in order to bring the vaginal apex closer to the sacral promontory. The mesh should then be affixed to the anterior longitudinal ligament using two to three 0 nonabsorbable sutures. These should be placed in a transverse fashion as it has the added effect of ligating any vertically oriented vessels at this location. The retroperitoneum is then closed over the mesh (retroperitonealization of mesh) with a running barbed suture.

#### Step 9: Closure

The uterus is removed at this point via the umbilical port, typically hand-morcellated in a plastic bag through the incision in a controlled fashion. Alternatively, the uterus can be removed whole by stressing the umbilical port. The abdomen is desufflated and the ports are removed. Fascia is closed in all 10–12 mm trocar sites with 0-Vicryl figure-of-eight sutures. Skin incisions are closed in a subcuticular fashion.

#### Step 10: Vaginal examination and cystoscopy

A vaginal examination is performed at this time to assess both apical support and to check for occult cystocele or rectocele. After repair of these defects, cystoscopy is performed to assess for any bladder wall injury and for ureteral efflux. The Foley catheter is then replaced and vaginal packing placed.

### Postoperative care

The Foley catheter and vaginal packing are removed in the morning of postoperative day 1. We generally employ a "fill and pull" technique, in which the bladder is filled with 300 ml of saline or as much as the patient can tolerate (whichever is less) and the Foley catheter is removed. The patient is generally discharged home on postoperative day 1 and then reassessed at one month and six months postoperatively.

We describe the robotic laparoscopic sacrocolpopexy approach in the next section as the basic steps are very similar to the laparoscopic approach.

### Robotic laparoscopic sacrocolpopexy

#### Step 1: Preparation

After induction of general endotracheal anesthesia, the patient is placed in low lithotomy position with the use of Yellowfin stirrups. The patient needs to be secured in order to allow for steep Trendelenburg position and the arms should be tucked in. All pressure points are padded. The patients breast should also be carefully padded and taped into position. Both the abdomen and the perineum should be prepped and a split drape should be employed to allow one assistant to manipulate the vagina while the other assists in the abdomen. A Foley catheter is placed in a sterile manner after draping to allow for further manipulation. A nasogastric tube may also be inserted at this time per surgeon preference.

#### Step 2: Abdominal access

The abdomen is insufflated with either a Veress needle or Hassan trocar in the periumbilical or supraumbilical region. At our institution, we prefer the use of a periumbilical Veress needle, unless there is concern for significant adhesions or chance of bowel injury. If that

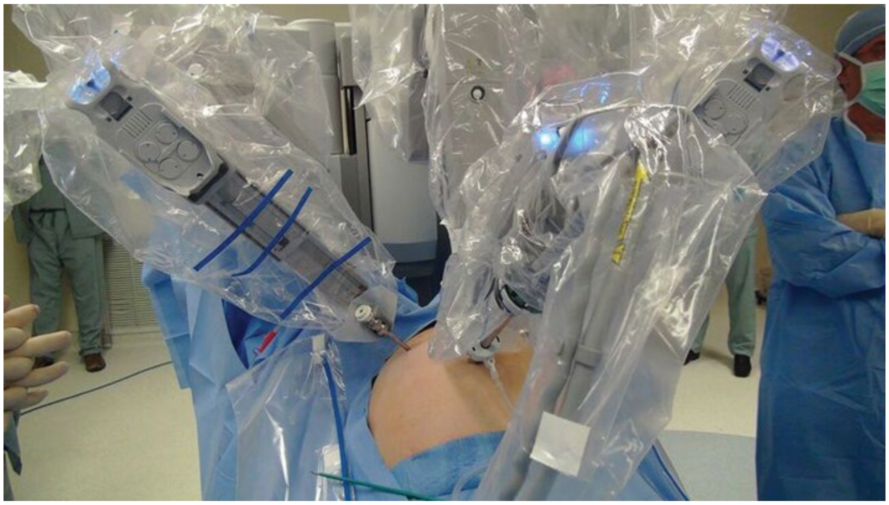

**Figure 106.4** One of the standard distributions of ports for robotic ASC. At our institution, we employ the AirSeal (SurgiQuest, Milford, CT, USA) system for constant pneumoperitoneum and smoke evacuation. *Source:* Wesley White. Reproduced with permission of Wesley White.

is the case, Veress needle access can be attempted two fingerbreadths below the costal margin at the level of the midclavicular line. After adequate insufflation, the trocar sites are marked out appropriately. Local anesthesia is administered at each trocar site for preemptive analgesia. A 12 mm camera port is then placed at the umbilical edge, depending on the robotic system being employed. If the patient has a shorter pubic symphysis to umbilicus length, the trocar can be placed in a supraumbilical fashion with a longitudinal incision. A da Vinci robotic 0° or 30° camera (Intuitive Surgical) is then used to inspect the abdomen. Two 8 mm robotic ports are then placed 9 cm lateral to the umbilicus at the same level. Another robotic port is placed 3 cm lateral and 3 cm cephalad to the left-sided 8 mm robotic arm. At our institution, we employ the AirSeal® (SurgiQuest, Milford, CT, USA) system for constant pneumoperitoneum and smoke evacuation. A 12 mm incision is made 3 cm lateral and 3 cm cephalad to the right 8 mm robotic port,and an AirSeal trocar is inserted (Figure 106.4).

**Step 3: Robotic setup**

The patient is now placed in steep Trendelenburg in order for the bowel to fall away from the pelvis. The patient cart of the robotic system is brought in either at the foot of the bed or docked at the patient's side. We prefer docking the patient cart at the patient's side in order to allow an assistant to be seated by the patient's perineum. We prefer to use right-handed monopolar shears and left-handed ProGrasp forceps. The fourth arm will use an atraumatic grasper such as a double fenestrated grasper. If needed, adhesiolysis is performed in order to have full access to the pelvis.

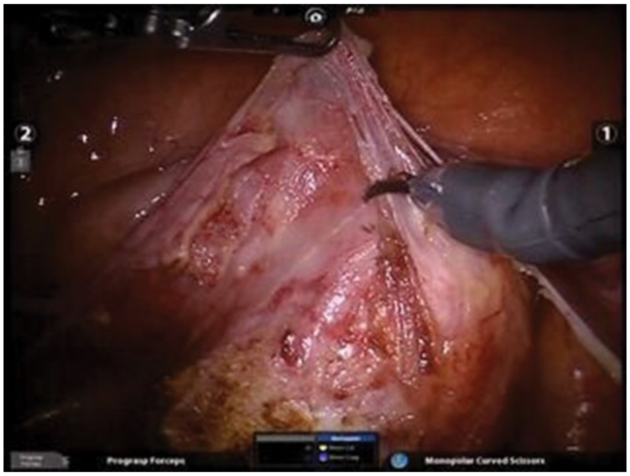

**Figure 106.5** The peritoneum is incised and the avascular areolar plane between the anterior wall of the vagina and the posterior wall of the bladder is developed. Much of this space can be bluntly dissected with minimal use of cautery for hemostasis. *Source:* Wesley White. Reproduced with permission of Wesley White.

**Step 4: Anterior vaginal dissection**

The assistant seated at the perineum places the vaginal manipulator, such as the EEA Reusable Sizer (Medtronic, Inc, Minneapolis, MN, USA), inside the vaginal vault. The ProGrasp is used to lift up the peritoneum at the vaginal apex following a hysterectomy or the cervical cuff following a supracervical hysterecomy. The peritoneum is incised and the avascular areolar plane between the anterior wall of the vagina and the posterior wall of the bladder is developed. Much of this space can be bluntly dissected with minimal use of cautery for hemostasis (Figure 106.5). Once enough of the peritoneum has been dissected, the third arm can be used to hold up the peritoneal edge and maintain countertraction. The dissection is carried distally to the level of the bladder neck and laterally to the lateral walls of the vagina. The bladder neck is identified by the location of the Foley balloon.

### Step 5: Posterior vaginal dissection

The posterior peritoneum is incised at the level of the cervical cuff or vaginal apex. The assistant at this point should shift the vaginal manipulator superiorly in order to allow for better exposure of the posterior vaginal wall. Once again, an avascular areolar plane is encountered and should be approached as described for the anterior plane. It should be noted that the rectovaginal space tends to be more areolar and may require more sharp dissection than the vesicovaginal plane. The lateral limits of dissection are defined by the uterosacral ligaments and the distal limits are either the peritoneal reflection or preferably down to the level of the peritoneal body. Once dissection has started, the surgeon may wish to change his endoscope to the 30° up position for better visualization, though this is not imperative.

### Step 6: Identifying and developing the sacral promontory

The third arm is used to sweep and retract the sigmoid colon to the left and expose the sacral promontory. In general, the sacral promontory is easily palpated once adequate retraction has been placed on the sigmoid colon and mesentery. The sacral promontory at the level of S1 will be moderately flat and then starts to curve inferiorly at the level of S2. The posterior peritoneum should be incised at the sacral promontory approximately 2 cm proximal to the palpable inferior curve. This peritoneal incision is carried distally and is connected to the posterior wall incision. Take care to stay medial to the ureter and lateral to the sigmoid mesentery throughout this maneuver.

Some surgeons prefer to create a retroperitoneal tunnel instead of opening the peritoneal incision completely. The proximal peritoneotomy is made and the ProGrasp forceps are placed inside the incision. Using blunt dissection, the forceps are advanced distally to the level of the posterior vaginal wall dissection. This is meant to allow for quick placement of mesh under the tunnel, but at our institution it has not been noted to significantly alter operative time.

### Step 7: Distal placement of mesh

Either a prefashioned Y-shaped polypropylene mesh or two single arms of mesh are trimmed to the anatomic specifications of the patient. The mesh is rolled and introduced into the abdomen. One arm is unrolled and placed upon the anterior aspect of the vagina and attached via multiple 2-0 Gore-Tex sutures. The sutures are placed in a configuration of three rows with two sutures each. The same is repeated on the posterior portion with the second arm of the mesh (Figure 106.6).

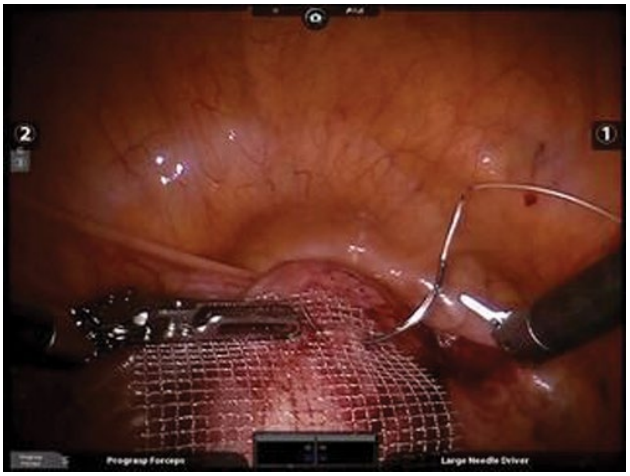

**Figure 106.6** Distal placement of the anterior arm of the mesh. The sutures are placed in three rows with two sutures each. The same is repeated on the posterior portion with the second arm of the mesh. *Source:* Wesley White. Reproduced with permission of Wesley White.

### Step 8: Fixation of the proximal mesh/coverage of mesh

The tail of the mesh should then be placed over the peritoneal incision. The assistant at this point should be placing pressure with the vaginal manipulator in order to bring the vaginal apex closer to the sacral promontory. The mesh should then be affixed to the anterior longitudinal ligament using two to three 0 nonabsorbable sutures. These should be placed in a transverse fashion as it has the added effect of ligating any vertically oriented vessels at this location (Figure 106.7). The retroperitoneum is then closed over the mesh (retroperitonealization of mesh) with a running barbed suture (Figure 106.8).

### Step 9: Closure

The uterus is removed at this point via the umbilical port, typically hand-morcellated in a plastic bag thorugh the incision in a controlled fashion. Alternatively, the uterus can be removed whole by stressing the umbilical port. The abdomen is desufflated and the ports are removed. Fascia is closed in all 10–12 mm trocar sites with 0-Vicryl figure-of-eight sutures. Skin incisions are closed in a subcuticular fashion.

### Step 10: Vaginal examination and cystoscopy

A vaginal examination is performed at this time to assess both apical support and to check for occult cystocele or rectocele. After repair of these defects, cystoscopy is

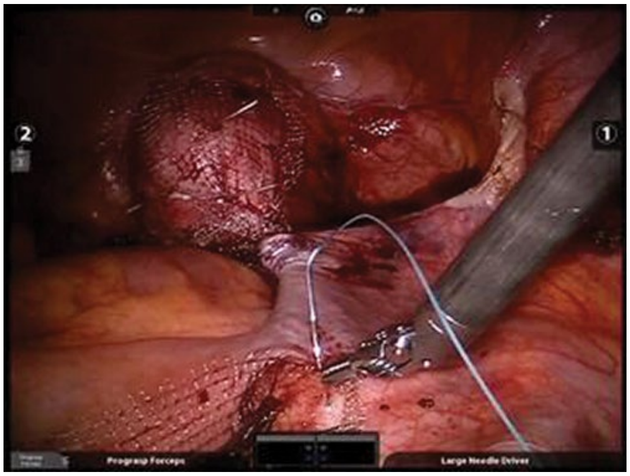

**Figure 106.7** The proximal placement of the mesh entails affixing the arm(s) to the anterior longitudinal ligament using two to three 0 nonabsorbable sutures. These should be placed in a transverse fashion as it has the added effect of ligating any vertically oriented vessels at this location. *Source:* Wesley White. Reproduced with permission of Wesley White.

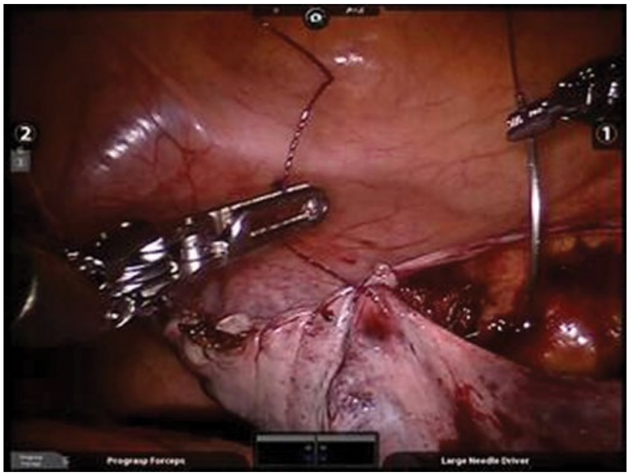

**Figure 106.8** The retroperitoneum is then closed over the mesh (retroperitonealization of mesh) with a running barbed suture. *Source:* Wesley White. Reproduced with permission of Wesley White.

performed to assess for any bladder wall injury and to assess for ureteral efflux. A Foley catheter is then replaced and vaginal packing placed. The postoperative care follows as described in the Laparoscopic sacrocolpopexy section.

### Robotic laparoscopic sacrouteropexy

In patients undergoing sacrohysteropexy, the general steps are similar when comparing laparoscopic and robotic approaches. The preparation and setup are as described earlier. The uterus can be retracted in the laparoscopic approach using a Keith needle or robot-controlled tenaculum. The posterior peritoneum is incised from the sacral promontory to the level of the posterior vaginal cervix. There are two main surgeon preferences for the use of mesh. One includes a single posterior arm, another a combination of a Y-shaped anterior arm of mesh along with a posterior arm. The dimensions of these mesh arms are typically 3–5 cm × 12–15 cm. When a single arm of mesh is used, the mesh is sutured to the posterior vaginal cervix using 0 nonabsorbable sutures. In cases using two arms of mesh, the Y-shaped mesh is passed through the broad ligament on either side, while the posterior arm of mesh is placed as previously described. The proximal arms of the mesh/meshes are then sutured to the sacral promontory as previously described.

## Outcomes

The main goal for the development of LSC and robotic ASC was to replicate the outcomes of ASC but with less morbidity. There have been many studies that have shown this to be the case. In their review, McDermott and Hale reported success rates between 90% and 96% [13]. Granese et al. reported a cure rate of 94.9% in their retrospective study of 165 patients [14], with 5.07% reporting recurrent vaginal vault prolapse and 3.62% reporting a recurrent cystocele. There have also been studies comparing ASC and LSC cohorts with respect to outcomes. Reoperation rates for prolapse were lower in the robotic ASC group compared to the ASC group in one study [15].

Similarly, there have been studies that have shown robotic ASC with cure rates similar to those for LSC. Geller et al. compared robotic ASC and ASC cohorts [16] in a retrospective study comparing 73 patients who underwent robotic ASC with 10 patients who had ASC. The patients had a pelvic exam and objective outcome was measured six weeks postoperatively. The robotic ASC group was found to have higher objective outcomes based on POP-Q score, with C point −9 compared to −8, with all other anatomic outcomes similar between the two groups. The robotic ASC had shorter length of stay (1.3 ± 0.8 days vs. 2.7 ± 1.4 days, $P < 0.001$) and less blood loss (103 ± 96 ml vs. 255 ± 155 ml, $P < 0.001$). The same authors reported on their almost 4-year mean follow-up in the same patient population [17]. Both groups maintained their anatomic success rates. Cure rates for the apex were 100%, with cure rates in the anterior and posterior compartments at 79%. Mesh erosion rates were similar in the robotic ASC and ASC groups (8% and 7%, respectively).

Finally, Paraiso et al. published the first randomized trial comparing robotic ASC to ASC or LSC [15]. At 1-year follow-up there was a difference in anatomical outcomes between the three groups. The study showed that the robotic ASC group had longer anesthesia time and surgical time. In addition, the robotic ASC group had higher rates of pain and required longer use of nonsteroidal anti-inflammatory drugs. From an economic standpoint, the robotic ASC group cost significantly more than the LSC group (mean difference of US$1936, $P = 0.008$).

## Complications

The Pelvic Floor Disorders Network has reported extensively on complications from ASC in the last couple of decades [18]. This comprehensive review reported on intraoperative complications, including cystotomy in 3.1%, ureteral injury in 1.0%, enterotomy or proctotomy in 1.6%, and bleeding or transfusion or both in 4.4%. The most common complication reported postoperatively was urinary tract infection in the median range of 10.9%, followed by wound infection, hematoma, or superficial separation in the median range of 4.6%. Other complications included ileus in 3.6% and deep venous thrombosis or pulmonary embolus in 3.3%. Erosion rate of mesh ranged from 1% to 8%. In terms of reoperation for nonprolapse indications, 1.1% required reoperation for small bowel obstruction and 5% underwent incisional hernia repair. These intraoperative and postoperative complications occurred at relatively the same rate in LSC and robotic ASC when compared to ASC [15].

## Summary

POP is a relatively common problem and may have a significant impact on a woman's quality of life. Several studies have shown that an abdominal sacocolpopexy leads to a more durable response compared to other surgical treatments. LSC and robotic ASC have developed a strong role in the management of POP. Recent data over the last decade has shown both these techniques to have outcomes equivalent to ASC, long considered the gold standard for apical POP repair.

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# 107

# Laparoscopic and Robotic Techniques for Repair of Female Genitourinary Fistulas

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## Introduction

Female genitourinary fistulas are abnormal communications that may occur between the ureter, bladder, or urethra and the uterus, cervix, or vagina. A genitourinary fistula can have devastating effects on the woman. Typically, they present with continual incontinence of varying degree; in some cultures the patient may be ostracized from their family and society, they may suffer depression, loss of employment, and become impoverished. In developed and developing nations alike there is often shame associated with incontinence. Women with fistulas often also develop dermatitis, recurrent urinary tract infections, infertility, and amenorrhea.

The most common cause of female genitourinary fistula in poorer communities is neglected, obstructed labor. Obstructed labor may lead to pressure necrosis of the anterior vagina and posterior bladder, with or without ureteral impingement, from compression between the baby's head and the mother's pubis. Obstructed labor rarely causes ureterovaginal fistula via the same compressive mechanism [1]. In contrast, genitourinary fistulas in developed countries are typically iatrogenic secondary to urologic or gynecologic surgeries for a variety of benign and malignant conditions, or radiation for pelvic malignancies. Iatrogenic fistulas include ureterovaginal, vesicovaginal, urethrovaginal, or vesicouterine fistulas. Rarely, fistulas may occur secondary to a granulomatous infectious process.

Urethrovaginal fistulas are increasing in prevalence due to increasing recognition and surgical treatment of urethral diverticula and the increasing use of midurethral slings [2]. Urethrovaginal fistulas are treated via a transvaginal approach and do not lend themselves to a transabdominal laparoscopic repair. Because of this, they will not be reviewed here.

Most vesicovaginal fistulas are successfully treated via a minimally invasive transvaginal surgery [3]. Vesicovaginal fistulas that have failed prior transvaginal repair, involve a fixed, fibrotic vagina, or are located high in the vaginal vault lend themselves readily to a transabdominal repair. Ureterovaginal fistulas and vesicouterine fistulas are most easily addressed transabdominally and, when appropriate, it is best to use a minimally invasive laparoscopic approach.

Indications are listed in Box 107.1.

## Incidence and prevalence of female genitourinary fistulas

Although the true incidence of vesicovaginal fistulas is unknown, they are estimated to occur in approximately 1/5636 of transvaginal hysterectomies, 1/958 of open hysterectomies, and 1/455 of laparoscopic hysterectomies [4]. Radiation-induced fistula can be divided into early postradiation fistulas caused by tumor necrosis and delayed fistulas secondary to capillary damage with subsequent tissue necrosis and sloughing [5].

## Clinical presentation

Genitourinary fistulas most commonly cause persistent urinary incontinence with an obvious inciting event such as recent obstructed delivery, pelvic surgery, or radiation.

Ureterovaginal fistulas typically present with continual incontinence as urine passes directly from the ureter to the vagina. They may be associated with partial ureteral obstruction, which may give the patient hydronephrosis and flank pain. Vesicouterine fistulas may present with

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**Box 107.1 Indications for transabdominal fistula repair.**

**Absolute indications**

- Involvement of the ureteral orifice by the fistula
- Small-capacity bladder requiring augmentation
- Vaginal stenosis from postsurgical scarring or previous radiation
- Involvement of the cervix or uterus
- Coexistent ureterovaginal fistula or ureteral stricture requiring ureteral reimplantation
- Vesicouterine or vesicocervical fistula

**Relative contraindications**

- Previously failed vaginal repair
- Large supratrigonal vesicovaginal fistula

cyclical hematuria, infertility, or amenorrhea (Youssef's syndrome). In the presence of a competent cervix, vesicouterine fistula may also present only with cyclical incontinence of urine during menses [6].

Vesicovaginal fistulas present with incontinence. Urine may pool in the vagina and periodically pass via the vaginal introitus with change in position or increasing abdominal pressure, thus mimicking stress urinary incontinence. Incontinence may be episodic as the fistula may be compressed and obstructed at low bladder volume and pressure and only open with evident incontinence at high pressure or volume. Patients may also develop urinary tract infections, pelvic pain with concomitant urinoma, flank pain if there is hydronephrosis, and perineal dermatitis due to constant moisture on the skin.

## Clinical diagnosis and evaluation

Typical preoperative evaluation at a minimum includes vaginal speculum exam to identify the location of the fistula and the health and viability of the affected portion of adjacent bladder and vaginal tissue. It is important to note during the visual inspection and bimanual exam the relevant vaginal anatomy, including a thorough assessment of vaginal length, signs of inflammation/infection, masses, atrophy, or prior scars. All of these can help aid in surgical planning. If the fistula location is uncertain and not clearly identified on vaginal speculum examination and cystoscopy there are a variety of imaging modalities and bedside tests to employ.

Vesicovaginal fistulas may be identified by instillation of methylene blue dye via a catheter into the bladder, compressing the urethra around the catheter and simultaneously observing for effluent into the vagina.

Ureterovaginal fistulas may also be detected by the double-dye tampon test. This test is performed by administering oral phenazopyridine, placing a tampon into the vagina, and filling the bladder with methylene blue dye. The apical portion of the tampon will reveal orange dye in the presence of a ureterovaginal fistula and blue dye in the presence of a vesicovaginal fistula.

Genitourinary fistulas are also readily identified on contrast-enhanced cross-sectional imaging. Ureterovaginal and ureterouterine fistulas may be identified on images in the pyelographic phase of an intravenously enhanced abdominal and pelvic CT scan or CT urogram. Importantly, the incomplete filling of the bladder as occurs with delayed images of the CT urogram is inadequate to exclude the presence of a vesicovaginal fistula.

A CT cystogram will appropriately distend the bladder and is highly sensitive for vesicovaginal fistula. Cross-sectional imaging may also reveal additional pathology such as urinoma, allow accurate lateralization of ureterovaginal fistula, identify congenital ureteral duplication, presence of hydroureteronephrosis, and thus significantly inform operative planning.

Endoscopic evaluation is also critical. Cystoscopy allows direct visualization of a vesicovaginal fistula, the health of surrounding tissue, and the proximity to the ureters and bladder neck. Cystoscopy may also reveal the presence of foreign material, such as suture, brachytherapy seeds, titanium vascular clips, or calculus. If patient history or clinical suspicions suggest carcinoma, fistula biopsy should be performed at time of cystoscopy. Retrograde pyelography may also reveal the location of ureterovaginal and ureterouterine fistulas.

Some tests for fistula evaluation are summarized in Table 107.1.

## Nonsurgical management

Small, benign, nonirradiated ureterovaginal fistulas may be initially managed by ureteral stent. If retrograde ureteral stent placement is not achieved due to associated stricture, percutaneous nephrostomy with antegrade ureteral stenting may be attempted. If successfully cannulated and stented, an initial trial of ureteral stent may be undertaken for perhaps 6–10 weeks prior to stent removal. If the fistula closes, serial imaging of the upper tract is necessary to observe for delayed stricture formation and need for subsequent endoscopic, laparoscopic, or open repair of the stricture or ureteroneocystotomy. Quality evidence supporting conservative management is poor and limited to case series and expert opinion. Irradiated, large, or malignant ureterovaginal fistulas are unlikely to close

**Table 107.1** Summary of tests for fistula evaluation.

| Fistula type | Test | Diagnostic findings |
|---|---|---|
| Vesicovaginal | Bladder backfill | Bladder is filled retrograde with dilute methylene blue or sterile milk while visualizing the anterior vaginal wall with the posterior speculum blade in place. If no fistula visualized, the catheter is removed and the patient is asked to Valsalva to evalute for stress incontinence |
| Vesicovaginal or urethrovaginal | Double-dye tampon test | Oral phenazopyridine is given and a tampon is placed in the vagina; bladder filled retrograde with methylene blue. Tampon inspected after 10 min: if orange dye is present on tampon, fistula likely urethrovaginal; if blue dye is present likely vesicovaginal. Both colors is combination of both fistulas |
| Urethrovaginal | Trattner double balloon catheter | The upper balloon is inserted through the urethra into the bladder and both balloons are inflated; one balloon is located at the urethrovesical junction and the second at the urethral meatus. Downward traction is placed on the internal balloon which occludes the urethrovaginal junction while the external balloon is pressed snugly against the external urethral meatus; methylene blue or sterile milk is then instilled into the catheter to identify a fistula between the vagina and urethra |
| Vesicovaginal, urethrovaginal, rectovaginal, or colovesical | Direct visualization or imaging | Cystoscopy, CT urogram, or retrograde pyelogram, colonoscopy, proctoscopy, endoanal or transperineal ultrasound, MRI |

with conservative management and are best managed with surgical intervention.

Ureterouterine fistulas may close with hormone therapy to prevent endometrial proliferation and maintain an amenorrheic state [7]. Typically, however, ureterouterine fistulas require transabdominal surgical intervention.

Small, benign, nonirradiated vesicovaginal fistulas may respond to prolonged Foley catheterization that diverts urine and prevents bladder distension. Success with this method ranges from 7% to 15% in case series. Fulguration of a fistula less than 3 mm in diameter is reported as successful in 73–100% of patients in two small series. Fibrin glue injection into the fistula tract has been reported, as has, more recently, fibrin glue combined with platelets and plasma. High cure rates of small fistulas with short-term follow-up are reported [8].

## Goals of surgery

Regardless of etiology, vesicovaginal fistulas can have a devastating impact on quality of life, sexual function, psychological well-being, physical discomfort from incontinence, and increase the risk for recurrent urinary tract infections and therefore damage to the upper tract urothelium. As is the case in most surgery, the first attempt at a surgical repair will be most likely to succeed. Therefore the goal with the surgical repair of vesicovaginal fistulas should be to minimize the number of surgeries, avoid complications and utilize precise surgical techniques to prevent recurrence.

## Timing of surgery for vesicovaginal fistula repairs

Optimal timing of fistula repair is unknown. Formerly, delayed fistula repair was advocated by many [9], but many now advocate for early surgical intervention [10]. Timing of fistula repair is determined by considering several factors, including the benign or malignant nature of the fistula, health and vitality of surrounding tissue, presence of concomitant abdominal or vaginal pathology, and the surgeon's experience and success with varying techniques and approaches. Surgical treatment of large or small, benign, nonirradiated fistula may be pursued without delay. Irradiated, large, or malignant fistula will not close with conservative management, delaying only long enough to optimize tissue health. The surrounding tissue may be optimized by treating any active infection, diverting urine as best as possible with Foley catheter and/or bilateral nephrostomy tubes, waiting for resolution of hematoma or edema, and (in the absence of a contraindication, such as hormonally sensitive cancer or thromboembolic disease) topical estrogen therapy in a low-estrogen state [11].

## Principles of repair

### Approach selection

High vesicovaginal fistula in the proximal vagina or at the vaginal cuff in post-hysterectomy patients may be addressed either transvaginally in experienced hands (not reviewed here) or transabdominally. It is reasonable to proceed to transabdominal repair if inexperienced in complex transvaginal surgery and the variety of interposition flaps raised for transvaginal fistula repair. Transabdominal repair is recommended if a prior transvaginal repair has been attempted previously and failed [12].

Successful extraperitoneal and intraperitoneal repairs have been described [13]. Intraperitoneal repair affords access to omental and peritoneal interposition grafts as well as the ability to perform ileocystoplasty when warranted. An extraperitoneal approach may offer the advantage of avoiding dense intra-abdominal adhesions, though it limits options for interposition grafts to peritoneum, rectus rotational flap, or allograft such as solvent-dehydrated human dura mater.

The best surgical approach is the approach that works best in the individual surgeon's hands. Regardless of the approach, however, the principles of genitourinary fistula repair are the same. Although excision of the fistulous tract is not necessary, debridement of any inflamed, nonviable tissue is critical. Next, wide mobilization of the tissue is required to reduce subsequent tension on the repair. This is followed by apposition of healthy tissue and a watertight closure of the urinary tract with absorbable suture and the closure of the other end of the fistula, be it uterine or vaginal tissue. Finally, it is our preference to deploy an interposition graft of healthy tissue to prevent overlapping suture lines. Urinary diversion with catheters and, when indicated, ureteral stents, is used to divert urine and prevent tension on the repair.

## Optimization for surgery

Early attempts at controlling urinary or bowel leakage can help mitigate skin breakdown and reduce psychological stress. The continuous leakage of urine can cause perineal dermatitis that may make postoperative skin healing more difficult. In the patient with vesicovaginal fistula, the surgeon can consider an indwelling catheter to help prevent perineal dermatitis. Patients often use incontinence products such as pads, diapers, and protective bedsheets to help manage their symptoms. The patient can be counseled on the importance of frequent pad changes to help minimize skin irritation. In addition, topical barrier products such as petroleum, zinc oxide, and dimethicone-based ointments can form an occlusive barrier to prevent skin damage [14].

In some cases, preoperative vaginal estrogen may help with spontaneous closure of the fistula in postmenopausal women with the caveat that there should be no other medical contraindications for the use of estrogen [11].

## Preoperative preparation

Preoperative urine cultures are obtained two weeks prior to surgery and treated according to culture and sensitivities of the infecting organisms. The day prior to surgery, patients are placed on a liquid diet and receive a mechanical bowel preparation with polyethylene glycol or magnesium citrate. Some surgeons advocate use of an enema the morning of surgery, and this is our practice as well. Patients requiring anticoagulation and antiplatelet therapy cease these medications 5–7 days prior to surgery. Prophylactic antibiotics (typically third-generation cephalosporin–cefoxitin at our institution) are given at the time of surgery, ideally an hour prior to incision.

## Operative technique of robot-assisted laparoscopic vesicovaginal fistula repair

Sequential compression devices are placed on the patient's lower extremities, general anesthesia is induced, and endotracheal intubation performed. The patient's arms are tucked alongside the abdomen. All pressure points are sufficiently padded. The abdomen is prepped with chlorhexidine and the genitalia are prepped with betadine scrub, or as dictated in accordance with patient skin sensitivities and allergies. The patient is draped as a single surgical field as the genitourinary fistula traverses both the surgically sterile field of the abdomen and the clean-contaminated field of the external genitalia and fistulized urinary tract. Cystourethroscopy is then performed if open-ended ureteral catheters are to be placed for ureteral access or if ureteral stents are planned. Ureteral catheters or stents are not typically required in the setting of an isolated vesicovaginal fistula high on the posterior bladder wall above the trigone in the midline. Vesicovaginal fistula near the ureteral orifices, trigone, or bladder neck are best addressed after at least placing open-ended ureteral catheters to facilitate later ureteral stent placement if warranted. A Foley catheter is then placed via the urethra into the bladder, balloon inflated, the bladder drained of any residual urine and the catheter clamped.

One may place a separate Foley catheter via the vesicovaginal fistula tract if possible, clamp it, and leave it indwelling to aid in further identification and manipulation of the fistula [3]. Many fistulas are too small to be cannulated this way and those that can accommodate a Foley catheter are typically quite apparent and, in our experience, a catheter is not needed for identification or manipulation. Catheters are clamped to maintain pneumoperitoneum upon later opening of the bladder and exposure of the fistula tract. In addition, the vagina is packed with a wet towel or gauze roll to maintain peritoneum.

The patient is placed in a steep Trendelenburg position. Pneumoperitoneum is achieved by Veress needle insufflation. In patients with few prior abdominal surgeries, the needle is typically placed at the umbilicus. In patients with multiple prior abdominal surgeries, including previous access at the umbilicus, the Veress needle may be placed anywhere below the costal margin as informed by preoperative axial imaging to avoid unexpected hepatomegaly or splenomegaly.

After achieving pneumoperitoneum, the robotic 12 mm optical trocar is placed just superior to the umbilicus and inspection of abdominal viscera performed upon entry. Any necessary adhesiolysis is performed and additional robotic and assistant's ports are placed under direct vision. Several port configurations are described. We use five transperitoneal ports. Two 8 mm robotic ports are placed 9–10 cm on either side of the optical trocar. An additional 8 mm robotic port is placed 4 cm superior to the left iliac crest, 9 cm from the adjacent robotic port, for the fourth robotic arm. An assistant's port, for which we use the 12 mm AirSeal® device (SurgiQuest, Milford, CT, USA), is placed on the patient's right side, 9 cm lateral to the adjacent port and 4 cm above the iliac crest.

The robotic surgical platform, currently da Vinci Si at our institution (Intuitive Surgical Inc., Sunnyvale, CA, USA), is then side-docked to allow ease of access by the bedside assistant to the urethral catheter, any ureteral catheters, vaginal packing, and, if needed, vaginal manipulation probe during the case.

Our starting instruments include two robotic Maryland bipolar forceps (one in the surgeon's nondominant control arm and the other in the fourth arm) and a robotic monopolar curved scissor under control of the surgeon's dominant hand. The assistant can then freely pass sutures and perform retraction via the AirSeal port on the patient's right side.

### Step 1: Delineate the anatomy

Genitourinary fistula patients often require extensive adhesiolysis because of their prior surgeries and the presence of any urinomas or phlegmon. Often, bowel is adherent not just to the peritoneum throughout the pelvis but also to the vaginal cuff or cervix in cases of prior hysterectomy or supracervical hysterectomy, respectively. Fastidious attention is given to mobilizing bowel from the pelvis while preserving posterior peritoneum and omentum, as each may later serve the critical role of interposition grafts to support the fistula repair. The omentum may require mobilization from the greater curvature of the stomach in order to reach the pelvis in as many as 70% of patients. Viability of the omental flap is dependent on preserving the right gastroepiploic artery and thus mobilization is begun high on the left side of the greater curvature. The distal end of the flap is then positioned in the pelvis for later use.

### Step 2: Accessing the fistula

Robot-assisted laparoscopic vesicovaginal fistula repair is a minimally invasive, transperitoneal technique to perform the classic transabdominal repair originally described by O'Conor and Sokol [15].

The peritoneum overlying the bladder is dissected laterally from a midline peritoneotomy. The transperitoneal cystotomy is performed in the midline of the bladder in the dome well above the vaginal wall and fistula site. Cystotomy may be made on a decompressed, empty bladder, but the bladder may also be distended with saline via the urethral catheter (or catheter via fistulous tract if placed previously) for ease of identification. The bladder is opened in the sagittal plain from the bladder dome to the level of the fistula using electrocautery. The current trend is away from a large bivalving of the bladder in favor of a limited cystotomy just above the fistula tract [16].

Polyglactin absorbable stay sutures may be placed through full thickness of the detrusor to facilitate visualization and fistula dissection. These sutures may be temporarily affixed to the superior and lateral abdominal wall using Weck™ hemoligation clips (Teleflex, Morrisville, NC, USA) or similar. Additional retraction may be performed with the fourth robotic arm and by the bedside assistant.

The cystotomy is extended to the level of the vesicovaginal fistula. The fistula itself may be incorporated into the cystotomy, or, if the tract is well epithelialized or necrotic, the fistula may be debrided or excised. We do not recommend wide excision of a benign, nonirradiated fistula tract as it has not been shown to be advantageous and increases the defect that must be repaired. Excision should be restricted to a minimum and only what is required to reach healthy, viable tissue circumferentially. Hemostasis is achieved using bipolar forceps diathermy to minimize thermal injury to surrounding tissue.

### Step 3: Separation of the bladder and vagina

Dissection of the posterior bladder wall from the underlying anterior vaginal wall or uterine segment is performed with blunt and sharp dissection. Posterior reflection of the vagina away from the bladder by the bedside assistant using a Haney retractor or vaginal probe may facilitate dissection. The bladder is reflected anteriorly and again visualization may be aided by additional polyglactin absorbable stay sutures affixed to the anterior abdominal wall. Wide circumferential dissection with a 3 cm radius from the fistula is ideal to facilitate tension-free closure and to anchor an interposition graft.

### Step 4: Closing colpotomy, interposing graft, closing cystotomy in vesicovaginal fistula

Our practice is to close the colpotomy with running, locking polyglactin or poliglecaptone suture, typically 3-0 on a small, tapered needle. A barbed unidirectional suture (V-Loc, Covidien, Minneapolis, MN, USA) is preferred by some surgeons [16].

An interposition graft is then advanced and secured with polyglactin sutures circumferentially around the colpotomy to the vaginal wall in order to completely cover the suture line. Omentum, as previously mentioned, is most often used. In the absence of adequate omentum, a peritoneal flap may be raised from the lateral pelvic wall and secured with polyglactin suture to the vagina. If peritoneum is also inadequately mobilized or of poor quality, a free bladder mucosal graft may be harvested from the luminal surface of the bladder dome, leaving underlying detrusor muscle *in situ*, and securing the graft in place with absorbable polyglactin suture, its mucosal surface toward the vagina [17]. The Gil-Vernet technique involves using a rotational bladder wall flap to slide into the apex of the cystotomy so that the suture lines of the colpotomy and cystotomy do not overlap, similar conceptually to a Y-V plasty that replaces bladder with bladder. This may obviate the need for a separate interposition graft [18].

If there is any suspicion of ureteral injury, ureteral patency is assessed and integrity suggested with intravenous administration of methylene blue or fluorescein dye while observing for dyed effluence of urine from the ureter and ureteral orifice.

The cystotomy is then closed in two layers of polyglactin suture. The first layer incorporates 2–3 mm of urothelium and approximately 7 mm of full-thickness detrusor with each passage of the 3-0 polyglactin suture on a tapered needle. This suturing is performed with a barbed unidirectional suture or in a running, locking fashion the full length of the cystotomy. The bladder is then distended by the assistant with methylene blue-dyed saline and examined for watertight integrity. The bladder is then partially drained and the second layer of closure is performed with 2-0 polyglactin or barbed unidirectional suture in a simple running manner to imbricate the first layer.

### Step 5: Ureterovaginal fistula repair

The technique for ureterovaginal fistula repair differs significantly from repair of a vesicovaginal fistula. The ureter distal to the fistula does not require excision, nor do the bladder and vagina require separation. The bowel is reflected superiorly from the underlying iliac vessels ipsilateral to the ureteral fistula. Dissection may be aided by the presence of a ureteral catheter or stent previously placed, but if the ureter cannot be catheterized, the ureter is identifiable as it crosses the iliac vessels. The peritoneum is incised and the ureter mobilized, taking care to preserve the lateral blood supply of the distal ureter and the medial blood supply of the proximal ureter. Iatrogenic ureterovaginal fistulas nearly always occur in the distal ureter and are amenable to direct ureteroneocystotomy without bladder mobilization and reconfiguration. If the fistula or injury has devitalized more than the distal 4 or 5 cm of the ureter, a psoas hitch or Boari flap are recommended to accomplish a tension-free anastomosis and reduce risk of ureteral distraction.

Direct ureteroneocystotomy may be performed by sharply transecting the ureter as distal as it is viable. An easily reached site on the bladder that ensures a tension-free anastomosis is selected for neocystotomy. The bladder is filled and a short cystotomy performed with the monopolar curved scissor. The medial wall of the distal ureter is incised, widely spatulating the ureter. The lateral half of the ureteral anastomosis is performed with a 4-0 poliglecaprone suture. A 5 Fr multilength double-J ureteral stent is then delivered via the assistant's robotic port and deployed first proximally within the ureter then distally within the bladder. The remainder of the ureteral anastomosis is completed with poliglecaptone suture.

If a tension-free direct ureteroneocystotomy is not possible because of the length of devitalized ureter or more proximal ureteral fistula, we prefer the use of a Boari flap. The apex of the flap is located on the anterior bladder surface with the base of the flap extending posterolaterally toward the affected ureter. The flap is then deflected superiorly and can be held outstretched and in place by the fenestrated grasper of the fourth robotic arm. The robot should be docked ipsilateral to the ureteral fistula for this purpose. The urothelium of the flap is incised in its midline from the apex for a length of 2 cm and the urothelium raised. The ureter then lies in the urothelial defect and is secured with poliglecaptone suture circumferentially. The urothelium of the flap is then closed over the distal 2 cm of ureter with interrupted poliglecaptone suture. A ureteral stent, typically 5 Fr multilength double-J, is deployed and the cystotomy closed in two layers as described above.

### Step 6: Exiting the abdomen

The abdomen is irrigated with saline and examined for hemostasis as pneumoperitoneum is reduced. Once hemostasis is assured, the robot system is undocked. We place a small, closed suction drainage tube via the lateral

8 mm port used for the fourth robotic arm and remove all ports under laparoscopic visualization. We close the 12 mm camera port and the 12 mm AirSeal assistant's port with 1-0 polydioxanone delayed absorbable suture. All port sites are infiltrated with 0.25% bupivacaine and then closed with subcuticular 4-0 poliglecaptone sutures on a cutting needle. Finally, the vagina is packed with a clindamycin cream-saturated gauze that is removed on morning of postoperative day 1.

### Postoperative care

We encourage early ambulation following surgery. Prophylactic antibiotics are continued for 24 hours after surgery while intravenous hydration is limited and diet advanced as tolerated. Most patients experience adequate postoperative analgesia with intravenous ketorolac (renal function permitting) and intravenous narcotics only for breakthrough pain.

Abdominal drain fluid is routinely sent for creatinine the next morning. If compatible with serum creatinine levels and not concerning for urinary extravasation, the drain is removed on the morning of postoperative day 1. Most patients are discharged on postoperative day 1 with the drain removed.

The detrusor is aggressively relaxed to minimize bladder tension and treat symptomatic bladder spasms with scheduled anticholinergic or beta-agonist medications for the duration of the catheterization, which is typically 10–14 days. A voiding cystourethrogram is obtained to ensure bladder integrity prior to catheter removal. If ureteroneocystotomy was performed, the ureteral stent remains indwelling for four weeks. We encourage pelvic rest with nothing placed per vagina for six weeks.

### Results

Since Nezhat and colleagues [19] first reported laparoscopic repair of a vesicovaginal fistula, several series have confirmed the success and reproducibility of the minimally invasive approach [20, 21].

Xiong et al. [22] recently reported their experience with open versus laparoscopic repair in 36 and 22 patients, respectively. The nonrandomized cohorts had similar preoperative characteristics. Patients receiving laparoscopic repair had less blood loss, shorter hospitalization, and equivalent success rates.

Miklos and Moore [23] analyzed their 15-year experience with laparoscopic extravesical technique in 33 patients and report a 97% cure in primary fistula, 100% cure (11 of 11) in recurrent fistulas at mean of 17 months follow-up. They used a three-layer closure without the interposition of a graft in 98% (43 of 44) and observed a 98% (42 of 43) success rate. They similarly had low mean estimated blood loss (39 ml) and short hospitalization (1.1 days mean).

Robot-assisted laparoscopic repair of a vesicovaginal fistula was initially reported by Melamud et al. [24]. Gupta et al. [25] reported on their series of 12 patients with recurrent, nonirradiated vesicovaginal fistula having robotic repair between 2006 and 2008. They found 100% cure rate, mean blood loss of 88 ml, and no complications at mean follow-up of six months [25]. The next largest published single-institution series to date is that reported by Agrawal et al. in 2015 [26]. This included 10 patients with nonirradiated fistulas, 3 with concomitant ureteral reimplantation. Mean operative time in this series was 214 minutes, median length of hospital stay was 1 day, and estimated blood loss ranged from 5 to 100 ml. There were no intraoperative complications. One patient had Clavien–Dindo grade I complication ileus and two had grade II complications of fever with atelectasis and *Clostridium difficile* infection, respectively. At median follow-up of 24 months, all patients were subjectively and cystographically cured [26].

## Ureterovaginal fistula repair

A multinational series of 12 patients undergoing robot-assisted laparoscopic ureteral reimplantation with psoas hitch included two patients with ureterovaginal fistula [27]. The authors reported a similarly low estimated blood loss of 48 ml, 208 minutes of operative time, no complications, and 100% success at 15 months.

## Conclusions

Genitourinary fistula repair is optimized with prompt diagnosis, the appropriate selection of least-invasive surgical approach, and use of interposition grafts as needed, according to the individual surgeon's experience. The vast majority of vesicovaginal fistulas are cured with transvaginal surgery, with or without interposition martius, gracilis, or other flaps. Vesicovaginal fistulas are also highly amenable to a minimally invasive transabdominal approach. Ureterovaginal, vesicouterine, ureterofallopian, and ureterouterine fistulas are nearly always treated with transabdominal approach and each has been successfully repaired in a minimally invasive fashion. Strict adherence to the principles of juxtaposing healthy tissue, a watertight suture line, interposition of viable tissue flap, avoiding overlapping suture lines, prolonged catheter drainage, and minimizing tension on the repair has delivered dramatic improvements in fistula cure rates since surgical repair was first attempted in 1663.

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# Laparoscopic, Laparoendoscopic Single-site, and Robot-assisted Living Donor Nephrectomy

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## Introduction

The first conventional laparoscopic living donor nephrectomy was reported in 1995 and was performed at the Johns Hopkins University. The authors reported that the kidney was removed via a 9 cm infra-umbilical incision, warm ischemia time was limited to under 5 minutes, and the patient was discharged on the first postoperative day [1]. Within 5 years of the initial report, laparoscopic donor nephrectomy was adopted by more than 100 transplant centers over five continents and had been demonstrated to result in shorter hospitalization, less pain, shorter convalescence, and earlier return to work and normal activities for patients postoperatively as compared to standard open donor nephrectomy [2, 3]. Since then, the technique for laparoscopic donor nephrectomy has evolved and spread such that it is considered the standard of care at most institutions for living renal donation. In this chapter, we review and discuss a modern approach to laparoscopic donor nephrectomy with special emphasis on the preoperative evaluation, intraoperative technique, and postoperative care.

## Preoperative evaluation

All potential renal donors should undergo a complete preoperative evaluation to ensure their suitability for renal donation. A thorough medical evaluation, generally coordinated by a transplant nephrologist, to assess for the presence or history of underlying renal disease, microhematuria or proteinuria, nephrolithiasis, transmissible infection (e.g. HIV, hepatitis B or C), hypertension, or other major comorbidities (e.g. diabetes, chronic obstructive pulmonary disease, heart disease, or immunologic disorders). Any abnormalities identified such as microhematuria or elevated blood pressure should be fully worked up prior to undergoing surgery. The comprehensive nature of this workup is critical as every care should be taken to avoid kidney donation in patients with a significantly increased likelihood of developing chronic kidney disease, endstage renal disease, or dialysis dependency following organ donation. In carefully selected renal donors, overall survival and incidence of endstage renal disease appear to be unchanged as compared to the general population [4]. The potential risk of developing chronic kidney disease and endstage renal disease should still be discussed with all patients preoperatively, however, as some studies have suggested that kidney donation may carry an increased lifetime risk of endstage renal disease as compared to healthy, similarly screened, matched control patients [5] or as projected by endstage renal disease models in the absence of donation [6].

A surgical history should be obtained preoperatively, and an abdominal exam should be performed by the operative surgeon to assess for abnormalities or any history of major abdominal surgery which may alter the surgical plan. Although a reported history of intra-abdominal surgery is not a contraindication for laparoscopic donor nephrectomy, it may change the surgeon's decision of extraction site planning or whether to utilize a hand-assisted laparoscopic technique.

It is imperative to obtain a thorough understanding of the renal anatomy prior to undertaking laparoscopic donor nephrectomy. An abdominal and pelvic computed tomography (CT) scan with both angiographic and excretory phases should be obtained. Axial, coronal, and, in many instances, sagittal reconstructions should be meticulously examined to determine the actual position of the renal arteries (and their origins) as well as the position of the initial segmental branches of each artery.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

The venous vasculature should be assessed for the position of the gonadal and adrenal veins as well as any lumbar veins in the region of the renal hilum. Magnetic resonance angiography is an alternative to CT for evaluation of potential kidneys. Renal scintigraphy is usually obtained when there is a discrepancy in renal size, contrast uptake or excretion, or renal scarring to ensure adequate renal function.

Although accessory renal veins can generally be sacrificed without consequence intraoperatively, they are generally spared quite easily provided they are appropriately identified on preoperative imaging. Finally, both kidneys, the remainder of the abdomen and retroperitoneum, and the great vasculature should be examined for abnormalities such as excessive perirenal adipose tissue, retrocaval ureters, retro-aortic renal veins, renal tumors or masses, nephrolithiasis, and complex renal cysts, which might complicate or contraindicate renal donation. Although the left kidney is traditionally preferred for donation due to the presence of a longer renal vein, the right kidney may be selected in the event of aberrant anatomy or other such patient-specific concerns. Multiple left renal arteries or anomalous left renal vasculature are not absolute contraindications to procuring the left kidney.

All potential donors should undergo routine psychiatric evaluation to rule out the presence of any psychiatric comorbidity that might impair their ability to provide informed consent for renal donation or the presence of any undue coercion from a third party affecting their decision to donate. It is often helpful to provide the renal donor with a "medical representative" unrelated to the transplant team to absolutely ensure that they have an advocate who is completely unbiased. Furthermore, all donors should be reassured that should they change their mind regarding their willingness to donate at any point, the recipient will be informed only that the transplant could not proceed due to "medical reasons." This is imperative in order to ensure that there is no element of coercion, either real or imagined, that clouds a potential donor's decision-making preoperatively.

A multidisciplinary transplant board should be convened to discuss any cases which might be complicated due to recipient medical or surgical history, aberrant renal anatomy, or ethical concerns.

## Surgical risks

Although the rate of major complications (≥Clavien II) following laparoscopic donor nephrectomy has been estimated to be only 1.8% [7], all potential donors should be presented with a comprehensive preoperative discussion regarding expected hospital stay, postoperative pain management, likelihood of blood transfusion, and all potential surgical risks including bleeding, injury to adjacent intra-abdominal structures (e.g. pancreas, spleen, colon, diaphragm, liver, stomach, and small bowel), standard wound-healing complications (e.g. infection, hernia), and the potential need for conversion to an open procedure. The potential for major and potentially catastrophic complications such as deep venous thrombosis, pulmonary embolism, myocardial infarction, stroke, or death should be discussed as well. If the potential donor has a change of heart following this discussion, they should be reassured that the reasons for the transplant cancellation will remain private and undisclosed from the intended recipient.

## Surgical technique

### Left laparoscopic donor nephrectomy

#### Patient positioning

After induction of general anesthesia and placement of an orogastric tube and Foley catheter, the patient should be positioned in a modified flank position with all pressure points adequately padded. We advocate using minimal, if any, flexion of the operating table, and avoiding the use of the kidney rest in order to limit the risk of postoperative positional complications such as rhabdomyolysis [8]. The abdomen should be sterilely prepped in its entirety. If a Pfannenstiel incision is to be utilized for extraction, then the skin should be marked prior to patient positioning in order to ensure an optimal cosmetic result, and then prepped into the surgical field as well.

#### Abdominal entry and trocar placement

Among the different approaches to donor nephrectomy, the transperitoneal approach is the most utilized. The surgical procedure is begun by entry into the abdomen using a closed Veress needle technique, an optical trocar, or an open Hasson technique. A Cochrane review of randomized controlled trials concluded that the open technique is associated with a lower rate of failed entry into the abdomen, but found no difference in the likelihood of visceral or vascular injury between patients undergoing closed versus open techniques [9]. Consequently, the method of primary entry into the abdomen is left to the operative surgeon's discretion.

The sizes and positions of the trocars is surgeon dependent, however a classic triangular configuration with the camera trocar in the midline is the traditional method. For left renal procurement, we prefer to place an initial 5 mm trocar in a periumbilical location which is used as a working instrument trocar. After placement of this trocar, the abdominal contents are inspected and the position of the upper and lower poles of the kidney are identified. Next, a 5 mm trocar is placed at approximately the level of the renal hilum, slightly lateral to the midline in the left upper quadrant, and used as the camera trocar. The third 12 mm trocar is placed at the midclavicular line below the level of the lower pole of the kidney and used as a working instrument trocar.

### Initial mobilization

For a left-sided donor nephrectomy, the descending colon is mobilized along the white line of Toldt. The superficial peritoneal attachments between the colon and lateral sidewall should be released initially. Lateral renal attachments to the sidewall should not be released at this point, as this maneuver would result in medial mobilization of the kidney and interfere with hilar dissection. The colon is further dissected medially, exposing the proper plane between the colonic mesentery and Gerota's fascia. Recognition of this plane is important, in that inadvertent entry into the mesentery can lead to bleeding as well as mesenteric defects with potential for internal herniation. The dissection is carried cephalad towards the upper pole of the kidney. Extensive splenic mobilization is required to provide adequate exposure of the upper pole of the kidney.

The psoas muscle is exposed below the lower pole of the kidney. This muscle functions as an important landmark for locating the ureter. The ureter and gonadal vein are identified along the medial border of the psoas muscle (Figure 108.1). Care should be taken to avoid entering the psoas muscle fascia, which may lead to unnecessary bleeding or damage to the genitofemoral nerve. The ureter is dissected to the level of the iliac artery bifurcation. Meticulous care is taken to avoid ureteral devascularization. Following distal ureteral transection, the remaining blood supply to the ureter arises proximally from the renal artery, and therefore excessive dissection of the periureteral tissue is avoided. The ureter is not divided at this time. By gently elevating the ureter and lower pole of the kidney with an instrument, the medial border of the kidney is dissected in a cephalad direction to the level of the renal hilum. The correct plane of dissection lies medial to the gonadal vein. As the ureter and lower pole of the kidney are elevated, the gonadal vein can be traced towards the renal hilum (Figure 108.2). Exposure of the renal vein, adrenal vein, gonadal vein, and lumbar branch is performed after the colon has been fully mobilized medially (Figure 108.3). When both lateral traction of the kidney and medial traction of spleen are needed, placement of an accessory trocar

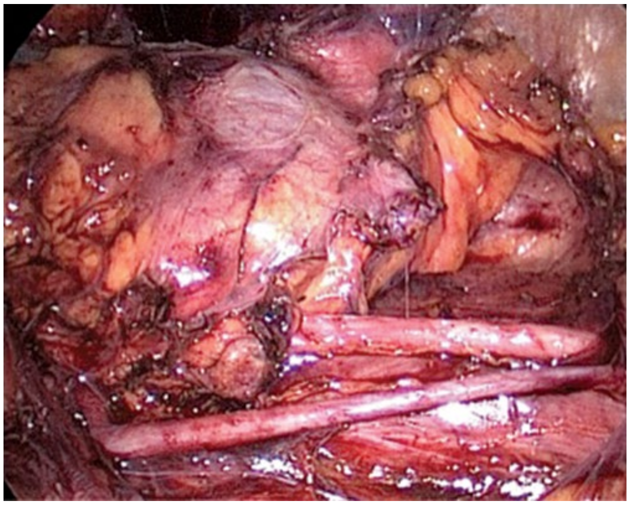

**Figure 108.1** Identification of the gonadal vein (medial) and ureter (lateral) on the psoas muscle inferior to the lower pole of the kidney.

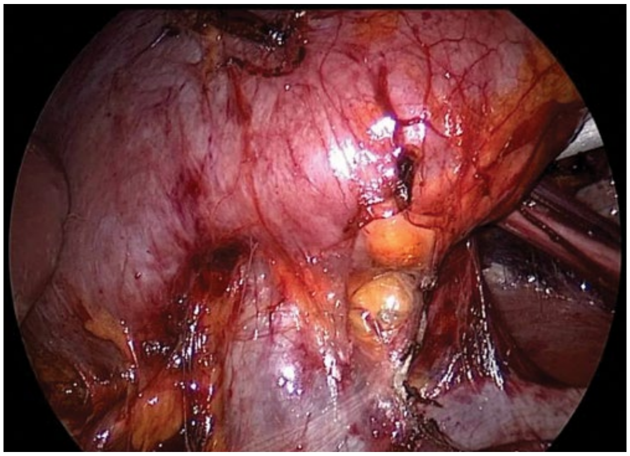

**Figure 108.2** Optimization of anterolateral retraction of the kidney and ureter using a laparoscopic instrument introduced through an accessory laparoscopic trocar.

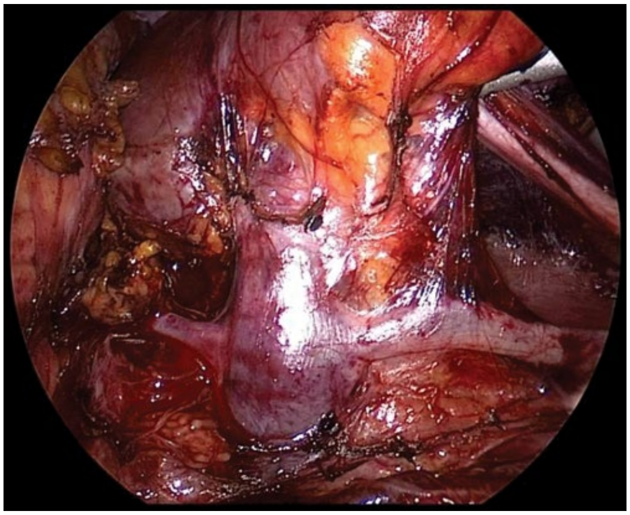

**Figure 108.3** Identification of the adrenal vein's ostium from the proximal, superior border of the left renal vein.

may be beneficial. This additional trocar can be introduced along the anterior axillary line at the inferior border of the kidney. A laparoscopic instrument can be introduced via this trocar to provide anterolateral retraction of the kidney so that the surgeon may use both working instruments to perform the hilar dissection.

### Hilar dissection

Once the kidney has been retracted anterolaterally, the gonadal vein is dissected at its insertion into the renal vein. The gonadal vein can be ligated and divided with a bipolar vessel-sealing device. Alternatively titanium or polymer clips can be utilized to ligate the vessel. The stump of the gonadal vein may serve as a handle for superior traction of the renal vein to help identify the lumbar vein and renal artery posteriorly. The adrenal vein is dissected at its insertion into the renal vein. The adrenal vein is ligated and divided with a bipolar vessel-sealing device or with clips. An advantage of a vessel-sealing device is that it eliminates the presence of clips that may interfere with subsequent placement of an endoscopic linear stapling device. The lumbar vein, when present, enters the renal vein posteriorly. This vein must be ligated and divided in order to identify the renal artery, which lies immediately posterior to the lumbar vein (Figure 108.4).

The renal vein is dissected from all surrounding perivascular tissues to a point medial to the adrenal vein stump. This maneuver provides maximal venous length for the vascular anastomosis. The renal artery is identified posterior to the renal vein and is dissected from the surrounding investing tissues. The renal artery must be carefully dissected in a retrograde fashion to its origin at the level of the aorta.

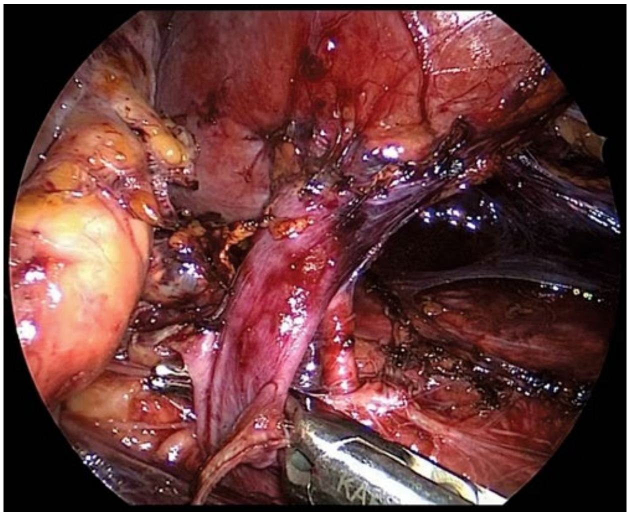

**Figure 108.4** Identification of the renal artery posterior and inferior to the renal vein and the divided stumps of the adrenal, gonadal, and lumbar veins.

### Dissection of the adrenal gland

After ligation and division of the adrenal vein, Gerota's fascia is entered along the anterior aspect of the upper pole of the kidney, exposing the renal capsule. With gentle displacement of the adrenal gland medially, meticulous dissection between the adrenal gland and the upper pole of the kidney is carried out. The use of a bipolar vessel-sealing device is beneficial in this area due to the highly vascular nature of the adrenal gland. If bleeding is encountered in this area, the application of gentle pressure is usually effective in obtaining hemostasis. In addition, renal artery branches to the upper pole of the kidney are not uncommonly encountered during this portion of the dissection, and one should be careful about inadvertent vascular injury. The upper pole of the kidney is released by dividing medial and superior attachments. The remaining posterior and lateral attachments of the kidney are released last. The kidney is rotated medially in order to expose the posterior surface of renal artery and vein. Any remaining perihilar tissue is dissected posteriorly. It is important to verify that all attachments to the kidney have been divided before hilar clamping.

### Specimen extraction incision

The specimen extraction incision is made prior to hilar clamping. A decision must be made as to whether the specimen will be extracted by lengthening an existing trocar incision site or via creation of a Pfannenstiel incision. A recent systematic review and meta-analysis comparing Pfannenstiel extraction versus extraction through an extended trocar site found no differences between cohorts in terms of incision length, morbidity, wound complications, or postoperative opioid consumption [10]. We routinely utilize both techniques depending on the preference of the patient and the recipient's transplant surgeon. Extraction through a periumbilical incision allows for rapid and facile utilization of an endoscopic TA linear stapling device (rather than a GIA linear stapling device) which may be preferable in cases where length of the renal vein may be lacking or in right-sided donor nephrectomy [11]. In this case, the periumbilical trocar incision should be lengthened to match the size of the kidney (generally 5–7 cm). A hand-access device can be placed to maintain pneumoperitoneum as a trocar is placed through the device. Alternatively, the surgeon's hand can be placed directly into the abdomen through this incision either with or without [12] the use of a hand-access device in order expedite extraction. In the case of a Pfannenstiel incision, a 5–7 cm is created and the fascia is incised in the midline to expose the peritoneum. A 15 mm trocar is placed through the peritoneum and a laparoscopic extraction bag is placed behind the kidney in order to elevate the kidney by providing lateral traction. Alternatively, the surgeon's hand can be placed directly into the abdomen as described for the periumbilical incision.

### Final preparations

At this point intraoperatively, final preparations are made in anticipation for hilar division and specimen extraction. The operating room staff should confirm that all appropriate equipment for specimen extraction and back table preparation are available in the room, including adequate staple reloads for the patient's hilum, an extra stapling device in the unlikely event of a stapler misfire, ice slush for rapid cooling of the specimen, and a completely furnished back table according to the transplant team's specifications. Ensuring the availability of all necessary components of the extraction will help minimize warm ischemia time.

Consultation should be performed with anesthesia to confirm adequate hydration and donor urine output prior to hilar ligation. If the patient has shown any signs of oliguria in the hour preceding this point in the case, it is best to wait for additional hydration prior to division of the renal hilum and specimen extraction.

The pneumoperitoneum created during laparoscopic surgery can have transient negative effects on urine output and renal function. This is cause for concern because low urine output in the donor may lead to delayed graft function in the recipient. Therefore certain measures during laparoscopic donor nephrectomy have been described to promote urine production and allograft function. Adequate hydration is mandatory, and many centers use loop or osmotic diuretics to promote a diuresis. Our preference is to administer one dose of 12.5 g of mannitol at time of the dissection of the gonadal and adrenal veins, and an additional 12.5 g of mannitol during renal artery dissection. Other groups have described the use of other combinations of mannitol and furosemide, as well as continuous infusions of mannitol and dopamine during laparoscopic donor nephrectomy.

The use of systemic heparin to prevent vascular thrombosis during donor nephrectomy remains controversial. An intravenous dose of up to 5000 U, with or without protamine reversal (up to 50 mg IV), is routinely advocated by many centers [13]. However, the literature suggests that the use of heparin, given either alone or with protamine reversal after the graft is removed, does not offer any clinical benefit in terms of preventing graft thrombosis or improving allograft function [14–16]. Some groups have abandoned this practice altogether because of the potential for exacerbating hemorrhagic complications.

Finally, in order to maintain adequate arterial blood flow during renal artery dissection, some surgeons advocate the topical application of papaverine (30 mg/ml solution, 10–20 ml total) to prevent arterial vasospasm.

### Hilar division

The ureter may then be ligated and divided at the level of the iliac vessels in order to maximize ureteral length to facilitate transplantation (Figure 108.5). A clip is placed on the ureter distally and the ureter is divided proximally. In a well-hydrated patient, urine is usually seen emanating from the proximal end of the ureter after transection.

An endoscopic TA linear stapling device is used to ligate the renal artery at its origin from the aorta. The artery is immediately divided lateral to the staple line using laparoscopic scissors. Length of the renal artery may be maximized by medial rotation of the kidney and application of the stapling device from a posterior approach (Figure 108.6). Alternatively, an endoscopic GIA linear stapling device can be used to the ligate and transect the renal artery, however this maneuver may compromise the length of the renal artery, as the staple line on the specimen side will need to be excised prior to initiating the vascular anastomosis. Hem-o-lok® ligating clips (Teleflex Medical, Bannockburn, IL, USA) are contraindicated for use in ligating the renal artery during laparoscopic nephrectomy in living donor patients. The manufacturers of the Hem-o-lok clip issued a memo in April 2006 stating that the Hem-o-lok ligating clips may become dislodged following ligation of the renal artery during laparoscopic donor nephrectomy which can lead to massive hemorrhage, open conversion, delayed hemorrhage requiring re-exploration, and even death [17, 18].

After division of the artery, an endoscopic TA linear stapling device is placed from an anterior approach and used to ligate the renal vein medial to the adrenal and gonadal branches (Figure 108.7). The vein is then divided lateral to the staple line using laparoscopic scissors. Once the specimen is free, it is either manually extracted through the planned extraction site or it is placed in a

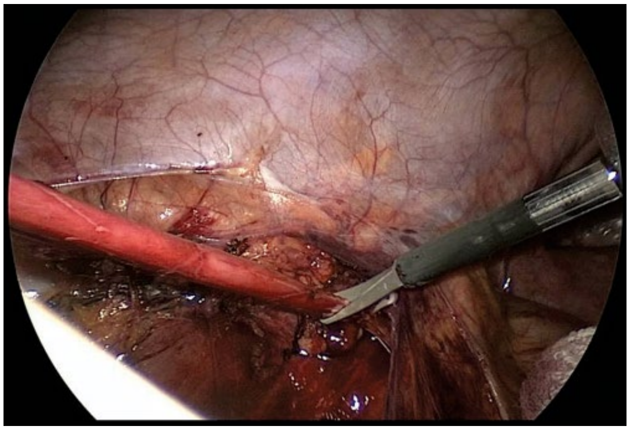

**Figure 108.5** Division of the ureter just proximal to the level of the iliac vessels.

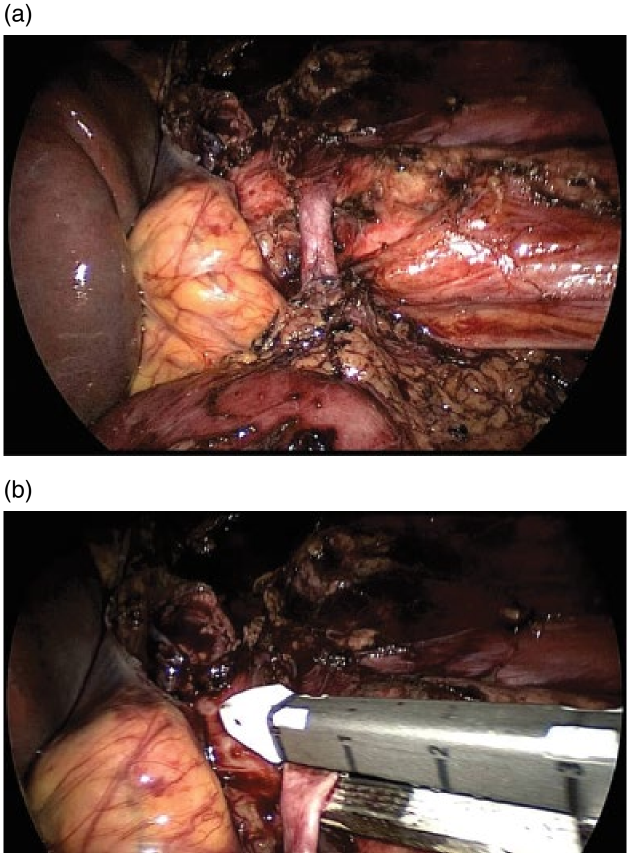

**Figure 108.6** (a) Renal artery visualization and (b) application of the endoscopic TA linear stapling device via a posterior approach.

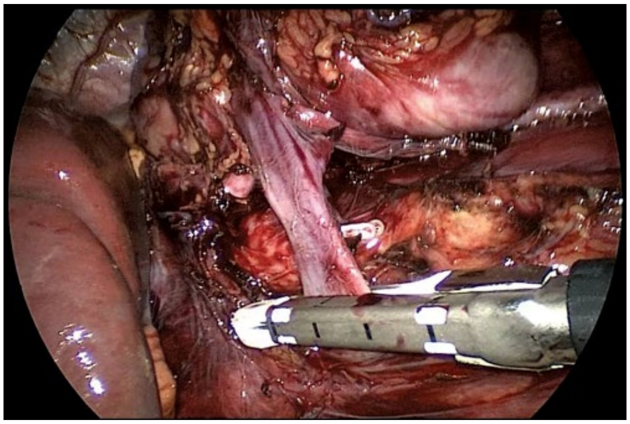

**Figure 108.7** Application of the endoscopic TA linear stapling device on the renal vein from an anterior approach.

laparoscopic extraction bag. The kidney is extracted and placed on ice. The kidney is then passed to the awaiting transplant surgical team.

Although exceedingly rare, stapler malfunctions have been reported. In such situations, an additional 12 mm trocar may be used to place a second stapling device. If possible, a second row of staples is applied across the bleeding vessel more proximally. When sufficient vessel length does not permit this salvage method, open conversion may be required.

### Closure

The extraction site fascia should be closed in standard fashion using either a running or interrupted fashion according to surgeon preference. After the extraction site fascia is closed, the abdomen is reinsufflated to 5 mmHg and the peritoneal cavity is laparoscopically inspected for bleeding or visceral injury. After inspection, all trocars are removed under direct vision and closure of all trocar sites 10 mm or larger is performed with a fascial closure device. Finally, the pneumoperitoneum is evacuated and the skin incisions are closed.

## Right laparoscopic donor nephrectomy

### Abdominal entry and trocar placement

Although the positioning and procedure for a right-sided donor nephrectomy is similar to a left-sided donor nephrectomy, some of the differences require clarification. A 12 mm trocar is inserted at the umbilicus and is used as the primary working trocar. A 5 mm camera trocar is placed slightly to the right of midline, approximately 2 cm below the xiphoid process. A 5 mm trocar is placed at the midclavicular line, and below the level of the umbilicus. An accessory 5 mm trocar is placed along the anterior axillary line below the costal margin and is used for liver retraction.

### Initial mobilization

The triangular ligament is incised to release the right lobe of the liver from the sidewall. A liver retractor is placed through the lateral subcostal trocar, and the liver is retracted superiorly to expose the upper pole of the kidney.

The right colon is reflected medially and a Kocher maneuver is performed to mobilize the duodenum medially. The peritoneal layer overlying Gerota's fascia is incised in a cephalad direction medially, and then in a lateral direction after reaching the upper pole of the kidney. The psoas muscle is exposed below the lower pole of the kidney. The ureter and gonadal vein are identified along the medial border of the psoas muscle. The ureter is dissected to the level of the iliac artery bifurcation. The ureter is not divided at this time. By gently elevating the ureter and lower pole of the kidney with an instrument, the medial border of the kidney is dissected in a cephalad direction to the level of the renal hilum. The correct plane of dissection lies lateral to the gonadal vein.

Gerota's fascia is entered along the anterior aspect of the upper pole, exposing the renal capsule. Meticulous dissection between the adrenal gland and the upper pole of the kidney is carried out.

#### Hilar dissection

The right adrenal vein enters directly into the inferior vena cava and is not dissected during a right-sided donor nephrectomy. The inferior border of the renal vein must be found by tracing the lateral aspect of the inferior vena cava to the ostium of the renal vein. Because of the anatomic limitations of a short right renal vein, a fervent attempt is made to salvage as much renal vein length as possible. The renal artery can be reliably identified posterior and inferior to the renal vein. Ligation and division of the ureter and renal hilum, and extraction of the specimen, is performed as described previously for the left-sided procedure.

### Hand-assisted laparoscopic donor nephrectomy

Hand-assisted laparoscopy has transformed the field of operative urology over the past decade, and its applications have been applied to a variety of procedures since its introduction. In this technique, the surgeon's nondominant hand is introduced into the surgical field through a hand-access device while the dominant hand uses laparoscopic instruments that are introduced through standard laparoscopic trocars. The nondominant hand facilitates dissection by providing the surgeon with tactile feedback and manual retraction, while additionally allowing prompt hemostasis, vascular control, and rapid specimen extraction.

### Laparoendoscopic single-site donor nephrectomy

Laparoendoscopic single-site (LESS) surgery has been adopted for a variety of urologic procedures and represents the next step in the evolution of conventional laparoscopic surgery. This surgery is performed through a single small skin incision, often partially concealed at the umbilicus. Several studies have shown that LESS living donor nephrectomy has been associated with decreased postoperative pain and better postoperative cosmesis, while providing equivalent graft outcomes when compared to the conventional laparoscopic approach. This technique, however, is far from the new standard of care due to the unique challenges posed by single-site surgery including problems with instrument clashing, difficulty with triangulation, and poor ergonomics.

There are several different techniques for performing LESS donor nephrectomy. The most commonly used technique utilizes a 5 cm periumbilical incision. The abdomen is entered through a vertical anterior rectus fasciotomy. The GelPOINT® device (Applied Medical Systems, Rancho Santa Margarita, CA, USA) is inserted into the abdomen with three triangulated trocars preplaced into the device (Figure 108.8). Typically, two 5–10 mm and one 15 mm trocars are used. If a right-sided LESS donor nephrectomy is being performed, a fourth trocar is placed through the GelPOINT® to allow for the use of a liver retractor. Pneumoperitoneum is then achieved. The remainder of the procedure is performed similar to what has been described above for conventional laparoscopic donor nephrectomy.

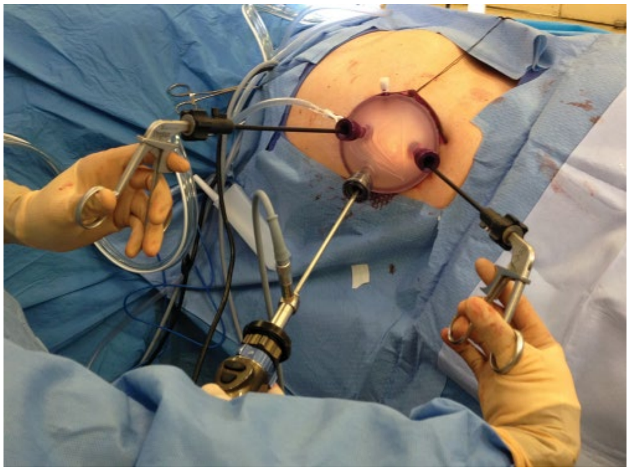

**Figure 108.8** Laparoendoscopic single-site (LESS) device and instrumentation for donor nephrectomy.

Once the renal hilum and all of the perinephric attachments have been carefully dissected, the gonadal vein and ureter are transected at the level of the iliac vessels, and the renal artery and vein are then ligated and transected. A laparoscopic extraction bag is then introduced to capture the kidney and the specimen is removed by removing the gel cap of the single-site device.

### Robot-assisted laparoscopic donor nephrectomy

Robot-assisted laparoscopic surgery has become widely accepted in urologic surgery as a revolutionary advance in operative technique due to the improved three-dimensional visualization of the operative field and the degrees of freedom offered by the robotic instruments. Several small studies have confirmed that robot-assisted laparoscopic donor nephrectomy is a viable, safe, and effective surgical technique. However, further studies are necessary to determine if robot-assisted surgery provides any advantages over traditional laparoscopic techniques.

## Postoperative management

### Hospital course

The orogastric tube is removed at the completion of the procedure. The patient is transferred from the recovery room to a regular room overnight. A Foley catheter is maintained overnight to permit strict monitoring of urine output. A chemistry panel and complete blood count are obtained in the recovery room and on the first postoperative day. The Foley catheter is removed on the first postoperative day. A clear liquid diet is started on the day of surgery and the diet is advanced as tolerated.

Most patients are discharged home with opioid pain control and a bowel regimen on the first postoperative day. Patients are generally seen for a routine evaluation seven days postoperatively. Unless abnormalities were noted during the hospitalization, there is no need for laboratory studies at this visit. Patients are advised to follow-up with either their primary care physician or transplant nephrologist at three months postoperatively for blood pressure measurement and routine laboratory studies. All donors should be advised to remain compliant with yearly routine annual follow-up with their primary care physician in order to monitor their blood pressure, renal function, and urine studies. Patients should also be counseled on avoiding chronic use of nephrotoxic medications (e.g. nonsteroidal anti-inflammatory drugs [NSAIDs]). It may be beneficial to arrange for donors to meet with a nutritionist postoperatively in order to help educate them on renal healthy diets and encourage healthy eating habits.

### Pain control

In most instances, we advocate the utilization of intravenous ketorolac in a scheduled fashion for the first 24 hours postoperatively as it has been demonstrated to reduce pain and opioid requirement postoperatively, shorten length of stay and quicken the return of bowel function postoperatively [19, 20]. It should be noted that the use of ketorolac in patients following donor nephrectomy is somewhat controversial due to reports that patients receiving the drug exhibit a lower creatinine clearance in the immediate postoperative period, but these differences do not persist at long-term follow-up [19]. After completion of 24 hours of scheduled intravenous ketorolac, most patients are discharged with a short supply of oral opioid medication (e.g. tramadol). They are further advised to avoid the use of NSAIDs in the future in order to protect their renal function.

### Complications

The overall postoperative complication rate following laparoscopic donor nephrectomy in large, contemporary series has been estimated at approximately 3.4–10.3% and primarily low grade in nature (e.g. wound infection or minor wound complications) [21–23]. The open conversion rate in most contemporary series is very low and has reported to range from 0.2% to 1.8% [21, 23–25]. Moreover, these reports of complications and conversion rates may actually represent slight overestimations today as many of these large case series report that the majority of conversion or complications occurred early in the laparoscopic donor nephrectomy experience (first 100–150 cases) [6, 14, 23]. Consequently, the rate of complications or open conversion can be reasonably believed to be even lower today.

## Conclusions

Laparoscopic donor nephrectomy has been demonstrated to be a safe alternative to open renal donation. Consequently, it is considered the standard of care at most transplant centers today. The reduced pain and opioid requirement, shorter convalescence, and improved cosmesis afforded by laparoscopic donor nephrectomy is likely partially responsible for reducing barriers to kidney donation and the increasing acceptance and performance of living donor nephrectomy with time.

See accompanying Video 108.1.

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# 109

# Robotic Kidney Transplantation

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## Introduction

The prevalence of chronic kidney disease (CKD) is rising along with increasing life expectancy. There has been a 30% increase in the prevalence of CKD in the United States in the last decade [1]. Similar data from developing countries such as India are scarce, but even conservative estimates reveal an age-adjusted incidence of 229 persons per million [2]. The numbers of endstage renal disease (ESRD) cases, and with that the number of patients waiting for a transplant, are increasing. Among the available methods of renal replacement therapy, kidney transplantation is associated with the best quality of life, best survival rates, and thus remains the treatment of choice for late stages of CKD [3].

Open surgery has been the gold standard for kidney transplant from the beginning and Carrel's technique of vascular anastomosis has been in use for over a hundred years. Although the introduction of minimally invasive techniques has completely transformed other surgical specialties, kidney recipient surgery has seen little change since its inception.

In recent years, the indications for minimally invasive surgery have expanded with the increasing use of surgical robots, and the field of kidney transplantation has not remained untouched. Evidence-based development of robotic kidney transplantation (RKT) in the last few years has opened a new frontier in recipient surgery. Reduction in perioperative complications remains a priority in frail, immunocompromised kidney recipients, who thus remain the ideal candidates for minimally invasive surgery. Obese transplant recipients in particular are a surgical challenge. Obesity leads to longer waiting times for transplant, higher risks of surgical site infections, and increased complications. In severe cases, such patients have been denied the opportunity for transplant in some centers. Early results of RKT have shown shorter convalescence times, less perioperative morbidity, and better cosmesis. In addition to these obvious benefits, RKT has been shown to be associated with decreased surgical site infections, and lower incidence of lymphoceles and vascular complications. This chapter reviews the development, technique, and current status of RKT.

## A brief history of robotic kidney transplantation

### History of laparoscopic kidney transplantation

The use of a surgical robot in kidney transplant was first described in a case of deceased donor transplant by Hoznek et al., from France, in 2001 [4]. The robot was used for vascular anastomosis and ureteroneocystostomy after making an open incision. Although the ability of the da Vinci® surgical robot (Intuitive Surgical, Sunnyvale, CA, USA) to handle fine sutures, such as 6-0 polydioxanone and 5-0 polypropylene, was demonstrated in this case, as was the ability of robotic instruments in dissection, lack of haptic feedback required the bedside assistant to follow the suture. Little enthusiasm was shown for this procedure in the next decade, until Antonio Rosales from Spain reported the first laparoscopic transplant in 2009. In this surgery, the kidney was introduced into the abdomen through a Pfannenstiel incision and the anastomosis was performed laparoscopically in 53 minutes. The cold ischemia time was 182 minutes [5]. Soon, Modi et al. from India described the procedure in four patients, in a deceased donor program [6]. They used the left kidney from the deceased donor for the laparoscopic procedure. A Carrel's patch was

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used to carry out a wide arterial anastomosis. The mean anastomosis time for laparoscopic procedure was reported as 65 minutes, which is not significantly longer than that for open surgery. More importantly, they reported equivalent renal function outcomes at 1 year, six months, and 1 year following surgery, for both open and laparoscopic recipients. The same group reported a series of 72 more cases in the following years [7]. The rewarming time (time taken after the graft is placed in the recipient until the graft is revascularized) was significantly longer in the laparoscopic group compared to the open group (60.3 vs. 30.3 minutes). Even though the estimated glomerular filtration rate (eGFR) at 7 and 30 days after transplant was lower in the laparoscopic group, the graft survival was excellent at six months. There was no difference in graft survival at 3, 6, 12, and 18 months postoperatively. Interestingly, since the graft was free-floating in the peritoneal cavity, there were two cases of torsion of graft leading to graft loss. The technique was subsequently modified to fix the graft using a peritoneal flap. Even as this study proved the feasibility of minimally invasive transplant, the operation remained extremely challenging. As a result, it did not see widespread adoption.

## Early development of robotic kidney transplant

The first RKT was reported from the University of Illinois at Chicago by Giulianotti et al. in 2010 [8]. A 7 cm periumbilical incision, and a hand-assist device was used for this procedure, in a morbidly obese patient with a body mass index (BMI) of 41 kg/m$^2$. Total operative time was 223 minutes and warm ischemia time was 50 minutes. The blood loss was less than 50 ml. Soon afterwards, the first case from Europe was reported by Boggi et al. A Pfannenstiel incision was used in this case, through which the ureterovesical anastomosis was performed in an open fashion. The operative time was 154 minutes and warm ischemia time 51 minutes [9].

The Chicago group subsequently reported RKT case series of 28 obese recipients (BMI 42.6 ± 7.8 kg/m$^2$). In the later part of the series, robot-assisted clamping was used instead of the hand-assist device used in the initial cases [10]. For the preparation of transplant bed and vascular anastomosis, a right flank position was used. For the ureteroneocystostomy, the patient has to be repositioned and the robot had to be redocked. The graft was left intraperitoneal and for a renal biopsy, when required, laparoscopy had to be used. According to this study, although there was no difference in cold or warm ischemia times between open kidney transplant (OKT) and RKT groups (RKT: 2.8 and 47.7 minutes; controls: 2.0 and 49.2 minutes; $P \geq 0.48$), the creatinine at discharge was higher in the RKT group than in the OKT group (2.0 mg/dl vs. 1.4 mg/dl; $P = 0.04$). The higher creatinine at discharge may be explained by poor allograft perfusion due to pneumoperitoneum [11]. The renal function at six months postoperatively was similar (serum creatinine 1.5 ± 0.4 mg/dl vs.1.6 ± 0.6 mg/dl; $P = 0.47$). Surgical site infections were found to be significantly less in the RKT group than in the OKT group (0/28 (0%) in RKT vs. 8/28 (28.6%) in OKT; $P = 0.004$).

These early experiences with minimally invasive transplant were pioneering, but critical analysis showed a slower return of graft function postoperatively. This was probably a result of increased anastomosis time, with the graft at body temperature, and lack of methods for intracorporeal cooling of the graft during anastomosis, which may cause slower return of graft function postoperatively. This effect could have been compounded by longer anastomosis times during the learning curve.

## Development of the Vattikuti Urology Institute RKT technique with regional hypothermia

The experimental studies by Wickham showed that the ideal temperature for maximal reno-protection during nonvascularized phase was around 20 °C [12]. Regional hypothermia using ice slush introduced into the pelvis was evaluated in >300 robotic prostatectomy patients at Vattikuti Urological Institute (VUI) in Detroit, USA. The ice slush was introduced through a GelPOINT® device (Applied Medical Inc., Rancho Santa Margarita, CA, USA). It was demonstrated that an average pelvic temperature of 15.8 °C could be achieved within 15 minutes of icing, with no change in core body temperature [13]. This finding led to the concept of regional hypothermia for RKT, which was then put into practice by collaboration between the VUI team and the Medanta team from India. The new procedure was developed according to IDEAL (idea, development, exploration, assessment, long-term follow-up) guidelines [14]. Phase 0 IDEAL studies were conducted in two fresh cadavers. This phase led to standardization of patient positioning, port placement, docking of the robot, and the choice of instruments and sutures. In this phase, the use of a GelPOINT device to introduce the kidney and ice slush into the pelvis was also established. The standardized pelvic docking also eliminated the need to reposition the robot for urethrovesical anastomosis, as was needed in previously reported efforts at robotic transplantation [15]. Phase 0 was followed by phase 1 study, during which seven patients underwent RKT with regional hypothermia by the combined VUI and Medanta team in India in January 2013. In this phase a mean kidney surface temperature of 22.5 °C could be achieved using regional hypothermia, with no patient developing systemic hypothermia. The mean arterial, venous, and ureterovesical anastomosis times were 14.4, 14, and 23.4 minutes, respectively. The mean rewarming time was 51.4 minutes, while the mean warm ischemia time was 2 minutes. Mean serum creatinine on postoperative days 1 and 7 were 2.2 mg/dl and 1.2 mg/dl, respectively. One patient required re-exploration due to increased drain output, but no specific bleeding point could be detected on exploration.

Next phase of the development of RKT consisted of 43 patients. Mean operative and console times were 214.1 ± 39.8 (156–293) and 135.4 ± 31.2 (94–201) minutes, respectively. Mean warm ischemia, rewarming, and arterial and venous anastomosis times were 2.4 ± 1.1 (1.5–6.0), 46.6 ± 9.3 (27–66), 12.0 ± 2.6 (7–17), and 13.4 ± 3.4 (8–21) minutes, respectively. The anastomosis times decreased in this phase compared to the phase 1 study. Mean intraoperative renal surface temperature was 20.3 ± 2.9 °C (14.5–27.8) and the mean blood loss was 151.7 ± 103.5 (50–450) ml. The average incision length was 6.1 ± 0.5 (5.4–7.1) cm. Mean serum creatinine at discharge was 1.3 ± 0.6 (0.8–3.1) mg/dl. No patient experienced delayed graft function, vascular or urine leaks, wound complications, or wound infections. There was no peri-graft collection on computed tomography in any patient at three months. No further complications were recorded at six months follow-up. One patient died at 1.5 months due to acute congestive heart failure secondary to a cardiac condition [11]. Presently, the evolution of RKT is in the IDEAL phase 3, and is being compared with OKT.

## Preoperative preparation of patients for RKT

Standard pretransplant medical evaluation includes assessment of the recipient for infectious and immunological risks, and malignancy. Modifiable risk factors for morbidity such as coronary artery disease, hypertension, and diabetes mellitus are then optimized. Patient education for relevant lifestyle modifications such as smoking cessation, risks of immunosuppression, and medication compliance is important. Surgical risk assessment is then done for RKT which includes evaluation for peripheral vascular disease and obesity. Obesity is an independent risk factor for surgical site infections [16]. The indications and contraindications for RKT are listed in Boxes 109.1 and 109.2.

**Box 109.1 Indications (standard for any kidney transplant).**

a) Irreversible kidney disease, defined as:
   i) CKD with glomerular filtration rate <20 ml/min
   ii) CKD with symptomatic uremia
   iii) CKD requiring dialysis
b) Anticipated ESRD, as defined as (a), within the next 12 months (preemptive transplant)
c) Absence of malignancy and/or active infection
d) Availability of appropriate kidney donor

CKD, chronic kidney disease.

**Box 109.2 Contraindications for robotic kidney transplantation in potential recipients otherwise suitable for kidney transplantation.**

- Significant atherosclerotic disease of the iliac vessels (>30% blockage)
- Previous major abdominal surgery with high suspicion for intra-abdominal adhesions (relative)
- Simultaneous dual or multiple organ transplant (relative)

## Step-by-step technique (Video 109.1)

### Step 1: Preparation of GelPOINT device

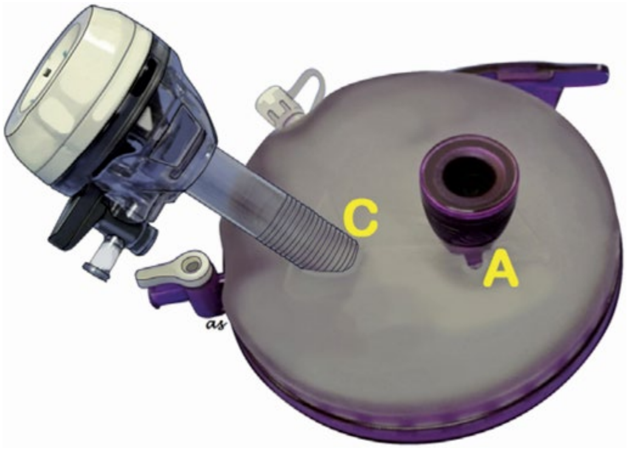

**Figure 109.1** Preparation of GelSeal cap, with a 12 mm camera port (C) and a 5 mm assistant port (A). *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

The GelPOINT device is placed through a 5–6 cm vertical midline incision curving around the umbilicus. The incision could be predominantly extended above the umbilicus in smaller patients. The GelSeal® cap is prepared with a 12 mm camera port and a 5 mm assistant port placed through it as shown in Figure 109.1. This 5 mm port will be the assistant's port. Optimal positioning of these ports into the cap is important, as placing these two ports too close to each other may lead to restriction of the assistant’s movement by the camera arm, and may hinder proper suctioning.

### Step 2: Port placement

After general anaesthesia and catheterization, with the patient in supine position, a 4–5 cm midline periumbilical incision is made for the GelPOINT device. The previously prepared GelPOINT device is placed through this incision. Pneumoperitoneum of 15 mmHg is created through this port. The rest of the port placement is identical to that for robotic prostatectomy (two 8 mm robotic ports along the left and right paramedian lines below the level of the umbilicus, a third 8 mm robotic port lateral to the left anterior axillary line just below the level of umbilicus, and a 12 mm assistant port along the right anterior axillary line) (Figure 109.2). For the da Vinci Xi robot, all 8 mm ports can be created in a single line, just above the level of the umbilicus, while the assistant port remains the same as described above.

### Step 3: Patient positioning

The patient is placed in a modified lithotomy as for robotic prostatectomy [17] if the Si or older models of da Vinci are being used. For the da Vinci Xi system, the patient can be placed supine, and in a 15–20° Trendelenburg position.

### Step 4: Docking of the robot

The robot may be docked between the patient’s legs if patient is in modified lithotomy. For the da Vinci Xi system, the patient can be supine, and the robot is docked from the side, usually the left side. The boom of the patient cart can then be adjusted to achieve the same position of robotic arms as in the standard docking of the previous surgical robots.

### Step 5: Instruments used

Authors find a “30 down” vision beneficial for this part of the procedure. Fenestrated bipolar forceps, and monopolar curved scissors are preferred instruments for preparation of the transplant bed. The peritoneum over the iliac vessels is incised, and the external iliac vessels are skeletonized from the level of the common iliac artery bifurcation to the inguinal ligament. With experience, it may become possible to reduce to minimal dissection, just freeing sufficient length for clamp and anastomosis. Some external iliac vein tributaries may, at times, need clipping and division to free up sufficient length (Figure 109.3).

The peritoneum distal to cecum is horizontally divided, starting from the center of the previously incised peritoneum over the iliac vessels. The proximal and distal flaps of the peritoneum are raised and used later to extraperitonealize and fix the graft.

Vision is changed to “30 up” and the urinary bladder is dropped from the anterior abdominal wall to the pubic

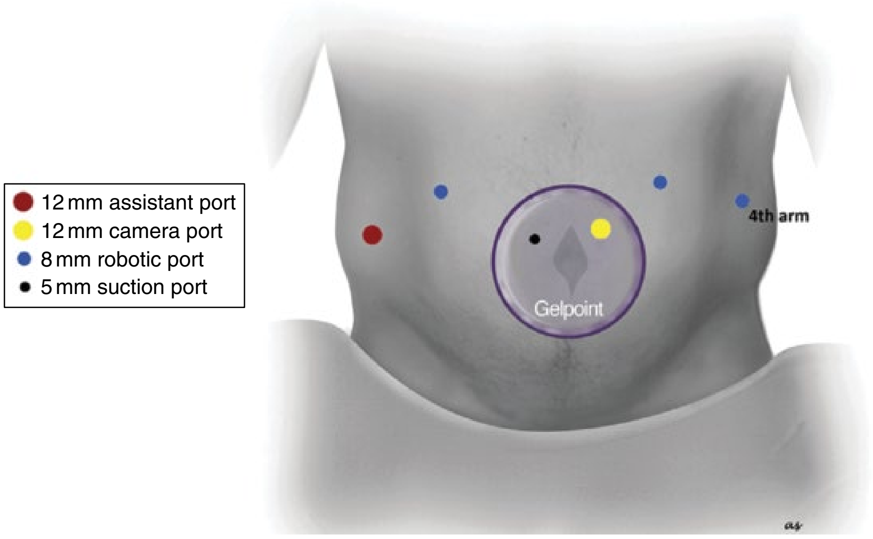

**Figure 109.2** Port placement. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

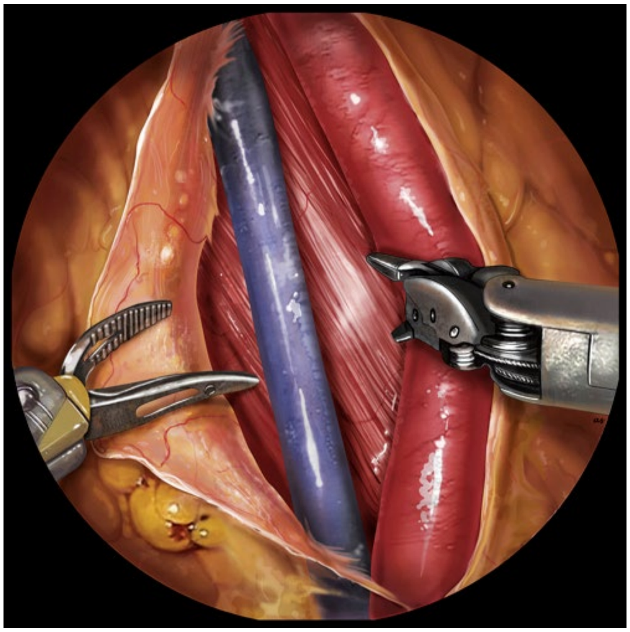

**Figure 109.3** Preparation of the iliac vessels (graft bed preparation). *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

symphysis. After filling the bladder with 200 ml of normal saline, a site is prepared for ureterovesical anastomosis on the anterosuperior aspect of the bladder ipsilaterally (Figure 109.4). A detrusor tunnel is made at the proximal end of the selected ureterovesicostomy site to give sufficient submucosal length.

## Step 6: Preparation of the graft kidney jacket

After harvesting, the graft kidney is enclosed in a jacket made of surgical gauze. Some ice slush is also enclosed inside the graft jacket around the graft (Figure 109.5). A hole is made in the jacket medially, which allows renal vessels to be brought out. The authors leave a long silk suture marker at the upper pole for correct orientation of the graft to identify the two ends when graft has been placed inside the peritoneal cavity. The jacket helps in maintaining intracorporeal cooling, as well as enabling holding and moving the graft without trauma to the graft. It also keeps the hilar fat retracted, thus presenting the vessels for easier anastomosis.

## Step 7: Regional hypothermia

After undocking of the robotic camera arm, and removal of the GelSeal cap, Toomey syringes with their front end cut off (Figure 109.6) are used to introduce 200–250 ml of ice slush through the GelPOINT device. The ice slush is placed on the pelvic bed, over the dropped bladder flap (Figure 109.7). Additional ice slush may be delivered onto the graft, immediately after the graft's introduction as well as between venous and arterial anastomosis, to achieve uniform cooling and prolonged effect (Figure 109.8).

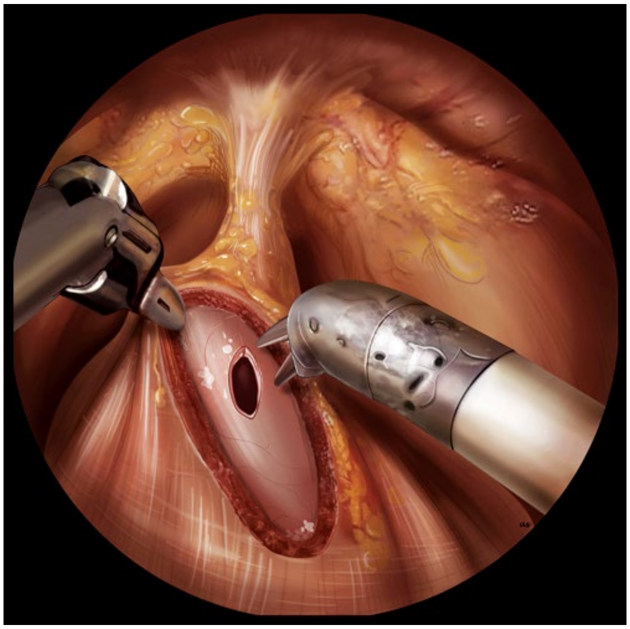

**Figure 109.4** Preparation of the site for ureterovesical anastomosis on the anterosuperior aspect of the bladder. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

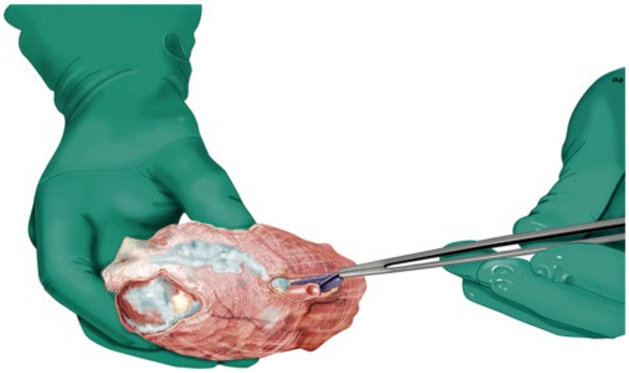

**Figure 109.5** Preparation of the gauze jacket. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

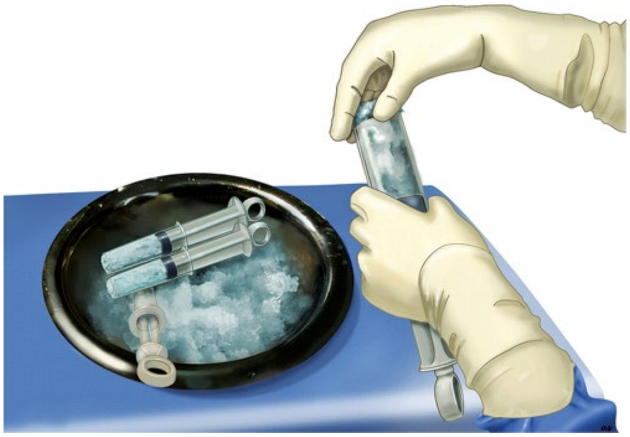

**Figure 109.6** Ice slush introduced into the abdomen using Toomey syringes with their front end cut off. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

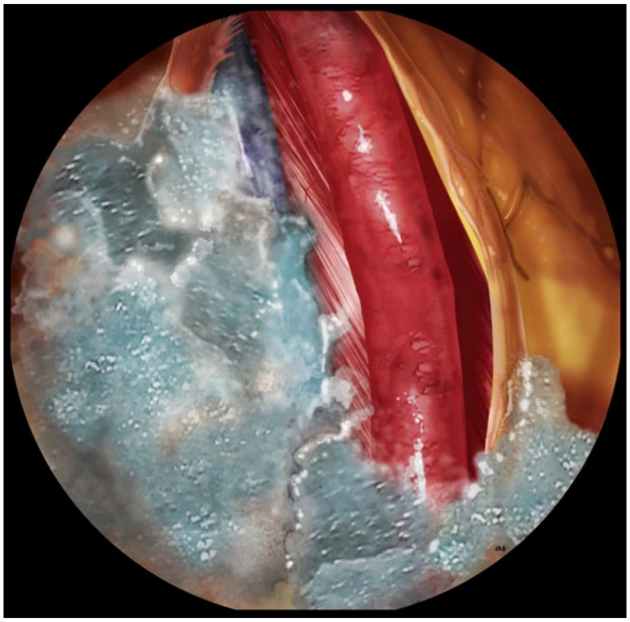

**Figure 109.7** Regional hypothermia with placement of ice slush on the bladder flap. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

## Step 8: Vascular anastomoses

The external iliac vein is now isolated both proximally and distally, with bulldog clamps introduced through the assistant port (Figure 109.9). Appropriate length venotomy is then made with scissors, and the external iliac vein flushed with heparinized saline. The external iliac

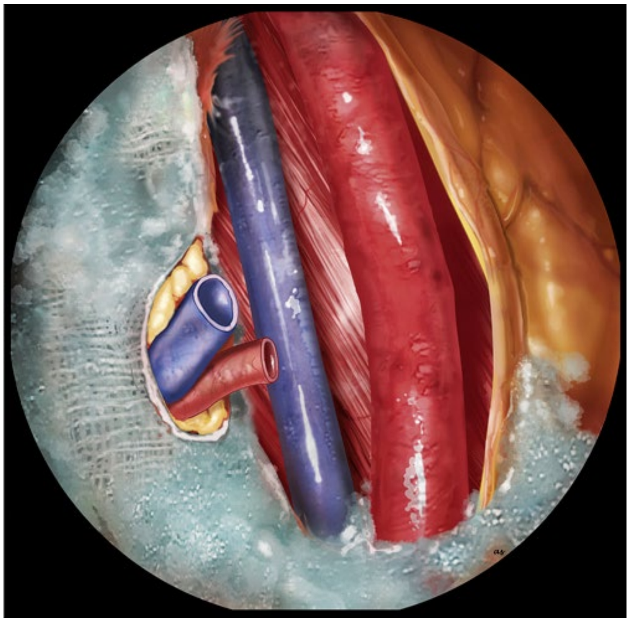

**Figure 109.8** Placement of additional ice slush on the graft. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

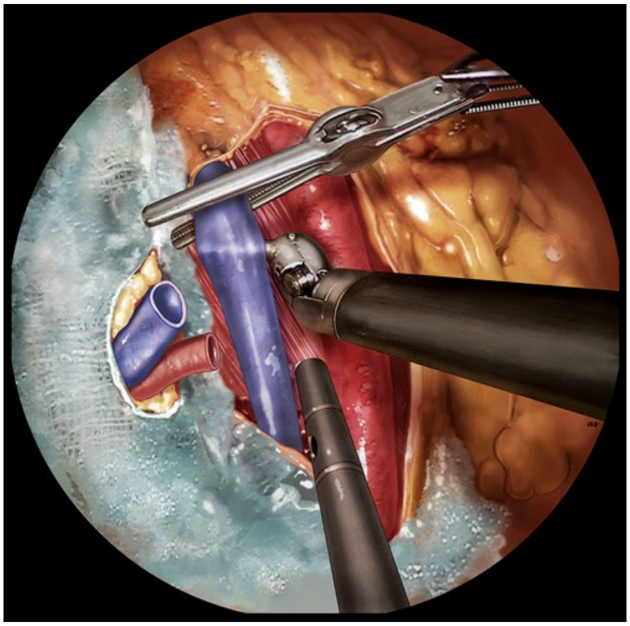

**Figure 109.9** Clamping of external iliac vein using bulldog clamps introduced through assistant ports. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

vein is anastomosed to the graft renal vein using Gore-Tex® 5-0 CV-6 suture with a 9 mm needle (Figure 109.10). The authors prefer this suture because of its many useful properties. It is a microporous, nonabsorbable, monofilament suture made of expanded polytetrafluoroethylene. It is soft and supple with no memory, and has sufficient strength for robotic handling. Needles at both ends are used, one each for venous and arterial anastomosis. The appropriate suture length is 15 cm for arterial and 18 cm for venous anastomosis. Black Diamond™ forceps are used in the nondominant hand similar to the use of DeBakey forceps in open surgery, to spread and handle vascular tissue for precise suturing, while a large robotic needle driver is used in the dominant hand during the anastomosis. An end-to-side anastomosis of the graft renal vein to the clamped external iliac vein is then performed. The authors prefer to start the anastomosis at the distal end, completing the posterior wall in a continuous manner. After turning the corner, and before proceeding to the anterior wall, a knot is tied.

A ureteric catheter introduced through the assistant port is used to flush the vein with heparinized saline before the final suture is pulled and tied. The graft renal vein is now clamped, and the clamps on the external iliac vein are removed. The bulldog clamps removed from the external iliac vein are applied to the proximal and distal end of the dissected external iliac artery. Robotic Snapfit® or a Pott's scissor is used to make a small arteriotomy, before using a 3.6 mm vascular punch inserted through GelPOINT device to make an adequate rounded opening (Figure 109.11). The authors have devised a long, metallic laparoscopic arterial punch for this step, as the standard commercially available arterial punches are limited in length, and it may not be possible to reach the external iliac artery from the GelPOINT device with them, especially in obese patients. An end-to-side anastomosis of the graft renal artery is done with external iliac artery using a technique similar to venous anastomosis (Figure 109.12).

The graft renal artery is now clamped, and the distal bulldog clamp on the external iliac artery removed to check for the integrity of the arterial anastomosis with the backflow from the distal external iliac artery. A major bleed can be tackled by taking extra sutures at this point. If there is no significant leak, the proximal bulldog clamp is removed from the external iliac artery to restore the flow continuity of the external iliac artery. Minor bleeding may be controlled by using Surgicel® over the bleeding point. The graft is then perfused by removing all of the clamps.

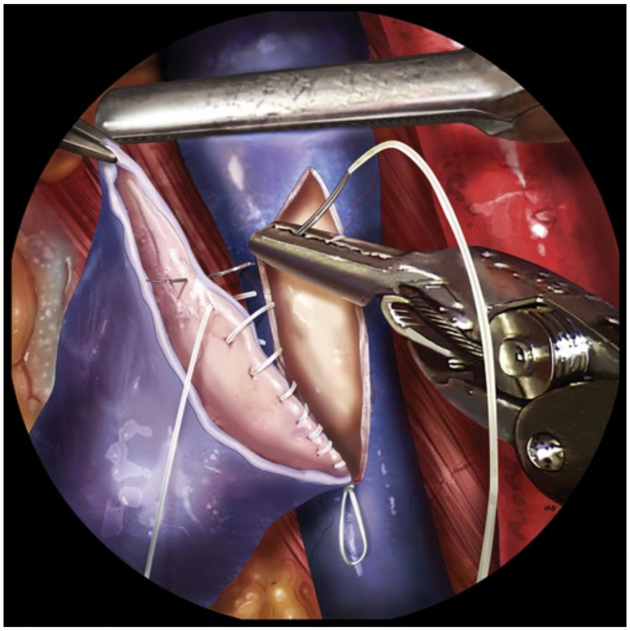

**Figure 109.10** End-to-side anastomosis of graft renal vein to the external iliac vein using Gore-Tex 5-0 CV-6 suture. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

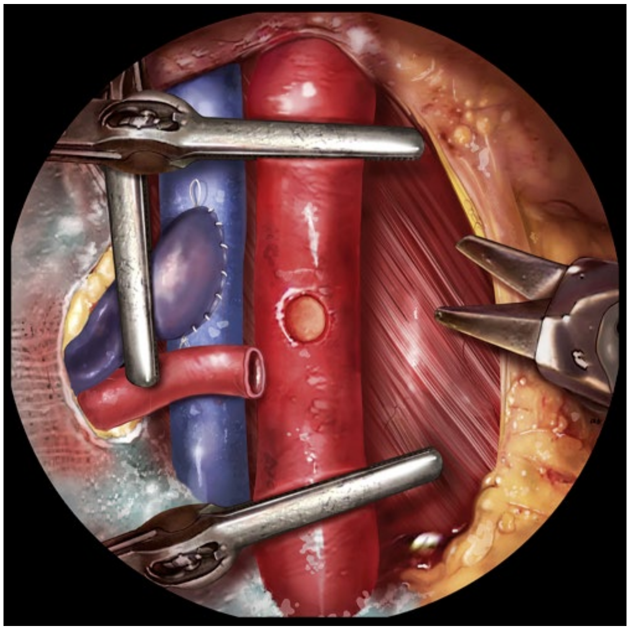

**Figure 109.11** Adequate rounded opening made on the external iliac artery using a Robotic Snapfit® or Pott's scissors followed by a 3.6 mm vascular punch. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

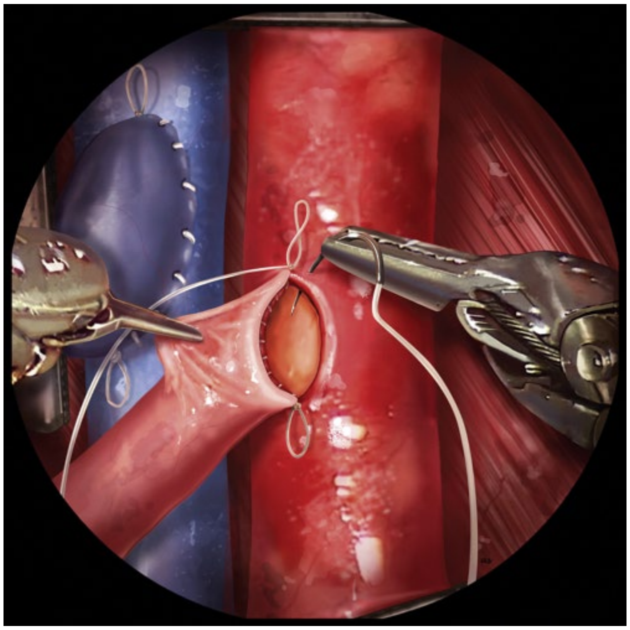

**Figure 109.12** End-to-side anastomosis of the graft renal artery to the external iliac artery. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

### Step 9: Cutting of gauze jacket and retroperitonealization of the graft

Scissors are used to cut the gauze jacket, which allows for visual inspection of the graft for color and turgidity. The graft jacket is now released, cutting it from its hilar opening proximally and distally to bare the graft and allow its visual inspection for color and turgidity. The graft is then flipped back into the right iliac fossa by turning it through 180° around the iliac vessels. This also allows for inspection of the other side of the anastomosis. The graft is then retroperitonialized by bringing the previously created proximal and distal peritoneal flaps over the graft, and using Hem-o-lok clips to keep them in place. The pneumoperitoneum is dropped to 8–10 mmHg at this stage to reduce its effect on graft perfusion.

### Step 10: Ureterovesicostomy

The ureter is brought out beneath the vas and the detrusor tunnel. A 4-0 polydiaxonone (PDS) or polyglactin (Vicryl) suture is used for the ureterovesical anastomosis. After completing the posterior layer, a 6 Fr, 16 cm double-J stent is placed before proceeding to the anterior layer of the anastomosis. A 3-0 barbed suture (3-0 V-Loc®) is used for detrusorrhaphy after the anastomosis is complete (Figure 109.13).

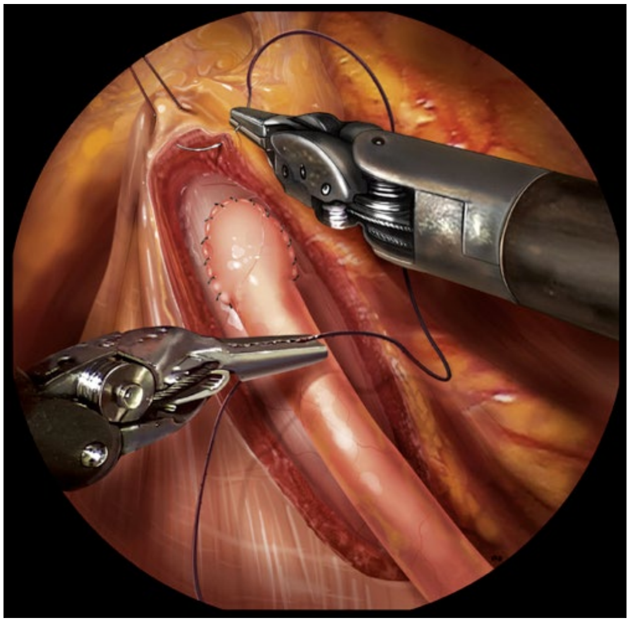

**Figure 109.13** A 3-0 barbed suture is used for detrusorrhapy after ureterovesical anastomosis. *Source:* Menon M, Sood A, Bhandari M et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta Technique (IDEA phase 2a). *Eur Urol* 2014;65(5):991–1000. Reproduced with permission of Elsevier.

### Step 11: Drain placement, undocking, and on-table Doppler

A flat drain is introduced through the fourth arm port, and is kept anterior to the urinary bladder. A 24 Fr drain is placed in the pouch of Douglas via the right 12 mm assistant port. The robot is then undocked and the ports are removed under vision before closing the wounds. It is possible that the anatomical relationship of the graft vessels and the external iliac vessels may change after pneumoperitoneum has been stopped, risking kinking of vessels. The authors routinely do an on-table vascular Doppler of the graft to confirm its vascularity before shifting the patient out to the transplant intensive care unit.

Prophylaxis for deep vein thrombosis is used as a part of protocol for any pelvic surgery. Postoperatively, calf exercises and early ambulation are encouraged.

## Evaluation of learning curve

The learning curve of RKT depends on two major factors: the experience of the surgeon in robotic surgery and their experience in kidney transplantation. Studying the learning curve is important not only to ensure the safety of the procedure during adoption at a new center, but also for appropriate timing of surgical trials.

The LC of RKT has recently been studied using the cumulative summation methodology, by comparing an established RKT center with a center which recently adopted this procedure. In this study, using target values derived from the established RKT center, it was found that the LC at the adopting center is short, with improving skill up to 20–25 cases. The functional outcomes were comparable at the two centers, with no increased complication rates during adoption [18]. The effect of robotic training and open transplant experience has previously been studied using target values derived from OKT [19]. This study showed that no learning curve existed for a surgeon who was experienced in, and actively performing robotic surgery as well as OKT. For a surgeon with limited robotic surgery experience but extensive OKT experience, a definite learning curve existed for all the steps (i.e. 3 cases for competency in graft function, 9–12 cases for venous and arterial anastomoses, 11 cases for rewarming times, and beyond 14 cases for ureterovesical anastomosis). For a surgeon with extensive robotic experience but not actively performing OKT, competency was attained in six cases, with a learning curve existing only for the ureterovesical anastomosis step.

Importantly, graft function was not adversely affected by either the lack of robotic training or kidney transplant experience.

## Renal function outcomes

The renal function outcomes are similar with OKT and RKT. The authors recently compared 125 RKT and 543 OKT patients over 3 years (unpublished data), and found no difference in fall of serum creatinine at discharge, as well as at three and six months after surgery. The mean creatinine at discharge was 1.2 mg/dl in RKT, compared to 1.3 mg/dl in OKT patients ($P < 0.71$). Delayed graft function was seen in 1.6% (2/125) patients in the RKT group, compared to 3.13% (17/543) in the OKT group ($P > 0.05$). The data comparing RKT versus OKT found no significant difference in graft survival as well as patient survival.

## Complications

RKT uses a smaller incision than OKT (6.1 cm vs. 15.6 cm, $P = 0.001$). A conference abstract on unpublished IDEAL stage 2b/3 studies indicated that the postoperative pain scores (visual analog scale [VAS] scores at 24 hours; $P < 0.001$), as well as analgesic requirements (16.9 vs. 29.7 mg morphine-equivalent patient-controlled analgesia; $P < 0.001$) are reduced in RKT compared to OKT [20]. Although various OKT series show the incidence of surgical site infections to be around 15% [21], stage 2b/3 studies show a 1.6% wound complication rate in a total of 125 patients. The blood loss is also reduced (296.8 ml vs. 151.7 ml; $P < 0.001$), partly due to the smaller incision, and also the effect of pneumoperitoneum in reducing venous blood loss. There is also a reduced risk of vascular complications in RKT, contributing to the reduced blood loss [20]. At a median follow-up of 19.1 months, no cases of vascular complications, transplant renal artery stenosis, or vascular thrombosis were reported.

Lymphocele is a common complication of OKT. The lymphatics along the iliac vessels and the graft itself lead to a constant 2.5% incidence of symptomatic lymphocele and a 20% incidence of ultrasound-detected lymphocele [22] in OKT studies. Stage 2b/3 studies of RKT show no lymphocele so far. Ureteric complications have been reported in 1–3% of OKT series [23]. A single case required a redo ureterovesicostomy after three months in our experience of 125 RKTs.

## Modifications of RKT

### Gasless robot-assisted retroperitoneal transplant

A gasless extraperitoneal approach for renal transplant has recently been reported by Tsai et al. from Taiwan [24]. This is a hybrid procedure, having steps of both open and robotic surgery. This technique has the potential advantages of the avoidance of pneumoperitoneum, and a smaller (7–9 cm), muscle-sparing Gibson incision. In case of conversion, the same incision can be extended for open surgery. The ureterovesical anastomosis is performed in an open fashion. Average anastomosis and operation time have been reported as 67.4 ± 22.3 minutes and 257.8 ± 52.7 minutes, respectively, and the average ischemia time was 283.3 ± 51.9 minutes. The mean creatinine at discharge in this series was 1.31 ± 0.31 mg/dl.

This technique is limited by the increasing difficulty in morbidly obese patients, limited working space, and, because it is extraperitoneal the theoretical risk of lymphocele remains as in OKT.

### Robotic transplant with vaginal insertion of graft

Both donor and recipient surgery was performed by Doumerc et al. via transvaginal access using an Alexis® (Applied Medical) retractor [25]. This method may be especially useful in multipara women. Only one case has been published so far, and a prospective study is currently underway to evaluate this technique.

## Current status and conclusions

The above results show that as it currently stands, RKT is a safe alternative to OKT with reduced postoperative pain, reduced analgesic requirements, similar graft function outcomes, and better cosmesis when compared to OKT. RKT is especially beneficial in obese patients. Even though the higher cost of surgery remains a concern, RKT has been adopted at multiple institutions around the world in recent years.

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# Minimally Invasive Surgery for Benign Prostate Disease: Laparoscopic and Robotic Techniques

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## Introduction

Benign prostatic hyperplasia (BPH) is one of the most common diagnoses in a majority of urologic practices. Although the treatment options for symptomatic bladder outlet obstruction have expanded dramatically over the past several decades, the simple prostatectomy remains the gold standard for complicated bladder outlet obstruction associated with a large prostate volume, generally greater than 80 g. Transurethral resection of the prostate (TURP) is a feasible option for the treatment of very large prostates, but this can lead to suboptimal results, and, especially for monopolar TURP, may predispose patients to post-transurethral resection syndrome [1]. It is also known that 12–15.5% of patients receiving TURP required further surgery, while only 1.8–4.5% of those treated with open surgery underwent reoperation within 8 years [2].

Simple prostatectomy is neither simple in technique nor indication and may have short- and long-term complications which are similar to and in some cases more clinically significant than those from radical prostatectomy. Simple prostatectomy is indicated for prostate glands of a volume that may far exceed those of the average prostate gland undergoing prostatectomy for prostate specific antigen (PSA)-identified prostate cancer. Men who undergo simple prostatectomy are on average older and carry more comorbidities than men undergoing radical prostatectomy. The advent of modern medical therapy for prostatic enlargement markedly changed the use of surgery for prostatic hypertrophy, including transurethral and open techniques. When open prostatectomy occurs in today's era, therefore, the patient has often had years of unsuccessful medical therapy, may have endured chronic urinary retention, along with the long-term effects of chronic bladder outlet obstruction. Open surgery in such men was classically associated with blood loss and a transfusion rate exceeding 25%, a prolonged hospital stay, wound healing, and incontinence [3]. Despite the success of the open prostatectomy, there are significant disadvantages, namely the need for an extraperitoneal incision, bleeding requiring transfusion, sphincteric, neurovascular bundle, or rectal injury, prolonged hospital stays, and increased catheterization time [4].

The modern era of minimally invasive surgery for BPH began several years and several hundred cases after the laparoscopic approach to prostate cancer was established. By 2005, groups with experience in robot-assisted laparoscopic prostatectomy (RALP) began adopting the approach to benign prostatic diseases, such as BPH [5]. The technique for BPH using laparoscopy and robotics is different enough from the approach for prostate cancer to warrant this chapter specifically devoted to the development, controversies, and potential future role of minimally invasive surgery in the management of benign prostatic disease.

## Historical context

Open prostatectomy was first performed via cystotomy in 1894 by Eugene Fuller and then popularized by Peter Freyer in 1900 and Robert Proust in the early 1910s. Hugh Hampton Young of Baltimore and Terrence Millin of Dublin, Ireland recognized that cystotomy may add undue morbidity to the procedure and often precluded visualization of the distal adenoma and sphincter [6]. Young proposed a perineal prostatectomy in 1904 to avoid cystotomy. Millin proposed a purely retropubic approach for more control over the prostatic apex during enucleation to avoid traction injury to the urethral sphincter, and more adequate prostatic exposure at the expense of bladder accessibility [2, 7]. The transvesical approach allows the

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urologist to treat concomitant bladder pathology via direct access to the bladder at the time of adenomectomy and may, therefore, be preferred over the retropubic approach when bladder calculi, large median prostatic lobes, or bladder diverticula are present [8]. Indications for prostatectomy include catheter-dependent urinary retention, bothersome lower urinary tract symptoms that is refractory to medical therapy, frequent urinary tract infections secondary to retention, severe hematuria secondary to prostatic bleeding, bladder calculi, and chronic kidney disease secondary to prostatic enlargement. Open simple prostatectomy may be preferred over TURP with prostates larger than 80 g because TURP was historically associated with morbidity and mortality rates of 55% and 6%, respectively, while the open prostatectomy had mortality rates of 3.3% [8, 9]. Additional indications for open surgery include concomitant surgically amenable bladder conditions, planned concomitant hernia repair, and patients in whom ankylotic or degenerative joint disease of the hip prevents the lithotomy position [2]. Today, mortality rates from both procedures approach 0%, an effect of medical optimization and clearance of most active urinary tract infections prior to elective surgery [2, 8, 10]. Furthermore, modern techniques, such as holmium laser enucleation of the prostate (HoLEP) and potassium titanyl phosphate crystal laser (KTP) have produced favorable results in large prostates and have further decreased the prevalence of open prostatectomy [11–13]. However, drawbacks to laser surgery for prostates >80 g include cost, steep learning curve, specialized equipment, prolonged urethral instrumentation with associated urethral complications (e.g. bladder neck contracture), and the need to morcellate laser-resected tissue free-floating in the bladder. Disadvantages of the open prostatectomy include need for extraperitoneal incision, bleeding requiring transfusion, sphincteric, neurovascular bundle, or rectal injury, prolonged hospital stays, and increased catheterization time [14].

The open surgical approach remained the gold standard for 100 years, the majority of subjects undergoing suprapubic approaches, followed by retropubic, and, least popular, the perineal prostatectomy, first performed by Young in October 1902. A major change came with the advent of laparoscopic radical prostatectomy, first performed by Schuessler in 1991, refined by Bertrand Guillonneau, Guy Vallencien, and Claude Abbou throughout the late 1990s. Mirandolino Mariano is generally regarded as the first surgeon to intentionally course along the retro-adenomatous plane to deliver obstructing adenomas and achieve a pure laparoscopic simple prostatectomy (LSP) of a 173 g prostate [15–17]. Reported advantages over the open approach included improved visualization of the adenoma and venous tamponade due to pneumoperitoneum during dissection and the avoidance of a major lower abdominal incision. Disadvantages were the mechanical challenge in laparoscopic manipulation of very large adenomas, steep learning curve, and complex suturing required in capsule plication and advancement of the bladder neck [4, 18]. Additional disadvantages were the lack of articulation of traditional laparoscopic instruments and the small working space for plicating, anastomotic, and hemostatic suture placement. LSP did, however, improve upon blood loss and length of stay compared to similar series of open prostatectomy and may be performed safely and effectively for the treatment of bladder outlet obstruction secondary to BPH. The advent of robotic surgery has largely supplanted straight laparoscopic techniques for benign disease as robotics has done for radical surgery as well [19].

The first radical robotic prostatectomy was performed by Binder et al. in Hanover in a collaborative effort that pioneered the use of the da Vinci® platform in 2000. This revolutionized an approach that is now performed three times more commonly than open surgery for prostatic cancer. Robotic prostatectomy greatly alleviated the burdens of laparoscopic techniques for cancer surgery and made the procedure more accessible. As applicability of robotics to cancer surgery grew, robotics was also considered for benign surgery. Sotelo et al. are regarded as the first group to have performed a simple prostatectomy robotically in 2008, after years of laparoscopic experience [5]. Robotic surgery offers the theoretical advantage over laparoscopy of a faster learning curve, especially regarding suture techniques, with the presumably shared benefits of laparoscopy, including less perioperative morbidity, improved visibility and precision, faster recovery, and ability to demonstrate technique and disseminate skills via the sharing of surgical videos on the internet and social media platforms. Disadvantages of the robotic approach include cost of the device, longer operative times, incomplete resections, and, when performed, the transperitoneal invasiveness of procedure [20].

## Technique

The technique of straight laparoscopic versus robotic simple prostatectomy is essentially the same, although there are minor differences in port placement, modifications that have occurred in the robotic era, and specific characteristics of robotics owing to its instrumentation. These are described in the text below.

### Port placement

Traditional multiple- and single-access laparoscopic techniques must all ensure an angle and depth of visualization and access to the surgical target, including the distal adenoma and pelvic floor. There are essentially no significant differences, therefore, in port placement for simple or radical laparoscopic prostatectomy. Traditional multiport access prostatectomy begins with placement of five trocars either extra- or transperitoneally [16, 21].

### The extraperitoneal approach

The extraperitoneal (EP) approach involves making a 12 mm infra-umbilical incision and dissecting down to the anterior rectus fascia. This fascia is incised transversely and the bellies of the recti abdomini are separated bluntly in the midline. Finger dissection inferiorly is carried out in the preperitoneal space, taking care to avoid incidental peritoneotomy by applying anterior pressure inferiorly when the posterior rectus fascia disappears below the arcuate line. A 12 mm balloon dissector with 10 mm visual optical channel is inserted and directed inferiorly toward the pubis and into the developed preperitoneal space. The balloon is slowly inflated under direct visualization. In the correct plane, the inferior epigastric vessels remain visible ventrally. The balloon is deflated and the balloon trocar is inserted, a 0° optical lens is inserted, and the space is filled with 10–15 mmHg of $CO_2$. Four additional trocars are inserted under direct vision with two 5 mm trocars close to the anterior superior iliac spines and two 10 mm trocars lateral to the rectus and 5–10 cm below the umbilicus. The proper space during development appears similar to that encountered in typical transperitoneal access. Joseph found that additional advantages of an extraperitoneal approach was the compartmentalization of any urinoma or hematoma, decreased rates of nonobstructive ileus, and decreased rates of early narcotic-dependent pain scores in those with ASA scores of 1–3 [22, 23].

### The transperitoneal approach

The transperitoneal (TP) approach enters the abdominal cavity directly via a midline or transverse supra-umbilical 10 mm incision. The rectus fascia is thinned with dissection using a Crile. A Veress needle is used to insufflate the abdomen through the fasciotomy and after pressures have reached 10 mmHg, the Veress is replaced with a 12 mm camera port. Visual inspection identifies the urachus and the medial umbilical ligaments, the pulsation of the iliac vessels and bladder in the midline. Placement of robotic ports occurs one handbreadth or 5–7 cm from the camera port in a line slightly inferior to a transverse perpendicular. Assistant 5 and 10 mm ports are placed in the right upper and right lower quadrant, respectively. Single-access devices allow for a camera port and two manipulator arm ports, typically through a midline para-umbilical incision but lateral 5 and 10 mm ports will be required for suction and assistant introduction of needle suture material during the case [24, 25].

## Planes of dissection

After successful insufflation of the space of Retzius in an EP approach, or release of the prevesical peritoneum in a TP approach, the arachnoid fibers and areolar tissue of the space are divided to identify the pubic rami. The endopelvic fascia is not punctured and the puboprostatic ligaments are not divided. Apparent in simple prostatectomy is the space in the deep pelvis occupied by the often markedly enlarged prostate not typically encountered in radical prostatectomy. Glands of >300 g may make even dissection to the symphysis pubis challenging and can be deferred. Manual inspection of the transition point between bladder and prostate is replaced by visual landmarks. Deformation of the "shoulders" of the prostate can be appreciated, but may be challenging with large prostates and without interrupting the fibers of the endopelvic fascia. Instead, careful manipulation of the bladder, filled with 200 ml NaCl, may be required to identify the transition to firm prostatic median and lateral lobes from the softer bladder wall. A Foley catheter, when withdrawn to the bladder neck, may not be visible owing to lateral deflection by the obstructing lobes. There is some variation as to the position of the cystotomy. Ideally, the camera will provide a view that is parallel with the planes of dissection and in larger prostates this may require a cystostomy far more cephalad than typically performed for radical prostatectomy.

Leslie et al. employed a "transvesical" approach in which a midline cystotomy is made at the dome of the bladder without development of the space of Retzius at all [26]. Alternatively, an appropriate transverse cystotomy is made that is large enough to expose the adenoma and preferably the ureteral orifices. The prostate must be elevated anteriorly away from the bladder neck and a large adenoma will be difficult to secure with ProGrasp® instruments alone. Instead, a CT-1 suture is often required through an untied figure of eight, secured with a large Weck clip which is then easier to manipulate with the #4 arm ProGrasp. It is not uncommon for the surgeon to make a cystotomy and be unable to identify the cephalad extent of markedly large median lobes with an intravesical component. The CT-1 suture technique will be helpful to bring the lobe up into cystotomy wound to better appreciate its extent.

Identification of the ureteral orifices (UOs) is critical but the use of methylene blue or indigo carmine is largely deferred owing to the obfuscation of landmarks by excreted dye. The operator needs to recall that it is not the prostate which one sees upon inspecting the deformed bladder neck but rather the mucosa and the muscularis of the bladder which are being elevated upwards by the hypertrophic adenomata deep to these tissues.

The critical incision is transverse and inferior to the UOs, allowing for enough remaining bladder neck tissue to be preserved for the plication step later in the case. Robotic "prostatectomists" see little difference between the initial transverse incision of a radical versus a simple case: the difference is what follows. Deep to the mucosa lie the fibers of the detrusor muscle and the soft tissue making up the posterior detrusor apron (PDA). Deep to the PDA lies Denonvilliers' fascia. In a radical prostatectomy, Denonvilliers' fascia is entered to identify and secure the structures of the ampulla, the vasa deferentia, and the seminal vesicles. In a simple prostatectomy, the fascia is not violated. The adenoma is anterior to the fascia and the surrounding prostatic capsule. A dissection too shallow in a radical prostatectomy may identify the potential plane between the true capsule and the adenoma. Similarly, a dissection too posterior (i.e. too deep) in a simple prostatectomy may enter Denonvilliers' fascia and bring into view the vasa deferentia. In the latter case, the operator needs to "course correct" without having to repair or reapproximate the bladder neck and PDA to the prostatic capsule but may need to do so later in the case. Transrectal ultrasound is generally not helpful in directing the operator into the correct plane posterior to the adenoma. In general, the operator proceeds parallel to the rectum once the bladder mucosa has been transversely divided. Anterior and upward traction by the fourth arm (and the retraction stitch secured by the arm or an assistant) will help tease or lead the surgeon into the correct plane posteriorly.

The operator will need to complete the transverse posterior dissection with a circumferential incision around the entirety of the lobes as they elevate the bladder neck. Bleeding in this region is often venous and may be difficult to prevent even with careful bipolar current and thermal energy because their lumens are held patent by surrounding fascial tissue. Once the posterior plane has been developed, the operator moves lateral to develop the similar planes of the lateral lobes. Robotically, or laparoscopically, the maneuver may be difficult as the lobes often occupy a large volume of the operative field. In an open case, the entirety of the prostatic adenomata may be removed en masse. In a laparoscopic case, each lobe may need to be removed separately, thus creating more working space for the subsequent lobes.

The anterior plane is then approached by incision across the 12 o'clock position following the dissection caudally. The operator should now consider that the dissection is to proceed toward the apex, slowly converging so that the posterior and anterior planes meet at the apical urethra. Capsule should surround the lateral aspects of the dissection at all points. For particularly large midline adenomas, the operator may perform a midline capsulotomy inferiorly from the bladder neck caudally. Bleeding through capsular venous branches would not be uncommon here and can be addressed or prevented by the placement of capsular plication sutures using 2-0 Vicryl on an CT-1 needle anteriorly. Care must be taken to avoid deep needle penetration which could enter the adenoma deep to it and prevent development of the dissection plane. Once the urethra is encountered distally, sharp dissection is performed across the urethra to encounter the Foley, which is withdrawn. The adenoma is resected free and placed into a specimen bag.

The operator should be able to appreciate the wide open bladder neck, a large space within the prostatic capsule, and the severed urethral tip in the deep pelvis. Unlike a radical prostatectomy, the preserved pelvic floor often prevents caudal retraction of the severed urethral margin and posterior plication or urethral withdrawal maneuvers are seldom necessary as one would consider prior to a Rocco maneuver. The next 30 minutes of surgical effort often predict the next week of clinical results. Although the field may not be dry, arterial bleeding is rare as the severed branches of the perforating capsular artery (a branch of the inferior vesicle artery) are generally in vasospasm at this point. Venous bleeding is often minimized by retraction of the PDA, the capsule, and the pneumoperitoneum. However, postoperative bleeding will be troublesome, problematic, and almost always clinically relevant, on a critical level, unless prophylactic hemostatic maneuvers are at this point performed. Such maneuvers, described below, will not only help minimize postoperative bleeding but also stabilize the bladder neck and posterior plate to facilitate neo-epithelialization of the created space.

## Retropubic approach

The limits of caudal dissection are the apex of the adenoma, which may be difficult to identify transvesically with large adenomata. An alternative approach is via the prostatic capsule itself. Sotelo et al. recommend the transverse incision just proximal to the prostatovesical junction to avoid disruption of the venous plexus along with resection of adenoma as separate lobes for improved visualization. Finger dissection through a modified suprapubic hand port to improve speed of resection and permit timely hemostatic control can be employed, although this becomes less relevant with operator experience. In an open case, a transverse capsulotomy incision is preferred to avoid caudal enlargement into the apical venous plexuses [18, 22]. Clavijo et al. reported their experience with so-called "intrafascial" prostatectomy for benign disease in prostates with an average size of 80 g. Here, a midline capsulotomy is made, resecting the entirety of the prostate with its adenoma while preserving the posterior fascia and structures of the ampulla, the neurovascular bundles, and the endopelvic fascia [27]. The lateral prostatic pedicles and anterior prostatic veins are first ligated with the latter suture serving as a traction suture during mobilization and dissection of the prostate. The endopelvic fascia is incised ventrally, medial to the puboprostatic ligaments, but high along the lateral prostate surface to allow the neurovascular bundles to be released. The incision is taken to the apex of the prostate and the dorsal vein complex is transected and suture ligated. The endopelvic fascia and neurovascular bundle are then peeled off the prostate using sharp dissection in a retrograde fashion. The urethra is transected as far proximally as dissection permits to maximize urethral length. The seminal vesicles are transected at the prostate base and the specimen removed. Remaining seminal vesicles and vas deferens are oversewn and closed. A vesicourethral anastomosis is performed in a manner similar to that of robotic prostatectomy. The residual anterior prostatic fascia is then sutured to the anterior bladder wall.

### Hemostatic maneuvers and bladder plication

Once the adenoma is removed, the pneumoperitoneum permits a clear field to inspect for arterial capsule bleeders, often amenable to fulguration. The temporary packing of the adenoma defect with Surgicel® (as one would with gauze in an open prostatectomy) is, in this case, logistically not feasible and may be deferred. Bleeders from the bladder neck are derived from the intravesical pedicle and require V-Loc™ hemostastic ligation or figure-of-eight surgical ligatures with a sliding, resorbable suture, such as a 3-0 Vicryl or Monocryl on an RB1 needle. The arterial bleeders are said to enter lateroposteriorly, best described as "at the 5- and 7-o'clock positions," although the operator is advised to oversew the entirety of the posterior intravesical fibers of the PDA as well. Next, plication of the bladder neck is performed to advance the mucosa of the bladder into the defect and further provide hemostatic force in a so-called "trigonization." Mucosal advancement is limited, however, by the attachment of the bladder neck to the laterally preserved prostatic capsule. Advancement can proceed far enough down the capsule to fix a mucosal flap to the posterior floor without undue tension. Coelho et al. have proposed a formal three-step urethrovesical anastomosis whereby a running van Velthoven anastomosis is created to the posterior urethra and the anterior prostatic capsule is sutured to the corresponding area of the bladder neck [28, 29].

### Closure

After simple prostatectomy and plication is completed, easy passage of a Foley catheter, traditionally a 22 Fr three-way catheter, must be demonstrated. Difficulty in passing a Foley will not improve after surgery. Better plication of the bladder neck or fixation of the posterior urethra to the posterior fascia with interrupted sutures may help. A suprapubic tube may be placed in addition to a transurethral Foley, in which case, both catheters can be smaller (e.g. 18 or 20 Fr), two-way catheters. A Jackson–Pratt or similar closed drain is placed near the anastomosis and emerges from the lateral inferior robotic ports. Extraction of the adenoma is best accomplished via surgical Endo Catch™ bags and removed by extending the midline supra-umbilical port through a transverse incision. Large adenomas may require longer incisions and when placed in the midline increases the risks of hernia. A transverse incision with rectus muscle preservation allowing for a running fascial closure anteriorly with 2-0 or 0-0 Vicryl on a UR-6 needle is better.

## Comparative studies

The literature surrounding minimally invasive simple prostatectomies generally suffers from a lack of long-term comparisons and "performance bias," in which the experience levels of the surgeons with their procedures are often not matched and controlled for. However, several attempts have been made in the literature to compare the minimally invasive techniques of robot-assisted simple prostatectomy (RASP) and LSP among each other and against open procedures. The results of such studies are outlined in Table 110.1 [24, 25, 30–33].

In general, open simple prostatectomy (OSP) has been associated with shorter operating room times. No significant difference in incidence or severity of complications or perioperative functional results have been noted. RASP and LSP are associated with shorter catheter duration, shorter bladder irrigation, and shorter hospital stay. In general, estimated blood loss (EBL) is similar between cohorts comparing OSP versus minimally invasive simple prostatectomy. Lucca et al. reported statistically significant lower EBLs in a minimally invasive simple prostatectomy group versus OSP group. Pavan et al. compared EBL among patients undergoing LSP (300 ml) versus OSP (250 ml). In the only study to date comparing LSP versus RASP, Pavan et al. found that both LSP and RASP offer similar operating room times, similar EBLs, and similar rates of major complications [32, 33].

**Table 110.1** Minimally invasive comparative studies.

| Author | Comparison | *N* | Method | Findings | Hospital stay | Foley time | Operative time | EBL |
|---|---|---|---|---|---|---|---|---|
| Baumert et al. (2006) [4] | Open vs. lap | 60 | Retrospective (30 lap vs. 30 open) for prostates >80 g | No significant difference in incidence or severity of complications or perioperative functional results | 5.1 (lap) vs. 8 (open) | 4 (lap) vs. 6.8 (open) | 115 min (lap) vs. 54 min (open) | 367 (lap) vs. 643 (open) |
| Porpiglia et al. (2006) [30] | Open vs. lap | 40 | Prospective RCT (20 vs. 20) | EP LSP provides results comparative to open, with the advantage of significantly lower blood loss | No difference (7.8 days lap vs. 7 days open) | No difference (6.3 days lap vs. 5.6 days open) | No difference (107 min lap vs. 95 min open) | 411 (lap) vs. 687 (open) ($P = 0.004$) |
| McCullough et al. (2009) [25] | Open vs. lap | 280 | Retrospective (96 lap vs. 184 open) | LSP associated with a longer operative time, shorter catheter duration, and shorter hospital stay. No difference in EBL between the cohorts | 6.3 (lap) vs. 7.7 (open) days ($P < 0.0001$) | 5.2 (lap) vs. 6.4 (open) days. ($P < 0.001$) | 95 min lap vs. 55 min open ($P < 0.0001$) | Similar EBL. Hemorrhage rates of 28% vs. 29% reported |
| Parsons et al. (2015) [31] | Open vs. MISP | 6220 | 6027 (OSP) vs. 193 (MISP) | Overall MISP and OSP showed no significant differences | No difference | Not reported | No difference | Not reported |
| Lucca et al. (2015) [32] | Open vs. MISP | 764 | Meta-analysis (27 studies with 764 total MISP) | MISP offers similar improvement in $Q_{max}$ and IPSS as OSP. Although it takes longer, it results in less blood loss and shorter hospital stay | WMD −1.6 days, $P = 0.02$ in favor of MISP | WMD −1.3 days, $P = 0.04$ in favor of MISP | WMD 37.8 min, $P < 0.0001$ in favor of open | WMD −187 ml, $P = 0.015$ in favor of MISP |
| Pavan et al. (2016) [33] | LSP vs. RASP | 319 | Retrospective review (189 lap paired to 130 robot) | Both LSP and RASP offer similar operative time, similar EBL, as well as similar rates of major complications. Age and BMI were found to be predictive of "trifecta" of surgery. "Trifecta" = combination of IPSS score <8, $Q_{max}$ >15 ml/s, and no perioperative complications | No difference (5 days vs. 5 days) | No difference (5 days vs. 5 days) | Similar OR time (120 min for LSP and 150 min for RASP) | Similar EBL (300 ml for LSP and 250 ml for RASP) |

LSP, laparoscopic simple prostatectomy; lap, laparoscopic; RASP, robot-assisted simple prostatectomy; MISP, minimally invasive simple prostatectomy; RCT, randomized controlled trial; OSP, open simple prostatectomy; EP, extraperitoneal; $Q_{max}$, maximal flow rate; IPSS, International Prostate Symptom Score; EBL, estimated blood loss; BMI, body mass index; WMD, weight mean difference.

## Expected complications and preventative measures

Patients who require simple prostatectomy are often older, heavier, and have more comorbidities than men undergoing radical prostatectomy who, presumably, do so because they have a >10 year life span. Medical evaluation for simple prostatectomy, therefore, may require a more extensive workup to identify any occult cardiac, pulmonary, or vascular disease that could complicate the intra- and perioperative course. Steep Trendelenburg positioning is generally tolerated by most men undergoing radical prostatectomy, whereas the older, more ill male undergoing simple prostatectomy may not tolerate Trendelenburg. Importantly, patients undergoing surgical planning for BPH should be screened for prostate cancer as rates of incidental prostate cancer can be found in 6–10% of specimens in larger series and may influence and in some cases limit postoperative therapeutic options [34–46]. Postoperative hemorrhage after open prostatectomy is generally ascribed to bleeding from the bladder neck. With its improved visualization, surgical ligation of suspected bleeders with robotic techniques may be more effective than through open approaches, but postoperative bleeding after robotic surgery is still prevalent (Table 110.2). Most report a minimal requirement of continuous bladder irrigation after robotic simple prostatectomy but one must be prepared for traditional maneuvers should gross hematuria become problematic. A secure posterior bladder neck plication, therefore, is critical to facilitate the easy passage of a Foley catheter into the bladder itself without undermining a poorly repaired PDA.

## Conclusions

Simple prostatectomy is a safe, effective, and well-tolerated procedure for the treatment of BPH and may be performed via several approaches. In the new era of healthcare, costs are becoming an increasingly important part of decision-making. The costs of investing in new technology or traveling to distant centers must be weighed against perceived and real benefits among the various technologies. Robotic simple prostatectomy offers the advantage of decreasing hospital stay and catheter time while providing outcomes consistent with those demonstrated by OSP of improved lower urinary tract symptoms and adequate bladder emptying.

See accompanying Video 110.1.

**Table 110.2** Hemostatic maneuvers.

| Author | Approach | Maneuver |
|---|---|---|
| Presman and Rolnick (1949) [47] | Transvesical | Pack the prostatic fossa with gauze for 5 min or more after prostate enucleation |
| O'Conor(1970) [48],<br>Magri (1975) [49] | Transvesical | Direct suture of bleeding vessels in prostatic bed, vesicourethroplasy with full-thickness bladder wall flaps to cover the denuded prostate |
| Hryntschak (Beck et al. 1970) [50],<br>Witherington (1974) [51] | Transvesical | Plication of the prostatic fossa: 2 separate 1-0 chromic sutures on GU needle used in running fashion from adjacent to bladder neck to the distal prostate just above verumontanum. Tie together in middle |
| Shaikh and Malement (1971) [52] | Transvesical | Bladder neck partition sutures: 1-0 Nylon pursestring suture around bladder neck starting from posterior margin of bladder neck (mucosa and muscle) and carried anteriorly to the midline where they exit through the entire thickness of bladder. Catheter placed in bladder and bladder closed carefully without involving pursestring sutures. Partition sutures brought out through abdominal wall. Tie around a gauze pad on abdominal wall. May remove on first postoperative day |
| Walsh and Oesterling (1990) [41] | Retropubic | Suture dorsal vein complex distally with a mass clamp ligature. Incise the puboprostatic ligaments and suture lateral pedicles at the bladder neck |
| Gregoir (1969) [53] | Retropubic | Place a suture at the distal prostatic apex through the adenoma to control all deep dorsal vein bleeding as well as ascending branches of the dorsal penile artery |
| Amen-Palma and Artega (2001) [54] | Retropubic | Place lateral pedicle and dorsal vein complex sutures only after prostate enucleation |

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# 111

# Laparoscopic Adrenalectomy

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## Development, indication, and anatomy of laparoscopic adrenalectomy

### Development of laparoscopic adrenalectomy and its efficacy

The adrenal grands are located deep in the trunk of the body. Therefore, large abdominal incisions are necessary to approach the adrenal by open surgery. Following the development of laparoscopic nephrectomy in 1990, several urologists and endocrine surgeons conceived of the idea of laparoscopic adrenalectomy (LA). The first LA was performed by Go et al. on January 17, 1992 in Japan [1], and the first publication was by Higashihara et al. in July, 1992 [2], followed by Gagner et al. in November, 1992 [3], who performed their first case in March, 1992. After these pioneers developed the technique independently, LA was became widespread as one of the most efficient laparoscopic surgeries [4, 5]. The small size of the majority of adrenal tumors accounts for the usefulness of the laparoscopic approach.

Nowadays, almost all clinical guidelines strongly recommend laparoscopic surgery as the gold standard approach for small benign adrenal tumors, including pheochromocytomas, if the tumor has not invaded the surrounding tissues [6–8]. Even though there is no high-level supportive evidence such as prospective randomized studies comparing laparoscopic and open adrenalectomies, it is generally believed that LA is associated with less postoperative pain, shorter hospital stay, earlier recovery, and similar long-term outcomes compared with open surgery [6–8].

### Indications for laparoscopic adrenalectomy

Indications for laparoscopic surgery for adrenal tumors vary depending on the surgeon's experience. In particular, large tumors, malignant tumors, and pheochromocytomas make laparoscopy more challenging. According to the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) guidelines, a tumor size ≥7.5 cm has been shown to be an independent risk factor for longer operating times, more blood loss, longer hospital stay, and a higher conversion rate to open surgery [6]. With regard to malignant tumors, the European Society for Medical Oncology (ESMO) clinical practice guidelines for adrenal cancer recommend LA as a safe and effective procedure for pheochromocytoma and for a select group of patients with small adrenocortical cancers (ACCs) (<8 cm) without preoperative evidence of invasiveness [9]. Metastatic adrenal tumors are also candidates for laparoscopic surgery when not invaded and not too large. A matched controlled study demonstrated similar clinical outcomes including capsular injury rate and cancer-specific survival with a median follow-up of 39.3 months for laparoscopic and open adrenalectomy for metastatectomies or ACC less than 10 cm diameter [10]. Most importantly, standard principles of oncologic surgical treatment should be strictly respected [9], and open conversion is warranted when difficult dissection is encountered due to tumor adhesion or invasion or when enlarged lymph nodes are seen. The Endocrine Society clinical practice guidelines for pheochromocytoma and paraganglioma recommend LA for most adrenal pheochromocytomas, but recommend open resection for tumors larger than 6 cm or for invasive pheochromocytomas [11]. It is recommended that paragangliomas be resected by open surgery because of the high incidence

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of malignancy, but laparoscopic resection can be performed for small, noninvasive paragangliomas in surgically favorable locations [11]. Again, the surgical indication depends on the surgeon's experience and the characteristics of the tumor.

The indications for surgical dissection of incidentally identified nonfunctioning adrenal tumors depends on the size of the tumor, increase in its size during follow-up, and the radiological findings. The Canadian Urological Association's guidelines recommend considering surgical excision for tumors more than 4 cm in diameter; this size has been shown to provide the best sensitivity (93%) in predicting malignant processes [7]. However, this marker has low specificity (42%) due to the low prevalence of ACC [7].

### Perioperative care

A full endocrine workup is mandatory for all adrenal tumors before surgery, even when there is apparent hormonal activity such as in patients with Cushing syndrome or pheochromocytoma. Some tumors simultaneously excrete more than one hormone, such as catecholamine plus cortisol or aldosterone plus cortisol. In these cases, appropriate perioperative management is required to prevent postoperative adrenal insufficiency [12]. In the case of a pheochromocytoma, preoperative treatment with alpha blocker administration for at least 7–14 days, a high-sodium diet, and fluid intake are required to normalize hypertension and to reverse catecholamine-induced blood volume contraction [11]. These management techniques are important to prevent severe hypotension after tumor removal.

Postoperatively, intensive monitoring is mandatory for pheochromocytoma cases to prevent hypotension and hypoglycemia. For cortisol-producing tumors, appropriate cortisol supplementation is required with close follow-up by endocrinologists.

### Vascular anatomy of the adrenals

Understanding the vascular anatomy of the adrenal is important for conducting safe LA, especially for large or highly vascularized tumors such as pheochromocytomas (Figure 111.1). Arterial supply to the adrenal comes from the aorta (the middle adrenal arteries), the renal artery (the inferior adrenal artery), and the inferior phrenic artery (the superior adrenal artery) [13]. All adrenal arteries are small in diameter and can be severed with sealing devices or ultrasonic scalpels without clips.

The left main adrenal vein comes from the anterior surface of the left adrenal, and inflows into the left renal vein. A communicating branch between the left inferior phrenic vein and the left adrenal vein is present in 34% of people according to a cadaveric study [14]. The left superior adrenal veins run into the left inferior phrenic vein, and the inferior left adrenal vein, which has a small diameter, runs into the renal vein just distal to the left adrenal vein. The right adrenal vein is very short, comes from the junction of the hepatic area and the area related to the inferior vena cava, and inflows into the posterolateral aspect of the vena cava. The right superior adrenal veins run into the right inferior phrenic vein, and the right inferior adrenal vein runs into the right renal vein. Several small veins from the adrenal run into the right renal capsular veins in both sides. A retrospective study of LA showed that a significant number of patients (13%) had variant venous anatomy such as no main adrenal vein, two adrenal veins, or drainage to the hepatic vein [15]. Because of the variations in venous anatomy, severing the adrenal vein does not result in the occlusion of all adrenal venous returns in a majority of patients. However, in the case of large tumors having a large blood supply, occlusion of the adrenal vein, the main venous return, may result in congestion of the adrenal and bleeding from the tumor surface. It is recommended that the main adrenal vein be occluded using clips, although it can be severed using electrosealing devices.

## Approaches to the adrenal and complications of laparoscopic adrenalectomy

### Laparoscopic approaches to the adrenal

LA was first developed using a transperitoneal approach [1–3], and the use of a retroperitoneal approach started later. There are anterior and lateral variants of the transperitoneal approach, and lateral and posterior variants of the retroperitoneal approach (Figure 111.2). The retroperitoneal approach was first reported in 1994 using the lateral approach in the lateral decubitus position [16]. The posterior retroperitoneal approach was first performed in 1994 [17]. It is performed with the patient prone, and is suitable for bilateral diseases. For large tumors, transperitoneal lateral approaches are the most widely used, whereas small tumors less than 5 cm in diameter are treated with various approaches. The transperitoneal anterior approach, where the spleen is not moved medially, is seldom used now for the left adrenals; however, it is still used for small right adrenal masses where the liver is not moved.

Comparing transperitoneal and retroperitoneal LA in a case–control study, longer operative duration and fewer perioperative complications were reported in retroperitoneal LA [18]. However, no differences between the two approaches were found in another study [19].

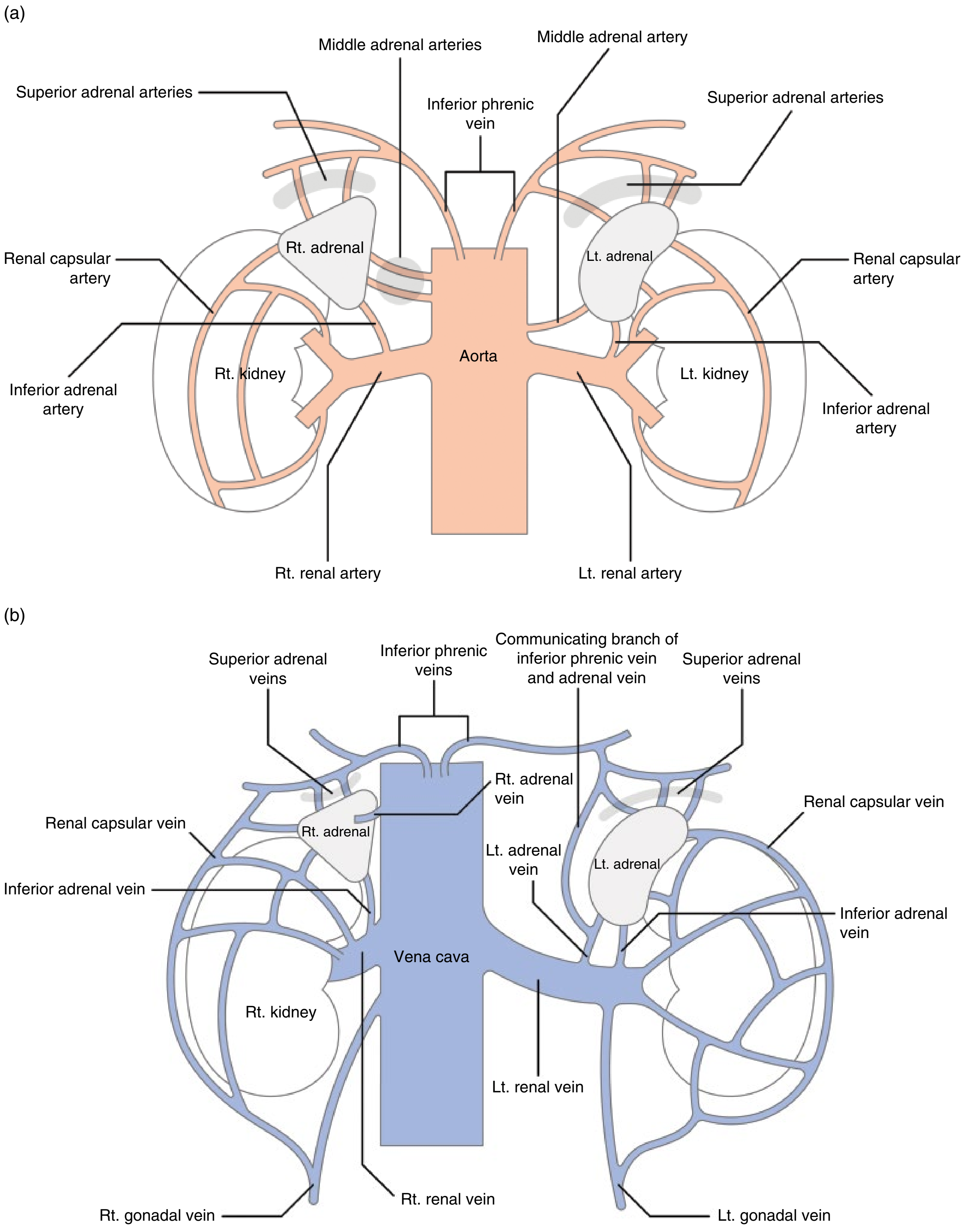
(a)
Middle adrenal arteries
Middle adrenal artery
Superior adrenal arteries
Inferior phrenic vein
Superior adrenal arteries
Renal capsular artery
Rt. adrenal
Lt. adrenal
Renal capsular artery
Aorta
Rt. kidney
Lt. kidney
Inferior adrenal artery
Inferior adrenal artery
Rt. renal artery
Lt. renal artery
(b)
Superior adrenal veins
Inferior phrenic veins
Communicating branch of inferior phrenic vein and adrenal vein
Superior adrenal veins
Rt. adrenal vein
Renal capsular vein
Renal capsular vein
Rt. adrenal
Lt. adrenal vein
Lt. adrenal
Inferior adrenal vein
Inferior adrenal vein
Vena cava
Rt. kidney
Lt. renal vein
Rt. gonadal vein
Rt. renal vein
Lt. gonadal vein

**Figure 111.1** Adrenal vascular anatomy. (a) Arteries; (b) veins.

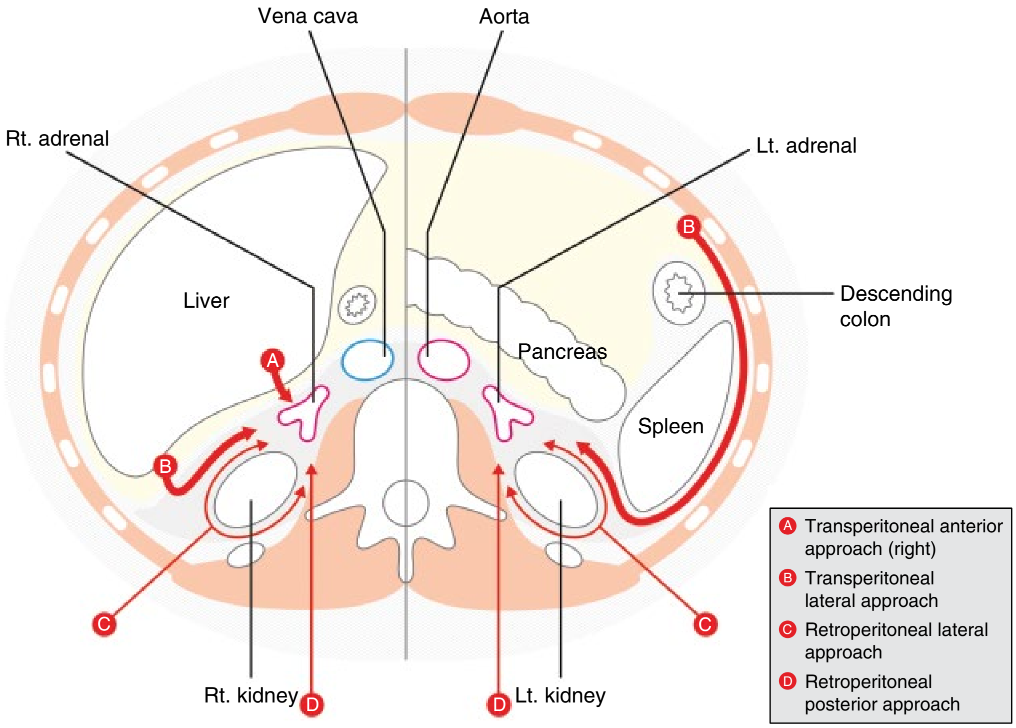
Vena cava
Aorta
Rt. adrenal
Lt. adrenal
Liver
Descending colon
Pancreas
Spleen
Rt. kidney
Lt. kidney
A
B
C
D
Ⓐ Transperitoneal anterior approach (right)
Ⓑ Transperitoneal lateral approach
Ⓒ Retroperitoneal lateral approach
Ⓓ Retroperitoneal posterior approach

**Figure 111.2** Laparoscopic approaches to the adrenal.

Two prospective randomized studies compared transperitoneal LA and lateral retroperitoneal LA [20, 21]. Both demonstrated similar operative times, estimated blood loss, postoperative analgesic use, hospital stay, and complication rates; however, convalescence was shorter with the retroperitoneal approach than the transperitoneal approach, probably due to less peritoneal irritability postoperatively. According to another recent randomized controlled trial comparing posterior retroperitoneal LA and transperitoneal LA, retroperitoneal LA is superior in operative duration, bleeding, postoperative pain, recovery from surgery, and postoperative hernia [22]. A recent report noted that outcomes of retroperitoneal LA for obese patients are the same as those of transperitoneal LA [23]. Retroperitoneal LA can be performed for patients with larger adrenal tumors [24].

Compared to the retroperitoneal approaches, the transperitoneal approach makes it easier to understand surgical anatomy and may be suitable for less experienced surgeons. It is recommended that the approach should be selected based on the condition of the patient, the characteristics of tumor and the surgeon's experience [8].

## Complications of laparoscopic adrenalectomy

Incidence of complications and open conversion depends on the indication and the surgeon's experience. It is reported that average blood loss, open conversion rate, and complication rate were 81 ml, 2%, and 8.9%, respectively [5]. Blood transfusions and organ injuries were both less than 5% [5]. Liver injury possibly occurs by retraction or during adrenal dissection on the right side. Hemostasis is usually achieved by coagulation by energy devices and hemostatic sheets. The spleen is so fragile that massive injury sometimes requires splenectomy. Unrecognized injury of the pancreas may result in pancreatitis (pancreatic fistula) in early postoperative days. Pneumothorax by diaphragm injury is recognized as a paradoxical movement of diaphragm. Sutured closure is required.

## Special concerns in laparoscopic adrenalectomy

Avoiding capsular injury during adrenal surgery is very important for all adrenal surgeries. This is especially true for cortical cancers, metastatic tumors, and pheochromocytomas that have more than a 10% incidence of malignancy. Even if preoperative diagnosis is adrenocortical adenoma, some could be ACCs, especially when the tumor is more than 4 cm in diameter. Only aldosterone-producing adenomas (APAs) have a very low incidence of malignancy. The incidence of capsular injury is relatively common during laparoscopic adrenalectomies [25], and local recurrences of pheochromocytoma after laparoscopic surgery are reported in the literature [26].

## Partial adrenalectomy

It is generally accepted that unilateral total adrenalectomy is the standard for adrenal tumors when the patient has a normal contralateral adrenal gland. Some authors have recommended partial adrenalectomy for unilateral APAs to achieve better adrenal function postoperatively [27]. However, it is reported that 27% of APAs have multiple microadenomas in the adrenal and 2 of 29 cases had persistent aldosterone production after partial adrenalectomy [28]. For bilateral tumors such as pheochromocytomas in multiple endocrine neoplasia type 2 (MEN2) cases, tumors arising after contralateral adrenalectomy, or hereditary pheochromocytomas, partial adrenalectomy is a treatment option. It was reported that Addisonian crisis occurred in 35% of cases and the mortality rate was 3% after bilateral adrenalectomies [29]. To prevent permanent postoperative cortisol substitution while preserving sufficient adrenal function, at least a third of the unilateral adrenal tissue should be preserved [30]. Because the incidence of malignant pheochromocytoma is less than 5% in MEN2 patients, less than 10% in von Hippel Lindau disease (VHL) patients, and 34–70% in succinate dehydrogenase B (SDHB) mutation patients, MEN2 and VHL are good candidates for partial adrenalectomy for pheochromocytoma [30]. The recurrence rate of pheochromocytoma in MEN2 patients after partial adrenalectomy in the ipsilateral adrenal was reported to be 3% (4/153 adrenals) after a median follow-up period of 10 years [30].

To preserve adrenal function in partial adrenalectomy, it is important to keep vascular supply to the residual adrenal tissue. Separation of the adrenal from the surrounding tissue should be minimized to preserve arterial supply and venous return. Keeping the main adrenal vein intact is not required to preserve adrenal function in partial adrenalectomy [31]. To control bleeding from the cut surface of the adrenal gland, bipolar or soft coagulation with or without hemostatic agents is effective in a majority of cases.

## Surgical techniques for laparoscopic adrenalectomy: transperitoneal approach

### Equipment

The instruments used in LA are highly dependent upon the surgeon's preference, surgeon's surgical style, or institutional equipment available.

- *Basic set*: These instruments may include: ports, graspers (e.g. Maryland type), right-angle dissector, scissors, monopolar generator, bipolar generator, suction–irrigation, liver retractor, hemoclips, gauze for laparoscopy.
- *Optional*: Sealing device, ultrasound scalpel, Veress needle, vascular-load endoscopic stapling device, and other instruments.

### Patient positioning

The patient is placed in the right or left kidney position (i.e. left or right lateral decubitus position, respectively). The authors prefer that the patient is rotated approximately 70–80° for the anterior approach, and full lateral decubitus position for the lateral approach. All pressure points should be padded to prevent nerve compression injuries. The surgeon, laparoscopist, and assistant usually stand on the patient's abdominal side. In right-sided adrenalectomy, the assistant is usually required to retract the liver.

### Right side

#### Anatomic considerations

The anatomy around the adrenal gland differs slightly between the right and left sides, and the surgical approach should be chosen with consideration of these differences. On the right side, the adrenal gland is located next to the inferior vena cava (IVC). After kidney position is taken, the duodenum moves medially. The anatomically important points to consider is the relationship between the adrenal gland and IVC or liver. The medial side of the adrenal gland is sometimes hidden behind the IVC. The upper side of the adrenal gland is placed behind the liver and, importantly, the upper part of the normal adrenal gland is sometimes physiologically fused with the normal liver tissue without a distinct border (adrenohepatic fusion) [32, 33].

#### Surgical technique

##### *Port position*

Port position is a very important issue in laparoscopic surgery, but it depends on the body shape of the patient and the surgeon's preference. The author places four ports during transperitoneal right-sided adrenalectomy: a 12 mm camera port, a 10 mm port for the right hand, a 5 mm port for the left hand, and a 3–5 mm port for liver retraction (Figure 111.3). The first port is placed by the Veress needle technique or open Hasson technique. The author prefers the open technique, in which the first port is placed slightly lateral to the midclavicular line and two fingerwidths away from the costal edge. Surgeons should be aware that the body surface landmarks (e.g. the umbilicus) are usually shifted to the

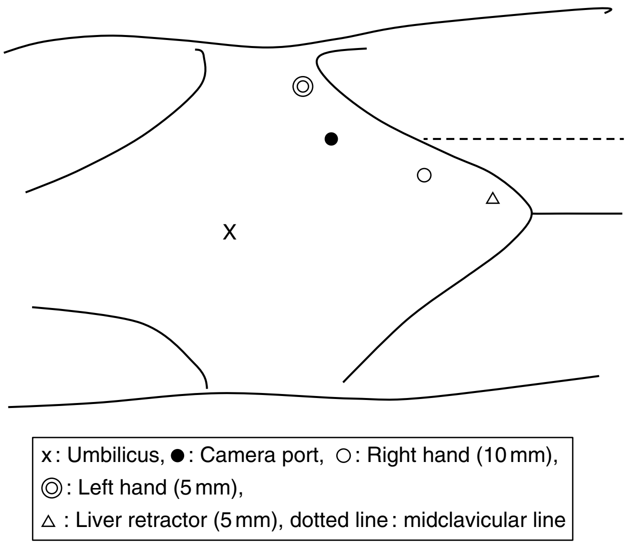
X
x : Umbilicus, ● : Camera port, ○ : Right hand (10 mm),
◎ : Left hand (5 mm),
△ : Liver retractor (5 mm), dotted line : midclavicular line

**Figure 111.3** Port position for transperitoneal right laparoscopic adrenalectomy.

left side in the right kidney position. The precise positions of the other ports are determined after the insufflation. The right- and left-hand working ports are usually placed parallel to and two fingerwidths from the costal edge. The left-hand port (5 mm) is placed four fingerwidths (6–8 cm) caudolaterally from the camera port, and the right-hand port (10 mm) is placed four fingerwidths (6–8 cm) medial-cephalad from the camera port. The port for the liver retraction (5 mm) is placed near the xiphoid process after confirming the liver size and falciform ligament. The ports are placed relatively lateral in the lateral approach compared to the anterior approach.

***Liver retraction and peritoneal incision***

The surgeons should first observe the surgical field in the upper abdominal quadrant. In some cases, the intestine is adhered to the abdominal wall or the peritoneum is adhered to the posterior surface of the liver. If the lateral side of the liver is attached to the diaphragm, a peritoneal incision is required to safely retract the liver in the medial-cephalad direction. After retracting the liver, the IVC may serve as a good landmark. Even in patients with a large amount of fatty tissue, the IVC may be recognized at the inferior edge of the liver. The peritoneum is incised at the lateral edge of the IVC from the upper edge of the right renal vein to the inferior edge of the liver (Figure 111.4, line b). The surgeon should take care to prevent duodenal injuries. The peritoneal incision is extended laterally along the inferior edge of the liver (Figure 111.4, line a). This incision may be done earlier, when retracting the liver.

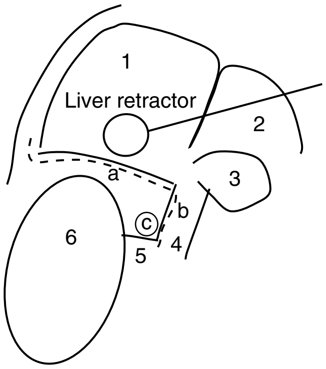

**Figure 111.4** Peritoneal incision in the transperitoneal anterior laparoscopic adrenalectomy. 1, Right lobe of liver; 2, left lobe of liver; 3, gall bladder; 4, inferior vena cava; 5, right renal vein; 6, kidney. Lines a and b, and circle c are explained in the text.

***Dissection around the adrenal gland***

The dissection is started at the median and inferior borders of the adrenal gland. To prevent injury to the adrenal gland, the dissection should be performed on the right-side surface of the IVC and the right kidney surface, not the surface of the adrenal gland. The author first dissects the fatty tissue in a wide and shallow manner, then more deeply dissects the fatty tissue at the junction of the IVC and renal vein (cephalad edge) to reach the surface of the psoas muscle (Figure 111.4, circle c). Small arteries and veins are located in this region, and the apical branch of the right renal artery is sometimes observed. Once the psoas surface is reached, the adrenal gland is easily elevated anteriorly, and the layer between the adrenal gland and psoas is usually avascular. Dissection between the adrenal gland and kidney is usually easily performed. The dissection between the adrenal gland and IVC progress cephalad, and the adrenal vein is then identified. Importantly, the surgeon should not completely dissect the lateral side (right side) of the adrenal gland before median dissection because the lateral retraction becomes difficult. This facilitates dissection between the IVC and median side of the adrenal gland and dissection and clipping of the adrenal vein, which can be elongated.

After dividing the adrenal vein, dissection progresses to the superior border of the adrenal gland. The adrenal gland and liver are sometimes tightly adhered, and histopathological examination shows intermingling of parenchymal cells (infiltration through the fibrous capsules). When the tumor is attached to the liver, the adrenal gland may be removed with the liver. Extensive coagulation and/or a hemostasis sheet is useful. The lateral side (right side) of the adrenal gland is easily dissected. After the adrenal gland is completely free, it is retrieved with a specimen bag.

## Left side

### Anatomic considerations

The left adrenal gland is located next to the aorta and right renal vein. The pancreas covers the anterior surface of the adrenal gland, and median replacement of the pancreas is mandatory. Other than its association with the pancreas, the left adrenal gland is usually isolated by surrounding fatty tissue.

### Surgical technique

#### *Port position*

The port position is usually the mirror image to that of right-sided adrenalectomy except for the liver retraction port. The authors use three ports: a camera port, right-hand working port (10 mm), and left-hand working port (5 mm).

#### *Mobilization of the spleen and descending colon*

The peritoneal incision is started at the splenic flexure of the colon. It is important to incise the peritoneum close to the colon; if the incision is too lateral, the left kidney moves medially and the dissection around the adrenal gland becomes difficult. The peritoneal incision progresses to the lower pole of the left kidney in the caudal and lateral attachment of the spleen to the cardiac notch of the stomach. Using this incision, the descending colon and spleen are mobilized medially. The spleen is very fragile, and care should be taken during its dissection. Injury to the spleen sometimes necessitates splenectomy.

#### *Dissection around the adrenal gland*

Dissection of the pancreas tail should also be carefully performed to prevent pancreatic injury, which is sometimes hard to recognize. Postoperative pancreatic fistulas may be severe. Dissection is usually performed between the Gerota's fascia and mesocolon. The authors sometimes dissect the pancreas from inside Gerota's fascia. This facilitates dissection of the left renal vein, which is usually recognized by the venous waveform, and the cephalad surface of the left renal vein is dissected. The left adrenal vein is easily identified. The dissection and ligation of the left adrenal vein is easier than that of the right side. After ligation of the left adrenal vein, the fatty tissue between the left renal vein and adrenal gland is dissected until the psoas muscle (or diaphragm) is reached. Upon reaching the psoas surface, the layer between the adrenal gland and psoas is usually avascular, and the adrenal gland is easily elevated anteriorly. The median and lateral sides of the left adrenal gland are dissected in the cephalad direction. The authors prefer to start from the median side. If the lateral attachment is divided, the adrenal gland moves medially and dissection of the medial side becomes difficult. After the adrenal gland is completely free, it is retrieved with a specimen bag.

# Surgical technique for laparoscopic adrenalectomy: retroperitoneal lateral approach

## Approach considerations

The retroperitoneal approach does not require entry into the peritoneal cavity, and thereby avoids potential injury to the intraperitoneal organs. Laparoscopic retroperitoneal adrenalectomy (retroperitoneal LA) can be performed for patients with a history of abdominal surgery. This approach can be indicated for younger patients who may have to undergo abdominal surgery in the future because peritoneal adhesions can be avoided. Retroperitoneal LA is reported to be a safe and feasible procedure for small benign adrenal tumors, as well as paragangliomas, in retrospective cohorts [34, 35]. However, the working space of this approach to manipulate forceps is narrower than that of the transperitoneal approach. For this reason, retroperitoneal LA is reported to be unsuitable for patients with large adrenal tumors. It also takes a longer time to learn this procedure for many inexperienced surgeons.

There are two approaches to retroperitoneal LA: the lateral flank approach and the posterior lumbar approach [16, 17]. In the latter, patients are placed in the prone position, with their head lifted up, allowing direct access to the central adrenal vein before separating the gland from perinephric fat tissue. However, because this approach is only used by experienced surgeons in a few centers, this chapter mainly describes the lateral flank approach.

## Patient positioning

In retroperitoneal LA with the lateral approach, the patients are placed in the full lateral decubitus position and secured in the standard manner. As necessary, the jackknife position is useful to extend the distance between trocars to manipulate forceps and scissors in the limited working space. The working space provided by the lateral flank approach is not enough to manipulate a large tumor [3]. The surgeon faces the back of the patient, the scopist stands on the same side, and the assistant stands on the opposite side.

## Surgical technique

### Port position

Port placement for retroperitoneal LA is shown in Figure 111.5. A skin incision (15–20 mm) is made at the midaxillary line above the iliac crest. The external and internal abdominal oblique muscles and the transverse abdominal muscle are expanded using surgical retraction

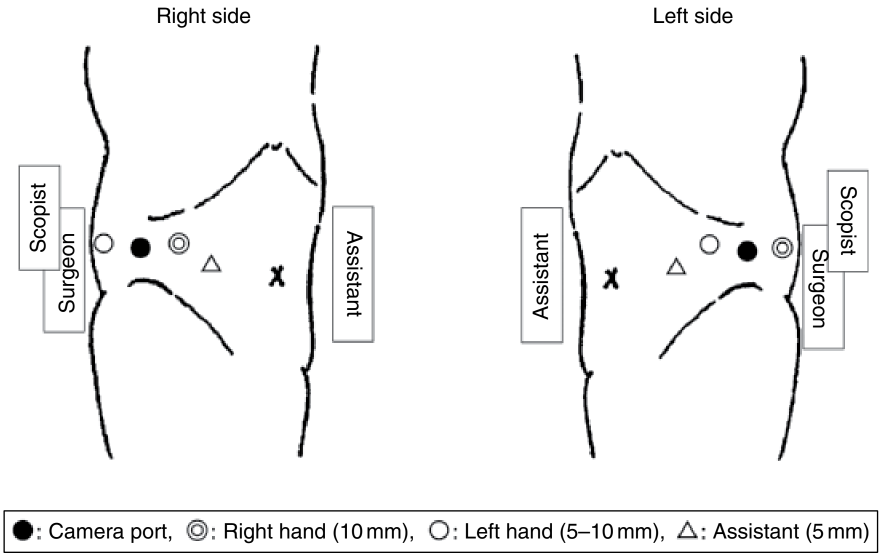
Right side
Left side
Scopist
Surgeon
Assistant
x
●: Camera port, ◎: Right hand (10 mm), ○: Left hand (5–10 mm), △: Assistant (5 mm)

**Figure 111.5** Port sites for the retroperitoneal lateral approach.

hooks. After the incision is deepened to the retroperitoneal space, the posterior perinephric space is developed using gentle digital dissection. The costal and iliac bones can be fingered at this time. To develop adequate working space, a balloon dilator can be used to expand the space outside the posterior lamina of Gerota's fascia. The working space is expanded while observing the retroperitoneal cavity by an endoscope through the balloon. A 10/12 mm trocar for an endoscope port is inserted, and the posterior perinephric space (outside Gerota's fascia) is expanded with $CO_2$ gas insufflation at a pressure of 10 mmHg.

The endoscope is inserted, and the second trocar (10/12 mm) is inserted at the posterior axillary line. The third trocar (10/12 mm, 5 mm is useful for experienced surgeons) is inserted outside the peritoneal reflection at the anterior axillary line under direct endoscopic vision. An additional trocar (5 mm) if needed may be placed above the iliac crest to retract the kidney.

#### Making working space in the retroperitoneal space

After the insertion of all trocars, the insufflation pressure is lowered. In obese patients, the flank pad might be removed out of the body to facilitate intraoperative manipulation. The posterior lamina of Gerota's fascia is incised widely along the attachment of the fascia to the psoas muscle to the origin of the diaphragm and separated from the iliopsoas muscle with careful attention to protection of the peritoneum from injury. The working space is more expanded by this manipulation. Then, further separating Gerota's fascia from the peritoneum allows identification of the conically shaped fat between the peritoneum and the diaphragm. If possible, it is better to separate Gerota's fascia from the peritoneum near the renal hilus. Gerota's fascia is incised, and the perinephric fat is dissected free from the diaphragm and the psoas muscle. After perinephric fat is separated from the peritoneum, the adrenal gland and the kidney become apparent.

#### Dissection around the adrenal gland

Perinephric fat is dissected to separate the adrenal gland from the kidney, and, if necessary, the upper pole of the kidney should be obvious. It is important not to expose the adrenal gland and tumor. The procedure should be to remove a loaf of adipose tissue surrounding the gland. A peritoneal injury would lead to severe difficulty in manipulating forces due to retroperitoneal working space contraction. On this occasion, holding up the peritoneal membrane with forceps through the additional trocar at the subcostal region is needed to expand the working space. Adipose tissue, including the gland, is separated from perinephric fat. If necessary, holding down the upper pole of the kidney with forceps through the additional trocar to the caudal side facilitates adrenalectomy. Small vessels excluding central veins can be ligated using an ultrasonically activated scalpel or a vessel-sealing device.

### Left side

The left renal vein is exposed and the adrenal vein is identified as an ascending branch of the renal vein. After securing the adrenal vein with three clips, the vein can be dissected keeping two clips secured in the central side of the vein. The inferior phrenic vein often communicates with the adrenal vein; ligation of the inferior phrenic vein is needed in such cases. The gland with adipose tissue is separated completely from perinephric fat and is bagged by a specimen retrieval bag through the second trocar.

After repositioning the endoscope through the third trocar, the bag is retrieved through the first trocar with forceps. If the gland and tumor are large, incision of the skin is needed to remove the bag from the body. Again, the endoscope is put through the first trocar to check for hemorrhage. If it is necessary to achieve adequate control of a hemorrhage, bipolar forceps and/or blood derivatives containing fibrin may be applied.

### Right side

Access to the right adrenal vein from the posterior or inferior-caudal side of the gland is feasible to separate the gland from the vena cava. Careful manipulation of the forceps is required because the right adrenal vein is short. When the right adrenal vein has a common vessel with the short hepatic vein, adequate exposure of the adrenal vein is necessary for ligation. After securing the adrenal vein with three clips, the vein can be dissected with two clips secured in the central side of the vein.

If it is not enough to separate the gland from the upper pole of the kidney, there is a risk of injuring the lower pole of the gland. The whole gland with adipose tissue is separated completely from perinephric fat and the subhepatic surface, and then it is bagged with a tissue retrieval bag. When the gland adheres firmly to the subhepatic surface, it will be necessary to resect the hepatic surface to separate the gland. When hemorrhage from the hepatic surface is difficult to control, covering it with a blood derivative containing fibrin can often be helpful.

## Laparoendoscopic single-site adrenalectomy

### History of laparoendoscopic single-site adrenalectomy

Since the first report of LA in 1992 [2, 3], this minimally invasive surgery to resect adrenal lesions has increased and spread widely. LA has been shown to be superior to conventional open adrenalectomy as its safety improved and morbidity decreased. Therefore, LA is now recognized as the gold standard procedure for the surgical resection of most adrenal tumors. Innovative techniques are continuously being developed in medical engineering fields, and new and revolutionary less-invasive surgery has emerged. One of the results is the emergence of laparoendoscopic single-site (LESS) surgery and natural orifice translumenal endoscopic surgery (NOTES) as minimally invasive and maximally effective cosmetic procedures.

Hirano et al. first reported LESS adrenalectomy (LESS-A) in 2005 by a retroperitoneal approach using conventional laparoscopic instruments [36]. Castellucci et al. in 2008 reported a transperitoneal LESS-A procedure using three 5 mm conventional ports [37]. Cindolo et al. then reported the first successful experience of transperitoneal LESS-A using a multichannel single port [38]. Since then, various multichannel single ports have been developed and LESS-A has become widely used [39]. A recent large international series study demonstrated that LESS represents the most commonly adopted technique as well as conventional laparoscopic adrenalectomy (CLA). From 2008 to 2013, LESS-A had the fastest increase in utilization at 6%/year among the techniques. Not surprisingly, LESS-A was used more often for benign indications compared to other adrenal surgeries, suggesting that surgeons approached this novel technique with some caution. Interestingly, institutions from Asia and South America reported high rates of LESS-A [40]. Whether adoption of LESS in these countries is driven by patient demand and a focus on cosmetic outcome is speculative and remains to be determined. Furthermore, safety and efficacy remain the key factors in the decision-making process of patients undergoing minimally invasive surgery [41].

### NOTES or LESS?

CLA requires at least three ports to complete adrenal excision since the surgeon uses two ports, and the scopist uses a port and sometimes a port for retraction when needed. Technical difficulty often increases the number of ports. Although LA is a minimally invasive surgery, a port site may induce pain or muscle spasm, or prolong recovery time, resulting in deteriorated patient quality of life. In order to improve these drawbacks, NOTES was developed. NOTES is based on the concept that the surgeon uses a natural orifice (mouth, anus, or vagina) as an access and approaches the intraperitoneal space through a small incision in the luminal wall. Since there is no wound on the body surface with NOTES, it was expected to be the ultimate minimally invasive surgery. However, NOTES is extremely hard from a technical standpoint and further improvements in the instruments are needed. Whether NOTES will be useful is still unknown. On the other hand, there has been increasing enthusiasm and growing interest in LESS over the last decade since LESS seems to be more reliable than NOTES.

### Techniques and instruments

LESS-A has two access routes: transperitoneal and extraperitoneal. The most common access route for LESS-A has been the umbilicus, for obvious cosmetic benefits. The umbilicus provides a place in which the scar can be partially hidden from view, resulting in improved cosmesis with LESS through the umbilicus.

Nevertheless, transperitoneal LESS-A through the umbilicus is still challenging because the distance from the port to the tissue is longer than in the conventional laparoscopic approach. The approach becomes more tangential in direction in LESS (Figure 111.6). The angle of approach of the instrument feels different compared with conventional laparoscopic surgery, and there is a tendency for the surgeon to grasp the second- or third-best site since it is difficult to approach the target tissue in a straightforward manner. This might contribute to an increase in tissue regrasping due to inadequate or insufficient countertraction. The articulating grasp has insufficient gripping power to allow the surgeon to continue grasping the tissue. Improvement in articulating instruments must be achieved to improve operability.

LESS-A involves a limited surgical space, which often results in the instruments interfering with each other, so-called "sword fighting." To reduce this, bent instruments are required to create a wider working space. A 5 mm flexible laparoscope (Olympus Surgical, Tokyo, Japan) should also be utilized to keep the scope away from the surgeon's instruments [42]. Even though sword fighting is still an obstacle in LESS-A and one-handed manipulation remains prevalent, these obstacles decease as experience increases. To avoid it, surgeons spend a greater proportion of an operation conducting one-handed maneuvers in the early phase after starting to perform LESS [42]. However, the use of one-handed maneuvers increases the pneumoperitoneum time and the risk of tissue damage. Because of this, the "crossover technique" was developed (Figure 111.7), in which the instruments are crossed at the platform (Figure 111.8). Although this can initially be confusing, after the surgeon has mastered the crossover technique, performing it with bent instruments creates an appropriate operative angle and adequate surgical space. Fukumoto et al. reported that it takes 30 cases to master LESS-A [43]. They found that tumor size and visceral fat prolonged pneumoperitoneum time, and patients with large tumors tended to lose more blood. However, the effects of these predictors of worse surgical outcomes were overcome as the surgeon gained experience.

The retroperitoneal approach has some advantages, including more direct access to the retroperitoneal organs, less need for visceral retraction, and elimination of the risk for intraperitoneal contamination with infectious organisms [20]. However, the retroperitoneal space is limited, and articulating and curved instruments are not as useful as they are in the transperitoneal approach. Taken together, the most common transperitoneal LESS

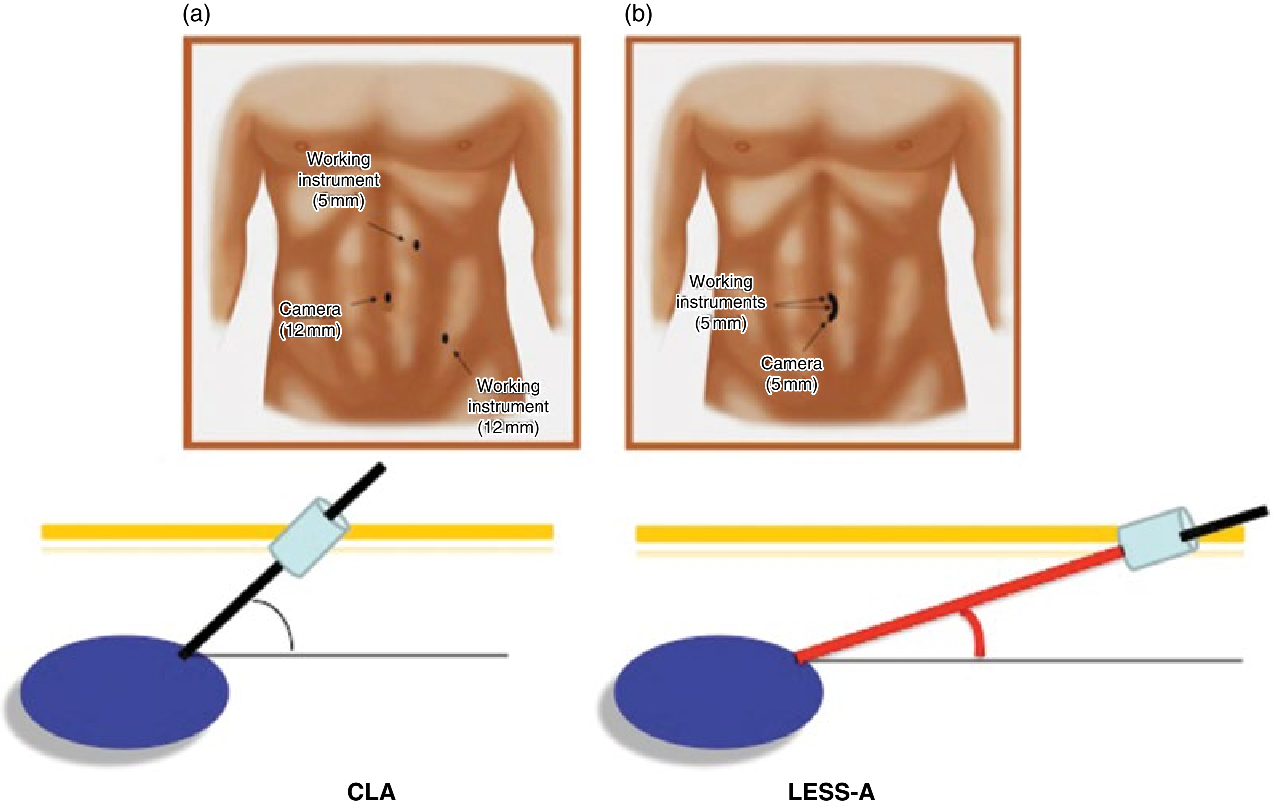
(a)
(b)
Working instrument (5 mm)
Camera (12 mm)
Working instrument (12 mm)
Working instruments (5 mm)
Camera (5 mm)
CLA
LESS-A

**Figure 111.6** The distance from the port to the tissue in laparoendoscopic single-site adrenalectomy (LESS-A) is longer than in conventional laparoscopic adrenalectomy (CLA).

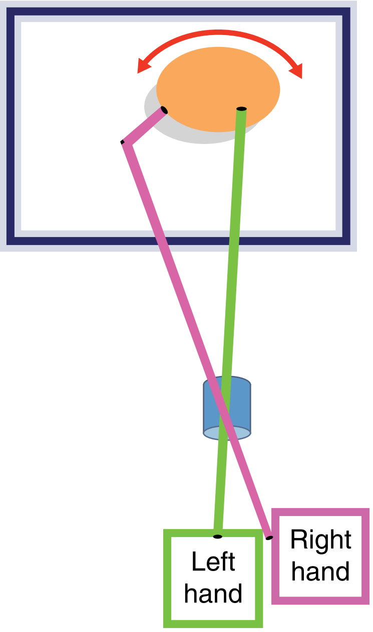

**Figure 111.7** In the crossover technique, the instruments are crossed at the platform and bent instruments create an appropriate operative angle and adequate surgical space.

through the umbilicus has a wider working space, although transperitoneal LESS requires the crossover technique using bent instruments.

## Indications

In general, all patients eligible for CLA can be considered for LESS-A depending on the surgeon's experience and technique. Benign adrenal tumors are a definite indication for CLA. Moreover, it is increasingly used for pheochromocytoma and some malignant cortical tumors preoperatively diagnosed as benign tumors. Nevertheless, Hasegawa et al. reported that factors prolonging pneumoperitoneum time in 50 early cases of LESS-A were patient visceral fat tissue, pheochromocytoma, and tumor diameter (>5 cm) [44]. When introducing LESS-A, patient selection criteria should be stringent. In addition to disease features (locally advanced or invasive), patient characteristics (visceral fat tissue, BMI, and previous surgical history) should be considered. According to these factors, the surgeon should choose relatively easier cases and may expand the indications with increasing experience. However, Fukumoto et al. found that no factor affects operative time as much as a surgeon with a lot of experience performing the crossover technique [43].

On the other hand, what kind of patient prefers LESS-A? Patient preference might depend on their characteristics. Inoue et al. reported that female and young patients were more satisfied with LESS-A than with CLA, suggesting that LESS-A may be recommended for female and young patients [45]. At this time, it must be mentioned that a LESS-A indication should be comprehensively decided upon based on these factors since urologists have to be skilled while there is a certain demand for LESS-A.

## Comparison of LESS-A and CLA

A single-surgeon series of transperitoneal LESS-A compared to CLA demonstrated that LESS-A had better pain control, faster recovery of bowel function, and better cosmetic satisfaction than CLA, although the operative time was longer with LESS-A [46]. Wen et al. also reported a single-surgeon series of retroperitoneal LESS-A compared with conventional retroperitoneal adrenalectomy. They found that retroperitoneal LESS-A was superior in terms of postoperative hospital stay and

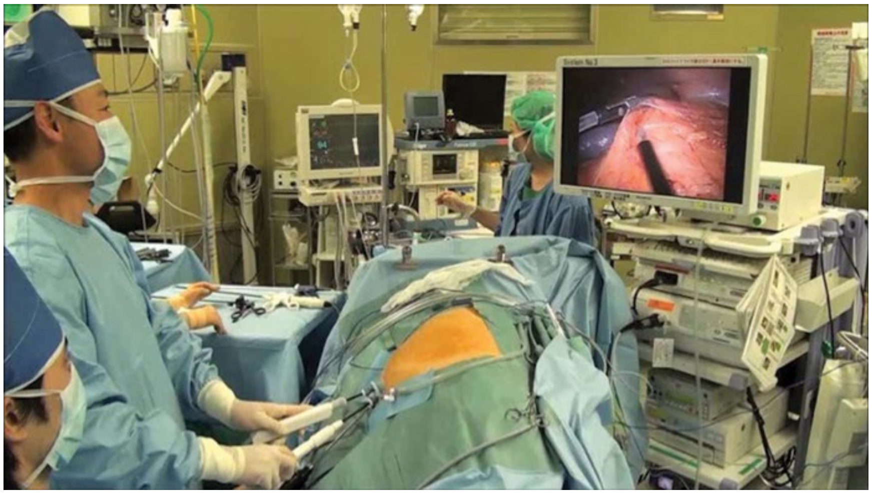

**Figure 111.8** In the crossover technique, the instrument in the surgeon's left hand is seen on the right side of the monitor, and that in the surgeon's right hand is seen on the left side of the monitor.

the time to resuming oral intake, although the operative time and opioid analgesic dosage were comparable [47].

A systematic review and meta-analysis comparing LESS-A and CLA revealed that operative blood loss and complications are similar, but that operative time seems to be longer in LESS-A. In addition, LESS-A has a shorter hospital stay after surgery and more acceptable perception of pain than CLA [48]. Another recent meta-analysis also suggests that LESS-A is a safe and feasible alternative to CLA due to its decreased postoperative pain, although the operative time is longer [49]. These results suggest that the operative time of LESS-A may be longer than that of CLA. Nevertheless, after a surgeon had experienced 30 cases of LESS-A, the pneumoperitoneum time was significantly decreased and the factors responsible for its prolongation had disappeared [43]. In summary, the technique for LESS-A, the crossover technique, appears to be not overly challenging but also not easy.

Hattori et al. compared 20 consecutive cases of LESS-A for pheochromocytoma with 30 cases of CLA for pheochromocytoma. They found no significant differences between LESS-A and CLA in terms of operation time, total fluid during the operation, estimated blood loss, first oral feeding, postoperative stay in the intensive care unit, and postoperative hospital stay. LESS-A could become one of the treatments of choice for resection of pheochromocytoma [50].

## Future perspectives

Since LESS-A first appeared, the instruments and techniques have been greatly improved. Bent instruments and sealing devices in particular have contributed to improving the operability and reducing the operation time. However, LESS-A is still not completely established. Lee et al. reported that they successfully carried out robotic single-site adrenalectomy using the da Vinci surgical system Si (Intuitive Surgical, Sunnyvale, CA, USA) [51]. The newest da Vinci surgical system, da Vinci Xi, has been designed for future techniques including single-site surgery. In the next decade, surgeons may face new challenges in adapting to new innovations in adrenal surgery.

See accompanying Video 111.1.

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# 112

# Laparoscopic and Robotic Surgery of the Seminal Vesicles

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## Anatomy

The seminal vesicles are paired tubular glands located superior to the prostate, posterior to the urinary bladder, and anterior to the rectum. Denonvilliers' fascia covers the posterior aspect of the seminal vesicles, separating the rectum from the bladder and prostate. Each vesicle forms as an outpocketing of the ampulla of its corresponding vas deferens, which is derived from the mesonephric duct. The excretory duct of each seminal vesicle joins the ipsilateral vas deferens to form the ejaculatory duct, which then enters the central zone of the prostate and opens to the urethra at the level of the verumontanum [1]. The vesiculodeferential artery – arising from the superior or inferior vesical arteries, which are branches of the internal iliac artery – provides the dominant blood supply to the seminal vesicle. The lymphatic drainage of the seminal vesicle is typically to the internal iliac lymph nodes [2].

Similar to its overall structure, a single tube folded and coiled upon itself, the lumen of the seminal vesicle is highly irregular. Histologically, the seminal vesicle is composed of mucosal and muscular layers. The convoluted mucosa consists of a pseudostratified columnar epithelium and underlying lamina propria, and the muscular layer consists of an inner circular and outer longitudinal layer of smooth muscle [3]. The secretions of the seminal vesicle are alkaline and comprise the majority of the ejaculate volume. Importantly, the seminal vesicle fluid contains factors necessary for sperm motility and survival, including fructose, prostaglandins, and coagulation factors [4].

## Pathology

### Benign disease

Benign diseases of the seminal vesicles include infection, stones, and cysts. Seminal vesicle amyloidosis has also been reported [5]. Infection of the seminal vesicles is more common in developing countries, as a result of tuberculosis and schistosomiasis [6, 7]. However, bacterial infection of the seminal vesicles may also occur as a result of instrumentation (e.g. during prostate biopsy), sexually transmitted diseases, or from a urinary source in an immunocompromised patient (Figure 112.1). Once the infection progresses to an abscess, surgical or percutaneous intervention is often required [8]. In the rare case of echinococcal disease involving the seminal vesicle, forming a hydatid cyst, treatment requires systematic antiparasitic medication, aspiration and injection of cysts with hydrogen peroxide and 10% formalin, followed by cyst excision [9].

Seminal vesicle calcifications (Figure 112.2) and stones may be a later sequela of infection and are associated with obstruction [10]. Intervention may be required for seminal vesicle stones associated with symptoms, such as chronic pelvic pain, hematospermia, ejaculatory pain, or infertility [11, 12].

Cysts of the seminal vesicle are rare, with estimated incidence of 1 out of 20 000 males [13]. Although typically asymptomatic, seminal vesicle cysts may cause pelvic pain, hematospermia, or urinary symptoms [14]. Congenital cysts occur as a result of Wolffian duct anomalies, and consequently are associated with ipsilateral renal abnormalities, such as agenesis or dysplasia,

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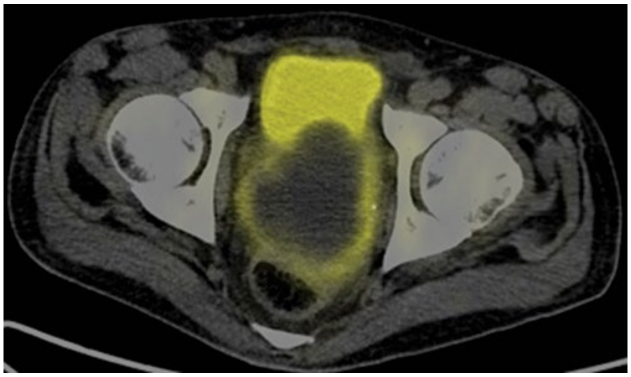

**Figure 112.1** Large seminal vesicle abscess detected on FDG-PET/CT scan in a patient with leukemia.

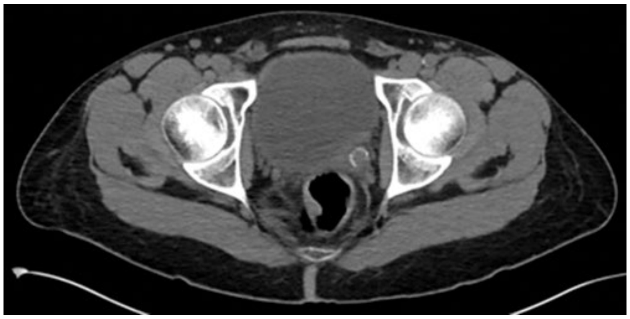

**Figure 112.2** Incidentally detected seminal vesicle calcification seen on CT scan.

polycystic kidney disease, ureteral ectopia, or ureterocele [13–16]. In the case of associated ejaculatory duct obstruction, the finding of unilateral renal agenesis and ipsilateral seminal vesicle cyst is termed Zinner syndrome [17]. Due to the close association with ipsilateral renal anomalies, the finding of a seminal vesicle cyst necessitates upper urinary tract imaging. Cysts of the seminal vesicle may also be acquired as a result of chronic ejaculatory duct or lower urinary tract obstruction [18, 19]. Surgical intervention is required in the case of superimposed infection and abscess (Figure 112.3), compression of urinary structures resulting in obstruction, or concern for malignant transformation [20–24].

## Benign tumors

Primary tumors of the seminal vesicle are rare, and include papillary adenoma and cystadenoma [25]. Schwannoma of the seminal vesicle has also been described [26]. Unlike malignant involvement of the seminal vesicle, benign tumors of the seminal vesicle demonstrate absence of adjacent organ involvement on imaging and do not cause elevations in serum tumor markers (e.g. prostate-specific antigen [PSA], carcinoembryonic antigen [CEA]) [27]. These tumors are often diagnosed due to symptoms, and pathologic diagnosis is made at the time of surgical excision [28]. Alternatively, if incidentally diagnosed and confirmed to be benign on biopsy, these tumors may be followed with serial transrectal ultrasound or cross-sectional imaging.

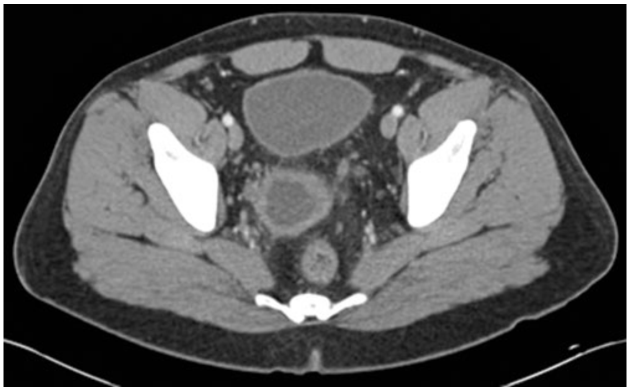

**Figure 112.3** Patient with history of seminal vesicle cyst found with an associated abscess on CT scan.

## Malignant tumors

Malignant involvement of the seminal vesicles from locally advanced pelvic tumors greatly outnumbers the frequency of primary malignancies of the seminal vesicles [29]. In the case of diagnostic uncertainty based on examination and imaging alone, serum tumor markers, cystoscopy, and/or sigmoidoscopy may be helpful in distinguishing prostate, bladder, or rectal carcinoma from a primary seminal vesicle malignancy. In the case of primary seminal vesicle malignancy, one would expect negative cystoscopic and sigmoidoscopic evaluations, normal PSA, normal CEA, and elevated cancer antigen 125 (CA-125) [30, 31].

Adenocarcinoma comprises the majority of malignant tumors of the seminal vesicle, with presenting symptoms including hematuria, hematospermia, dysuria, urinary retention, and rarely ureteral obstruction [29, 32]. In the case of advanced disease, pathologic diagnosis may be made by transrectal ultrasound-guided needle biopsy or transurethral resection. However, in the case of organ-confined disease on cross-sectional imaging, the pathologic diagnosis is often made at the time of surgical excision. Immunohistochemical profile includes positive CA-125, positive cytokeratin-7, and negative cytokeratin-20 staining [29–31]. In the case of CA-125-producing seminal vesicle carcinoma, the response to therapy may be monitored by serum CA-125 levels [31]. Other malignant tumors of the seminal vesicle include cystosarcoma phyllodes [33], sarcomas (rhabdomyosarcoma, leiomyosarcoma, and fibrosarcoma) [34, 35], extragastrointestinal stromal tumors [36], and primary germ cell tumors [37, 38]. Some have proposed that cystadenomas, cystosarcoma phyllodes, and sarcomas represent an increasingly aggressive spectrum of mixed epithelial stromal tumors [39].

## Diagnosis

### History and examination

The signs and symptoms of seminal vesicle pathology are vague and nonspecific; furthermore, seminal vesicle cysts and tumors may be completely asymptomatic. Reported symptoms, as described above, may include perineal or pelvic pain, pain with ejaculation, hematospermia, lower urinary tract symptoms, hematuria, infertility, and symptoms consistent with urinary tract obstruction. Physical examination of the seminal vesicles is limited. Digital rectal examination may be revealing in the case of infection or abscess due to exquisite tenderness, and a large seminal vesicle mass may be palpated. Urinalysis may reveal microscopic hematuria in some cases, prompting further evaluation with imaging and cystoscopy. Cystoscopic evaluation may reveal distortion of the ipsilateral trigone (i.e. asymmetric elevation of the trigonal ridge) or of the ipsilateral prostatic urethra [40].

### Imaging

Given the limitations of history and physical examination for seminal vesicle pathology, radiographic imaging is often necessary for accurate diagnosis. Transrectal ultrasound is the most commonly employed imaging modality for seminal vesicle pathology, and is the recommended initial study of choice for its cost, relative availability, and avoidance of ionizing radiation. The seminal vesicles are well visualized on transrectal ultrasound, and are normally symmetric, paired cystic structures located immediately superior to the prostate [41, 42]. Although cystic and solid components can be distinguished on ultrasound imaging, no specific imaging characteristics differentiate benign from malignant seminal vesicle tumors. This distinction can only be made with histopathology on either transrectal ultrasound-guided biopsy or surgical excision of the specimen. Secondary involvement of the seminal vesicle may be appreciated as lesions contiguous with the adjacent organ of primary disease, often affecting both seminal vesicles.

Cross-sectional imaging, either computed tomography (CT) scan or magnetic resonance imaging (MRI), provides greater anatomic information than transrectal ultrasound. The surrounding pelvic organs can be well visualized, and tissue planes between adjacent structures can also be delineated. On CT scan, cysts can be identified as well-defined structures filled with fluid (Hounsfield unit characteristics consistent with fluid). On MRI, cyst fluid would have high intensity on T2-weighted imaging, while hemorrhagic cysts would also have high intensity on T1-weighted imaging [42]. On both CT and MRI, abscesses would demonstrate rim-enhancement after administration of intravenous contrast and with surrounding soft tissue stranding. Neither imaging modality can reliably distinguish between benign and malignant tumors. Once again, this distinction can only be made with histopathology from either image-guided biopsy or surgical excision of the lesion. Obliteration of the surrounding tissue planes and involvement of both seminal vesicles may suggest secondary malignant involvement of the seminal vesicles from an adjacent tumor.

## Surgery

### Indications

Operative intervention of the seminal vesicles is indicated when any of the pathology discussed above (i.e. cyst, abscess, stone) becomes symptomatic or for tumors of the seminal vesicles. As transrectal ultrasound and cross-sectional imaging are unable to reliably differentiate benign from malignant tumors, accurate diagnosis requires surgical excision followed by histopathologic evaluation. Finally, surgical excision of the seminal vesicles is routinely performed during radical prostatectomy.

### Endoscopic interventions

For cases of seminal vesicle obstruction or cysts and abscesses near the prostatic urethra, transurethral resection of the ejaculatory ducts may provide decompression. Using a resectoscope and electrocautery or a rigid cystoscope with a holmium laser, the proximal verumontanum is excised until fluid is expressed. Care must be taken to remain distal to the bladder neck and proximal to the external sphincter. Although this approach has been shown to be effective for the treatment of seminal vesicle cysts and abscesses [43, 44], patients must be counseled on the risks of recurrence and infection, including epididymitis due to future on-going urinary reflux. Stones of the seminal vesicle can also be accessed in an endoscopic fashion by introducing conventional ureteroscopic instruments into the ejaculatory ducts [45].

### Laparoscopic or robotic approaches

Because of decreased postoperative pain, patient morbidity, and hospital length of stay compared to traditional open approaches [46, 47], laparoscopic (and robotic) approaches are the preferred method of seminal vesicle extirpative surgery. The laparoscopic approach to the seminal vesicles was first described in 1993 by Kavoussi et al. [48]. The transperitoneal route is utilized for isolated seminal vesicle surgery, while the retroperitoneal (extraperitoneal) route can be utilized during radical prostatectomy. Extraperitoneal access and port placement for laparoscopic radical prostatectomy is described elsewhere.

As with any abdominopelvic surgery under general anesthesia, deep vein thrombosis prophylaxis and appropriate antibiotics are administered prior to induction of anesthesia. The patient may remain supine with or without lower extremity spreader bars or the patient may be placed in lithotomy position. Importantly, the patient must be well secured to the operating room table as steep Trendelenburg position will be required to facilitate bowel mobilization out of the pelvis. A Foley catheter is placed to decompress the urinary bladder. Once the skin has been shaved and prepped, pneumoperitoneum is established with Veress needle or Hasson technique, and the 10 mm port is placed 1–2 fingerbreadths above the umbilicus. After adequate pneumoperitoneum is ensured and the underlying bowel is examined for injuries under direct visualization using the laparoscope, two 5 mm (8 mm in the case of robot-assistance) working ports are placed inferolaterally, at least 8 cm on either side of the 10 mm port, at the level of the umbilicus. In the case of robot-assistance, an additional 8 mm port and 12 mm port may be placed 8 cm lateral to either working port at the level of the umbilicus. For the nonrobotic laparoscopic approach, assistant ports should include a 12 mm port placed 8 cm lateral to the right working port at the level of the umbilicus and a 5-mm port placed superolaterally to the camera port (Figure 112.4).

Once the ports are placed, the patient is put into steep Trendelenburg position. In the case of robot-assistance, the robot is docked and instruments are placed, typically monopolar scissors in the robot one arm, bipolar Maryland forceps in the robot two arm, and ProGrasp® forceps in the robot three arm [49, 50]. The assistant uses the suction–irrigator and provides countertraction when necessary, and uses the clip-applier through the 12 mm port. For traditional laparoscopic surgery, the surgeon may use a variety of energy sources. Although the authors prefer to use monopolar scissors and bipolar Maryland forceps, the use of a harmonic scalpel or laparoscopic LigaSure™ may also be considered. Lysis of adhesions is performed, and the sigmoid colon is mobilized out of the pelvis and retracted with the robotic fourth arm or by the assistant. The peritoneal fold at the junction of the rectum and bladder is noted (i.e. the peritoneal cul-de-sac), and the peritoneum is incised at the midline in a transverse fashion (Figure 112.5). The seminal vesicles or vas are identified with a combination of sharp and blunt dissection. If these structures are not readily apparent, the ipsilateral vas can be traced from the inguinal ring as it crosses below the medial umbilical ligament and over the ureter. Once the vas is identified, it is retracted medially and divided without extensive lateral dissection to avoid potential ureteral injury (Figure 112.6). Particularly in the case of a large seminal vesicle mass that extends laterally, the use of temporary ureteral catheters or double-J stents may be beneficial to reduce the risk of ureteral injury. The vas is retracted in a medial and cranial direction to bring the seminal vesicle into the operative field. Combination blunt and sharp dissection is performed on the seminal vesicle circumferentially and strictly on the plane of the seminal vesicle. Dissection proceeds in a medial to lateral direction (Figure 112.7). Continuous adjustment of retraction to ensure medial and cranial force on the seminal vesicle is important, as care must be made to avoid injury to the neurovascular bundle or the ureter, which lie near the lateral tip of the seminal vesicle. The dominant blood supply to the seminal vesicle is also located in this region: the vesiculodeferential artery

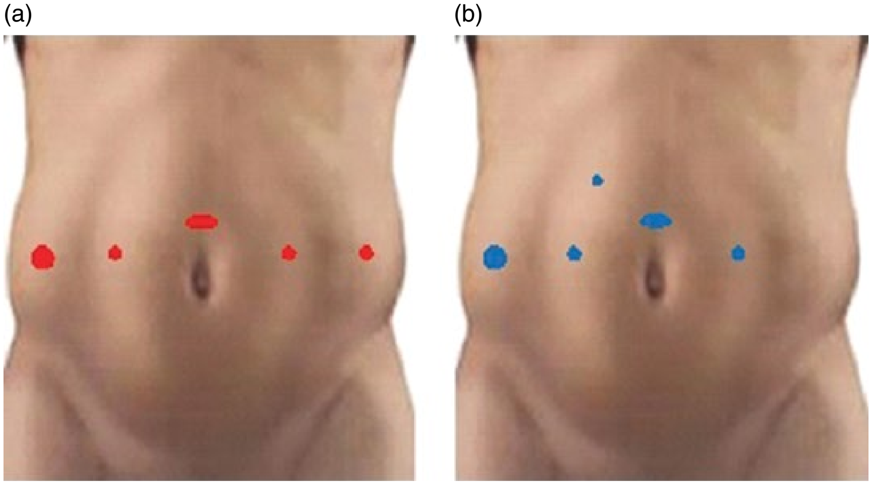

**Figure 112.4** Port configuration for robot-assisted (a) and traditional laparoscopic (b) approaches to the seminal vesicle. Please see text for port sizes and relative distances from one another.

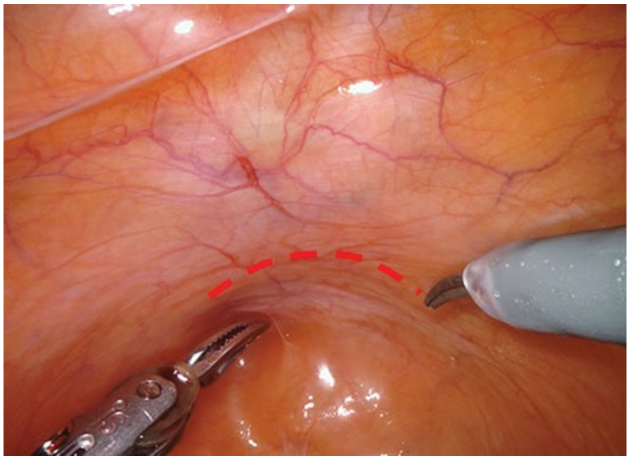

**Figure 112.5** Appearance of the pelvic peritoneal fold and location of incision to approach the seminal vesicles from a transabdominal laparoscopic (or robotic) approach (red dashed line).

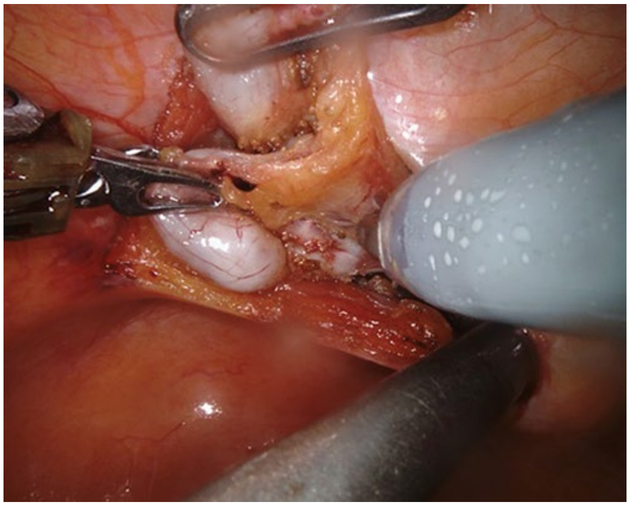

**Figure 112.7** Dissection of the right seminal vesicle with the right vas retracted medially and superiorly.

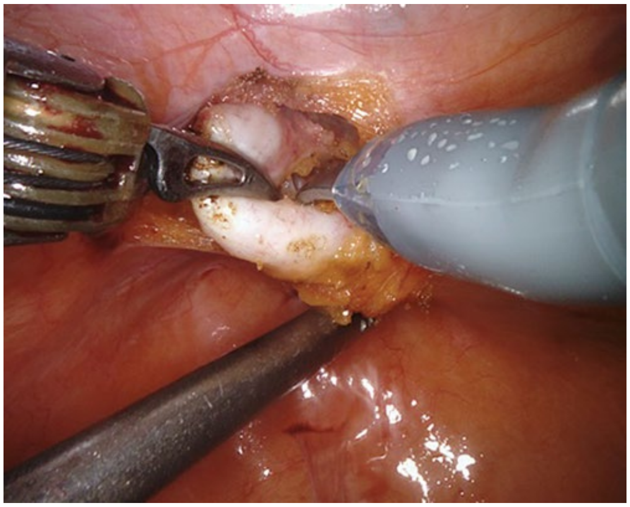

**Figure 112.6** Dissection of right vas deferens prior to division.

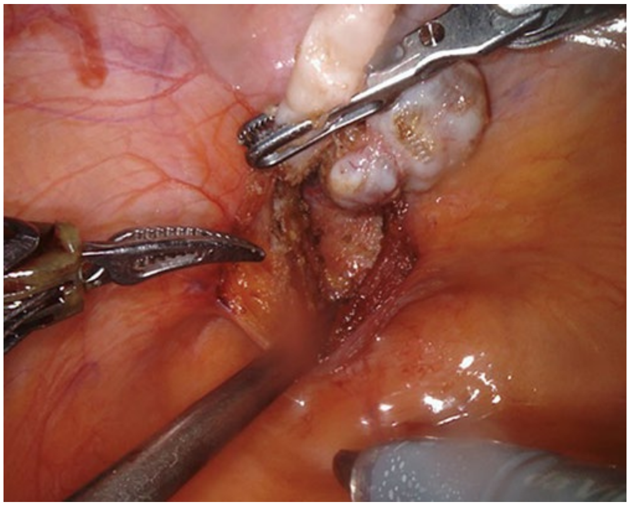

**Figure 112.8** Completed dissection of the right seminal vesicle and vas.

typically arises from the inferior vesical artery, which is a branch of the internal iliac artery. These vessels may be divided with clips or with judicious electrocautery.

Once the seminal vesicle and vas have been completely dissected (Figure 112.8), the ejaculatory duct may be transected at the entrance to the prostate. Plication of the prostatic tissue on either side of the ejaculatory duct may be performed but is not imperative. In patients with seminal vesicle cysts who desire fertility preservation, the seminal vesicle can be dissected without division of the ipsilateral vas deferens, and the cyst can be divided at its base with reapproximation of the seminal vesicle defect. The specimen is placed in an Endo Catch™ bag and extracted through either the midline camera port or the lateral assistant port. Some recommend reapproximation of the overlying peritoneum, but this is not absolutely necessary. The 10 and 12 mm port sites should be closed with 0 Vicryl suture, and the skin incisions reapproximated with absorbable suture, staples, or skin glue. The patient should be observed overnight, with diet advanced as tolerated. Foley catheter can typically be removed the following morning, except in the case of large prostatic defect with urethral exposure or entry.

## Conclusions

Various seminal vesicle pathologies exist that require surgical intervention. Although diagnostic imaging may provide insights, histopathology is required to differentiate benign from malignant tumors. In these cases, laparoscopic (or robotic) approaches are preferred.

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# 113

# Modern Techniques in Abdominal Wall Hernia Repair: a Guide for the Practicing Endourologist

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## Introduction

Abdominal wall hernias are the most common surgical condition for which patients seek care. In the current healthcare environment, a significant proportion of general surgical practice is devoted to the repair of hernia. The last three decades have witnessed significant advancements in both surgical technique and prosthetic implants to aid the hernia surgeon. As in other specialized fields of medicine, there are now centers of excellence devoted to both complex abdominal wall reconstruction and the study of the physiology of the abdominal wall.

The use of prosthetic materials in hernia repair has become ubiquitous throughout the United States and Europe. In short, the mesh implant industry has grown to a 1 billion dollar plus business with some individual prosthetics costing in excess of US$10 000 [1]. From a surgical perspective, an experienced well-trained "herniologist" should be able to perform both laparoscopic and open techniques. There is no longer a one-size-fits-all approach. A hernia specialist should be able to evaluate the patient and decide on either a laparoscopic or open approach with consideration given to complicating medical issues, technical factors, and cosmesis. One thing has become very clear in the management of abdominal wall hernia – the use of mesh implants has decreased the rate of recurrence, but has simultaneously introduced a range of potential complications.

From the standpoint of the practicing endourologist, there will be preoperative considerations in performing laparoscopic/robotic procedures in patients with existing hernia. This will require management of both abdominal adhesions and trocar placement with consideration to simultaneous repair of the hernia itself. The remainder of this chapter will be devoted to current laparoscopic techniques utilized in some of the more common hernias of the abdominal wall.

## Laparoscopic techniques

As part of the patient's medical history, the endourologist should be cognizant of both the patient's surgical history and the presence of abdominal wall hernia. If there is a plan to repair the hernia, the surgeon should have a working knowledge of the types of mesh prosthetics currently in use and be familiar with potential complications of mesh implantation. There are currently both biologic and synthetic meshes available for use in repair of abdominal wall defects (Tables 113.1–113.3).

## Technical principles

Every hernia of the abdominal wall has one common denominator: a musculofascial defect through which abdominal contents or preperitoneal structures can herniate. The repair of the musculofascial defect has evolved over the last century in an attempt to decrease postoperative discomfort, provide earlier return to activity, and decrease the rate of recurrence. The repair of inguinal, incisional/ventral, and parastomal hernias all require the defect either be closed primarily, bridged with a prosthetic, or most commonly, a combination of primary closure with prosthetic reinforcement.

Surgical literature has clearly shown that the use of mesh implants decrease the overall rate of recurrence [2, 3]. In addition, especially in dealing with midline defects, it is preferred to restore continuity of the musculature by

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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 113.1** Synthetic mesh implants commonly used in hernia repair.

| | Commercial mesh name | Material | Manufacturer |
|---|---|---|---|
| 1. | Vicryl™ Woven Mesh | Polyglactin 910 (polyglycolic acid) | Ethicon (Somerville, NJ, USA) |
| 2. | PROLENE™ 3D Patch Polypropylene Mesh | Polypropylene | Ethicon |
| 3. | PROLENE™ Polypropylene Mesh | Polypropylene | Ethicon |
| 4. | PROLENE™ Polypropylene Hernia System | Polypropylene | Ethicon |
| 5. | MERSILENE™ Polyester Fiber Mesh | Polyethylene terephthalate | Ethicon |
| 6. | ULTRAPRO™ Partially Absorbable Lightweight Mesh | Monocryl (poliglecaprone 25) and polypropylene | Ethicon |
| 7. | ULTRAPRO™ Plug | Monocryl (poliglecaprone 25) and polypropylene | Ethicon |
| 8. | ULTRAPRO™ Hernia System | Monocryl (poliglecaprone 25) and polypropylene | Ethicon |
| 9. | PVP™ Device | Oxidized regenerated cellulose (ORC) and polypropylene | Ethicon |
| 10. | PROCEED™ Surgical Mesh | Oxidized regenerated cellulose (ORC) and polypropylene | Ethicon |
| 11. | Parietex™ Composite (PCO) Mesh | Macroporous polyester, with a 3D weave material with resorbable collagen film | Covidien (Mansfield, MA, USA) |
| 12. | Parietex™ Composite Open Skirt (PCO OS) Mesh | Macroporous polyester, with a 3D weave material *with* resorbable collagen film | Covidien |
| 13. | Parietex™ Composite (PCO) Parastomal Mesh | Macroporous polyester, monofilament material | Covidien |
| 14. | Parietex™ Composite (PCO) Hiatal Mesh | Macroporous polyester, with a 3D weave material *with* resorbable collagen film | Covidien |

**Table 113.2** Current biologic implants used most often in infected wounds but used rarely for noninfected primary hernia repairs.

| Product and origin | Manufacturer |
|---|---|
| Alloderm (cadaveric dermis) | Lifecell, Branchburg, NJ, USA |
| AlloMax (cadaveric dermis) | CR Bard, Providence, RI, USA |
| CollaMend (porcine dermis) | CR Bard, Providence, RI, USA |
| FlexHD (cadaveric dermis) | Ethicon Inc., Somerville, NJ, USA |
| Permacol (porcine dermis) | Covidien, Mansfield, MA, USA |
| Strattice (porcine dermis) | Lifecell, Branchburg, NJ, USA |
| SurgiMend (fetal bovine pericardium) | TEI Biosciences, Boston, MA, USA |
| Surgisis (porcine small intestinal submucosa) | Cook Medical, Bloomington IN, USA |
| Veritas (bovine pericardium) | Synovis, St. Paul, MN, USA |
| XenMatrix (porcine dermis) | CR Bard, Providence, RI, USA |

direct suture or with some form of myofascial release, facilitating midline closure. It is clear that most forms of direct closure will place tension across the wound even with fascial release procedures. For this reason, it is proper to reinforce the closure with some form of prosthetic "buttress."

Prosthetics used in hernia repair have evolved rapidly over the last 20 years. The use of polypropylene mesh for abdominal wall closure was first reported in 1962, and for many years was the only viable option in hernia repair [4]. The material elicits a strong inflammatory reaction in the surrounding tissues, with scar plate formation.

It soon became apparent that although mesh implants decreased overall hernia recurrence rates, the use of plain, heavyweight polypropylene created potential problems. If polypropylene is placed in an intra-abdominal location, it can cause severe inflammatory reaction in adjacent organs, leading to dense impenetrable adhesions with potential erosion and fistula formation. In addition, the use of mesh or foreign material in any form can exacerbate wound infection and can

**Table 113.3** Results of biologic implant usage in difficult wounds.

| Product | Description | Overall complication rates | Recurrence rates | Rates of postoperative infection | Need for explantation |
|---|---|---|---|---|---|
| AlloDerm | Noncrosslinked human dermis | 12–15% | 46% | – | – |
| | | 30% (early) | 47% | – | 9% |
| | | – | 15% | – | – |
| | | – | 17% | 40% | – |
| | | – | 27% | 27% | – |
| Permacol | Crosslinked porcine dermis | 32% | 11% | 7% | 0% |
| | | 48% (early) | 32% | – | 11% |
| | | 50% | 15% | 10% | – |
| | | 53% | 0% | 11% | 0% |
| | | – | 66% | 37% | 25% |
| Strattice | Noncrosslinked porcine dermis | 24% | 0% | 2.4% | 0% |
| | | 28% | 0% | 8% | – |
| | | 31% | 5% | 19% | 0% |
| | | 57% | 43% | 14% | 0% |
| Surgisis | Noncrosslinked porcine small intestine submucosa | 25% | 7% | 0.7% | – |
| | | 25% | 0% | 25% | 25% |
| | | 33.3% | 8% | 8% | – |
| Tucomesh and Veritas | Bovine pericardium | 12.5% | – | 4.2% | – |
| | | 18% | 0% | 3% | – |
| | | 20.8% | 8% | – | – |
| | | 23.3% | 16.7% | 3% | 3% |
| Surgimend | Bovine acellular dermal matrix | 25.5% | 3.9% | 9.8% | – |

necessitate removal with potential catastrophic results. Often this requires multiple surgical procedures for resolution.

With consideration of these findings, prosthetic research and development has evolved with the following principles:

- Tensile strength must be maintained to avoid prosthetic rupture.
- An adhesive barrier should be placed for potential use in any intra-abdominal location adjacent to viscera.
- Implants should be designed for easy deployment using either open or laparoscopic techniques.
- Potential resistance to infection should be considered.
- Using prosthetic material which contracts over time can be a source of abdominal pain and lead to recurrent herniation.

The technical aspects of mesh placement have also been studied carefully with reference to the rate of recurrence and complications.

- Mesh can be placed intraperitoneally, preperitoneally (retromuscular), or as an onlay over the muscular closure (Figure 113.1).
- It is imperative to overlap the defect by at least 4–6 cm in all directions.

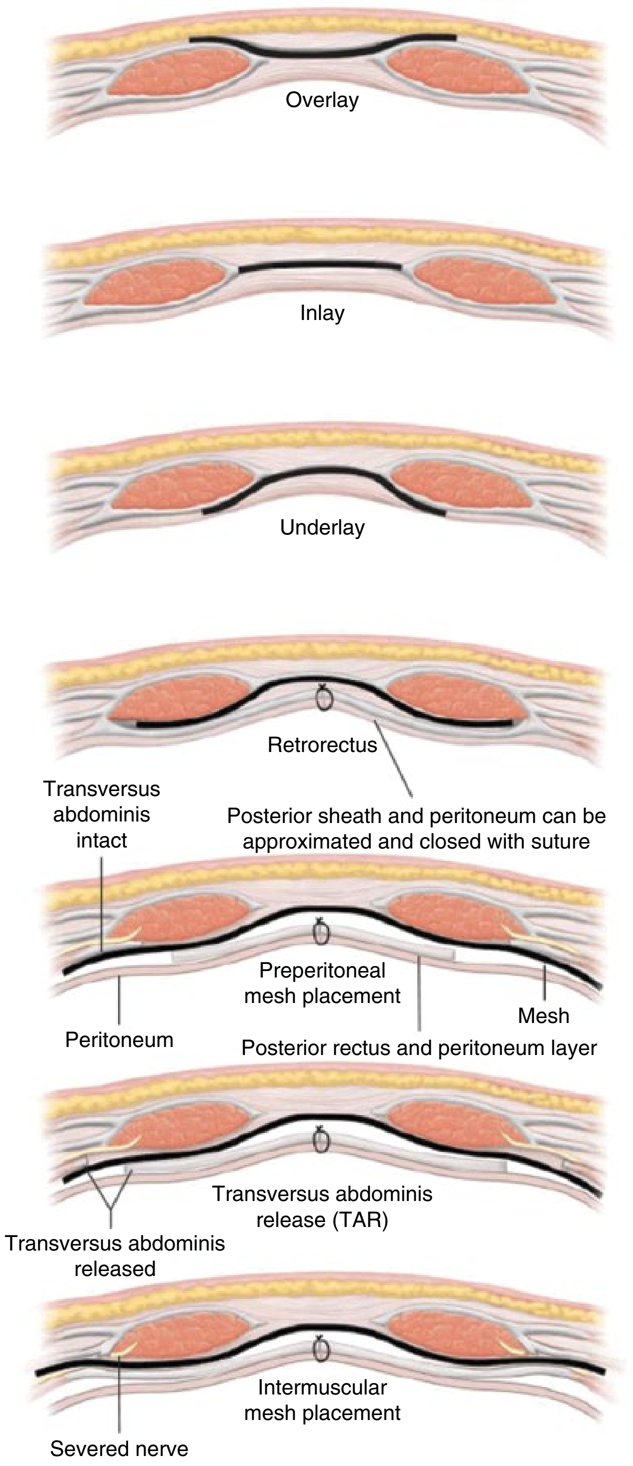
Overlay
Inlay
Underlay
Retrorectus
Transversus abdominis intact
Posterior sheath and peritoneum can be approximated and closed with suture
Preperitoneal mesh placement
Mesh
Peritoneum
Posterior rectus and peritoneum layer
Transversus abdominis release (TAR)
Transversus abdominis released
Intermuscular mesh placement
Severed nerve

**Figure 113.1** Various locations of mesh placement.

- Depending on location, the mesh must be fixed to the abdominal wall with sutures, staples, fibrin glues, or the use of self-fixating mesh.
- Inlay techniques that do not overlap the repair, but merely bridge the defect should be avoided.

## Laparoscopic repair of incisional/ventral abdominal wall hernias

### Incisional hernia

Incisional hernias can develop in any region of the abdominal wall where previous fascial closure has been performed. The incidence of the midline hernia has been reported to be 11–23% after midline laparotomy [5]. Causes of incisional hernia are most often a combination of technical and patient-related factors. Wound infection, obesity, smoking, and malnutrition are the most common related factors in incisional hernia occurrence. Correct technique in fascial closure is imperative. It is important for the laparoscopic surgeon to note that incisional hernia can develop in port sites, most commonly when 10 mm or larger ports are used. It is not clear from the literature that fascial closure of 10 mm or larger port sites decreases the incidence of hernia, but generally, most surgeons advocate fascial closure both in the midline and laterally, especially below the semilunar line.

#### Preop consideration

As stated previously, there are two aspects to consider when performing a laparoscopic urologic procedure in patients with concurrent ventral hernia. Is the hernia within the surgical field of the proposed urologic procedure? Will it present a hazard secondary to adhesions and the presence of incarcerated structures? This can be defined with preoperative contrast computed tomographic (CT) scans if necessary. At our institution, general surgery is often consulted preoperatively and simultaneous repair of the hernia is often completed at the time of the urologic procedure. In fact, smaller ventral hernia sites have been used to extract the operative specimen followed by open repair of the hernia.

#### Laparoscopic repair

Laparoscopic repair of incisional hernia should be performed selectively based on the size of the defect and its location. In a general sense, the larger the defect the more difficult it is to restore muscular continuity and provide a symmetrical appearance of the abdominal wall with relief of symptoms.

We employ laparoscopic repair most often in patients with smaller defects where the defect is bridged and overlapped, but the defect itself is not closed. With proper patient selection, this will provide symptomatic relief and prevent incarceration of the hernia.

Technically, access to the abdominal cavity is chosen at a site remote from the defect, allowing for visualization of the defect and its contents (Figure 113.2).

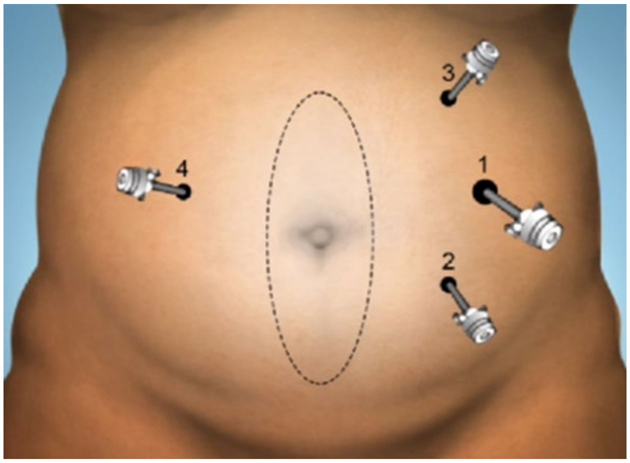

**Figure 113.2** Port placement for midline incisional defect.

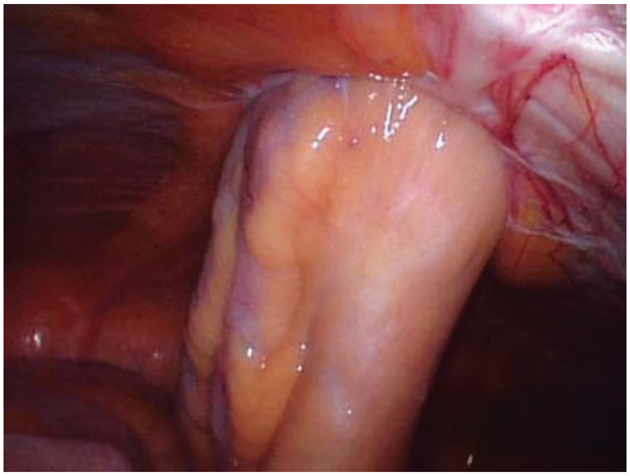

**Figure 113.3** Incarcerated incisional hernia.

We generally employ a 5 mm, 30°, or 0° scope which can be placed initially in the access site and can be rotated to any working port to facilitate dissection and mesh placement. After initiation of pneumoperitoneum and placement of working ports the defect is inspected, complete reduction of hernia contents (Figure 113.3) and lysis of adhesions is initiated, and adequate clearance of the surrounding abdominal wall is assured (Figure 113.4). The hernia sac is generally left in place and the inner dimensions of the defect are measured with a flexible ruler placed intra-abdominally. A prosthetic barrier-type mesh is chosen to overlap of the defect by 6 cm in all directions. Multiple stay sutures of 0 long-term dissolvable material are used circumferentially at the edge of the defect (Figure 113.5). The mesh is then introduced through the access site and placed under the defect. A suture assist device is used through minute incisions in the abdominal wall to elevate the mesh and ensure adequate overlap of the defect. The stay sutures are tied beneath the small incisions in the subcutaneous tissue and the mesh is elevated to the peritoneal surface (Figure 113.6).

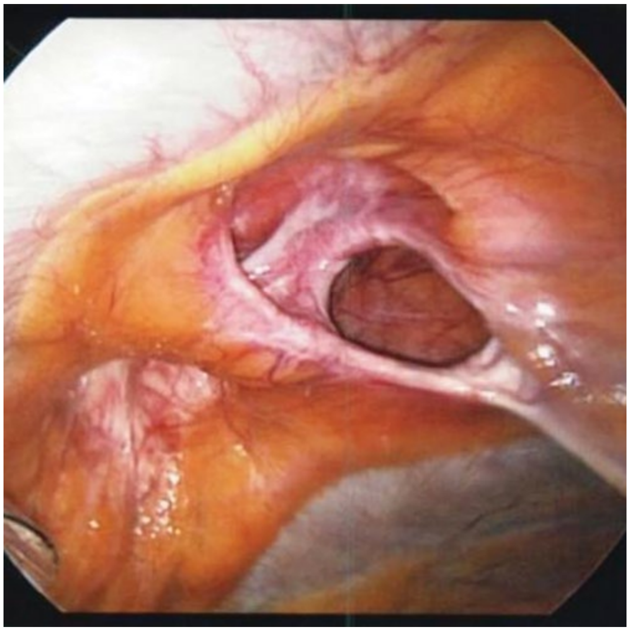

**Figure 113.4** Defect after reduction and enterolysis.

Additional fixation is then commenced with a surgical tacker with at least three rows of long-term dissolvable tacks placed around the material in the abdominal wall (Figure 113.7). This is generally completed with a reduced intra-abdominal pressure of 8–10 mmHg. Reducing the pressure helps to ensure flush contact with the peritoneal surface and minimizes redundancy and buckling of the material. It is imperative to make sure that the barrier side is facing the viscera and that the mesh edges are secured, preventing the viscera from herniating between the mesh and the abdominal wall. The trocars are then removed and an abdominal binder is placed to theoretically reduce seroma formation and promote adherence of the hernia sac.

### Other laparoscopic techniques

Recent advances in laparoscopic technique, including robotic surgery, have introduced modifications to the preceding technique with attention to repair of large defects and closure of the abdominal musculature. This is based on improvements in intracorporeal suturing technique and abdominal wall myofascial flap release procedures. Ramirez et al. first described the technique of component separation where the anterior rectus fascia is incised lateral to the semilunar line on one or both sides of the midline [6] (Figure 113.8). Laparoscopically assisted component separation is a technique employing a myofascial advancement flap, whereby muscular closure can be

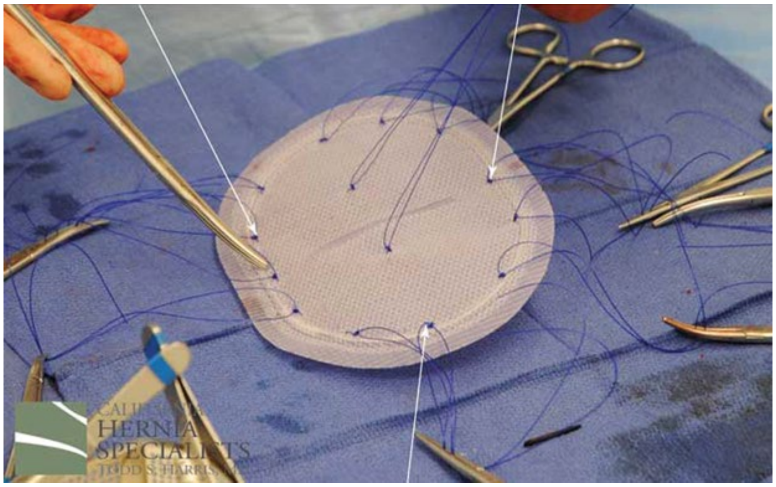

**Figure 113.5** Placement of stay sutures in mesh. The appropriate size mesh is selected for the particular patient. Sutures are placed at intervals around the mesh. These sutures ultimately will be brought through the muscle to secure the mesh in place under the newly repaired muscle wall.

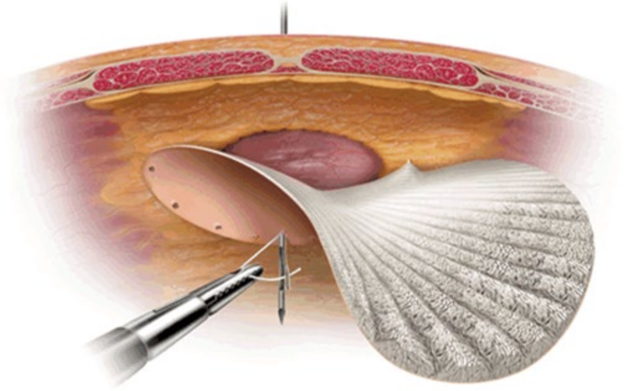

**Figure 113.6** Mesh fixation to abdominal wall.

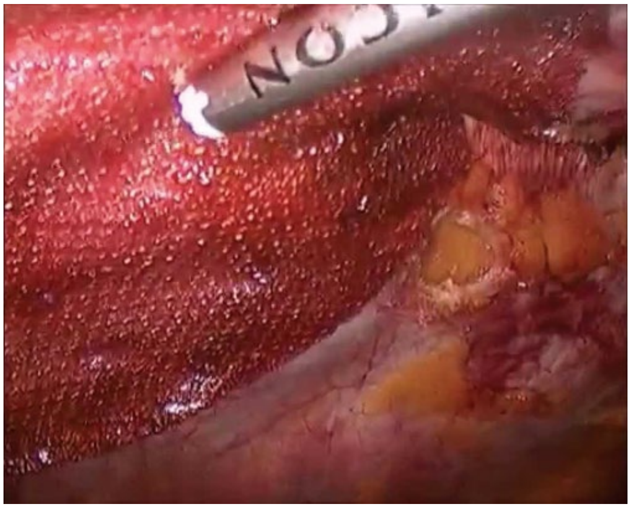

**Figure 113.7** Reinforcement of mesh to abdominal wall with tacks.

accomplished in the midline [7]. This technique can add as much as 20 cm advancement to facilitate midline muscular closure [8]. After closure, mesh reinforcement of the repair is generally used to buttress the closure. If done open, the mesh can be placed as a sublay, in the retromuscular (retrorectus) position, or as an onlay. Laparoscopically, the options are retromuscular or as a sublay.

### Results

In general, over the last quarter century, there has been vast improvement in both functional and cosmetic results of ventral hernia repair. The most significant parameters of improvement are the lower rates of recurrence in both open and laparoscopic repairs utilizing mesh. In addition, reestablishing continuity of the abdominal musculature and the ability to manage large defects improve symptoms and functional results. When evaluating results, it is clear that there is no current consensus on one particular methodology.

As stated, multiple series in the literature have clearly confirmed the superiority of mesh repair when compared to simple suture with respect to recurrence. It is important to note that although mesh repair has decreased overall rates of recurrence, hernias can recur up to 10 years after the original repair [9]. Especially in large, >10 cm defects, even repairs with mesh have been reported to recur in as many as 20% of patients. The increased use of myofascial advancement, although yielding superior cosmetic and functional results, has not been shown to be superior to other mesh techniques with regard to recurrence [10].

### Laparoscopic versus open technique

Multiple randomized trials have demonstrated that the laparoscopic technique has low rates of wound infection when compared to the open technique. Importantly, the

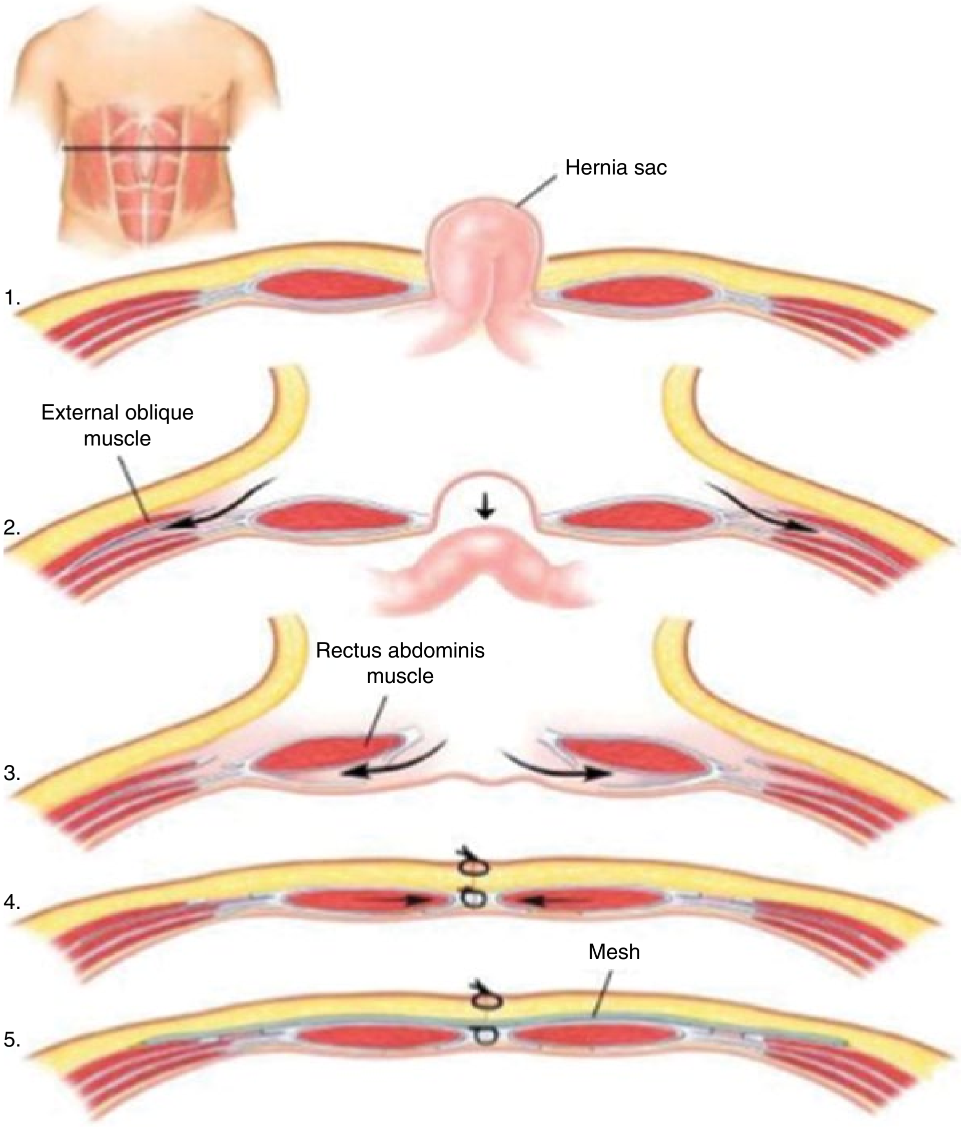

**Figure 113.8** Component separation to facilitate midline muscular closure.

rate of complications, including bowel obstruction in addition to rates of recurrence, shows no statistical difference. Of note, the incidence of bowel injury is higher in the laparoscopic repair group [11] (Table 113.4).

### Complications of laparoscopic surgery

Wound seroma is a common result of laparoscopic repair which generally occurs between the mesh and retained hernia sac. In the vast majority of cases, these will resolve spontaneously with no sequelae. General avoidance of drainage is preferred to mitigate the potential for wound infection. In symptomatic collections, after adequate skin preparation, the fluid can be drained with direct needle puncture. In rare cases, ultrasound guidance may be necessary (Figure 113.9).

Wound infection, generally the most feared result in any procedure requiring implants, is a rare complication of laparoscopic ventral hernia repairs. Wound infection when prosthetic material is exposed often requires explantation of the material. If PTFE is used, generally, implant removal is required. Infections in derivatives of polypropylene mesh or polyester mesh can sometimes be managed with drainage and antibiotics without removal of the material.

### Bowel injury

Laparoscopic repair can often require extensive enterolysis for reduction of incarcerated hernia contents. In the course of enterolysis inadvertent enterotomy can occur. Once recognized and repaired, there are a number of

**Table 113.4** Comparative meta-analysis comparing laparoscopic versus open repair for incisional hernia.

| Outcomes | No. of studies | No. of patients | HG, $\chi^2$ | HG, *P* value | Model | RR/WMD | *P* value | 95% CI |
|---|---|---|---|---|---|---|---|---|
| Recurrence | 11 | 1003 | 2.66 | 0.91 | Fix | 1.21 | 0.41 | 0.77, 0.91 |
| Wound infection | 11 | 1003 | 0.25 | 10.26 | Fix | 0.19 | <0.00001 | 0.11, 0.32 |
| Seroma | 9 | 893 | 23.55 | 0.003 | Random | 0.99 | 0.97 | 0.46, 0.10 |
| Hematoma | 8 | 768 | 6.77 | 0.45 | Fix | 0.94 | 0.82 | 0.53, 0.65 |
| Bowel injury | 10 | 977 | 4.78 | 0.57 | Fix | 3.68 | 0.003 | 1.58, 0.67 |
| Bowel obstruction | 6 | 711 | 1.72 | 0.79 | Fix | 1.58 | 0.40 | 0.55, 0.58 |
| Postoperative bleeding | 3 | 473 | 0.32 | 0.85 | Fix | 1.88 | 0.42 | 0.41, 0.71 |
| Reoperative | 4 | 431 | 2.79 | 0.42 | Fix | 0.42 | 0.07 | 0.16, 0.09 |
| Wound drainage | 8 | 752 | 19.31 | 0.007 | Random | 0.06 | <0.00001 | 0.03, 0.09 |

RR, risk ratio; WMD, weighted mean difference; HG, heterogeneity; Fix, fix effect model; Random, random effects model; CI, confidence interval.

options to consider. If the contamination is significant it is generally preferred not to place an implant. In which case, the procedure can be abandoned and the patient can be brought back to surgery at a later date.

As with all laparoscopic procedures, unrecognized bowel injury is a potential devastating complication. In any procedure where extensive enterolysis has been performed, it is imperative to pay attention to the patient's complaints of pain and anorexia. Postoperative temperature elevations and tachycardia are significant findings and often should be worked up with early postoperative CT scans. The presence of free fluid, free air, and/or ileus should alert the clinician to the possibility of bowel injury. If suspected, immediate surgical intervention is required.

## Inguinal hernia

Hernias of the inguinal region are extremely common and have a reported incidence of up to 25% in males. Over the last quarter century, improvements in inguinal hernia repair have focused on three main factors: less postoperative discomfort, early return to full activity, and decreased rate of recurrence. The use of prosthetics in both open and laparoscopic inguinal hernia repairs has become extremely popular. The routine use of mesh in primary open inguinal hernia was strongly advocated by Lichtenstein et al. in the 1990s [12]. The technique includes reduction of the hernia sac, closure of the defect in the transversalis fascia, and onlay mesh to cover the pubic tubercle and entire inguinal floor (Figure 113.10). There are many current derivatives of the above

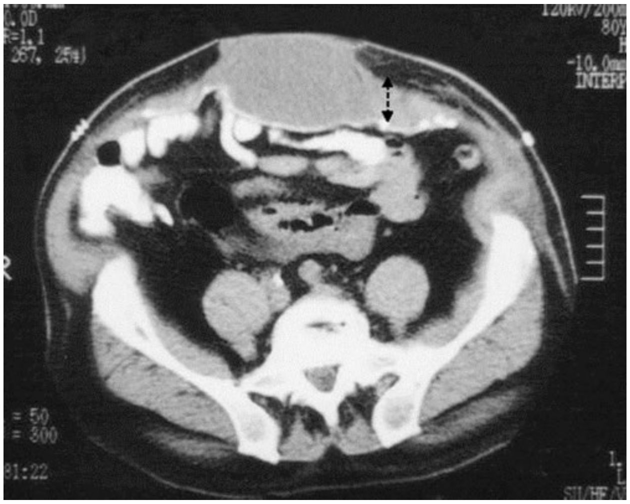

**Figure 113.9** Abdominal CT scan showing seroma between mesh and hernia sac.

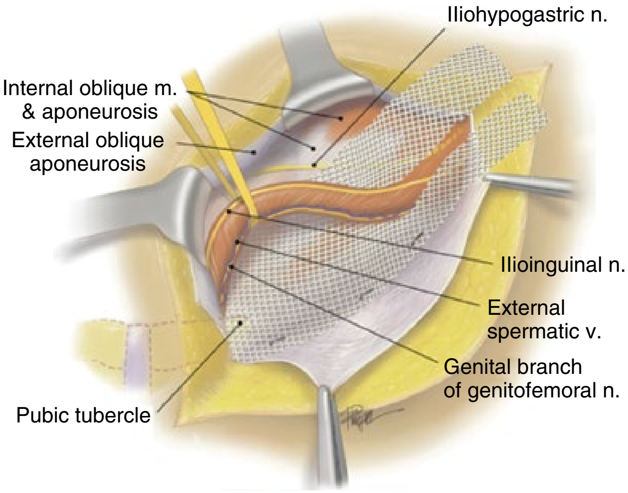
Iliohypogastric n.
Internal oblique m. & aponeurosis
External oblique aponeurosis
Ilioinguinal n.
External spermatic v.
Genital branch of genitofemoral n.
Pubic tubercle

**Figure 113.10** Lichtenstein hernia repair. Mesh placement over inguinal floor.

technique including the Bard PerFix® Plug (CR Bard, Murray Hill, NJ, USA), which is placed in the defect and sutured to the transversalis fascia with an onlay over the inguinal floor (Figures 113.11 and 113.12). In addition, the Ethicon Prolene® hernia system, with combined preperitoneal and onlay patches, has also become popular (Figure 113.13).

As in repair of incisional/ventral defects, there is no generally accepted preferred method of inguinal repair. Only one caveat applies, the rate of recurrence should be comparable in the evaluation of different techniques. In high-volume centers and individual practices, the rate of recurrence should be comparable in either open or laparoscopic repairs and should clearly be under 5%. The decision to perform either open or laparoscopic repair is essentially up to the operating surgeon. It is not clear from the literature that laparoscopic repair for unilateral inguinal hernia offers superior results with respect to early recovery and recurrence rates. Therefore, many surgeons will perform open repair for unilateral hernia, reserving the laparoscopic approach for bilateral hernia and recurrences. Large or incarcerated inguinal hernias can be difficult to perform laparoscopically and are therefore done open or with an intraperitoneal laparoscopic technique. In addition, previous lower midline abdominal surgery can make laparoscopic repairs difficult.

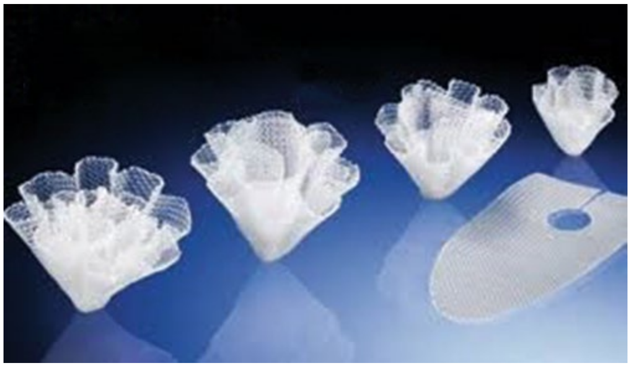

**Figure 113.11** Bard PerFix® Plug.

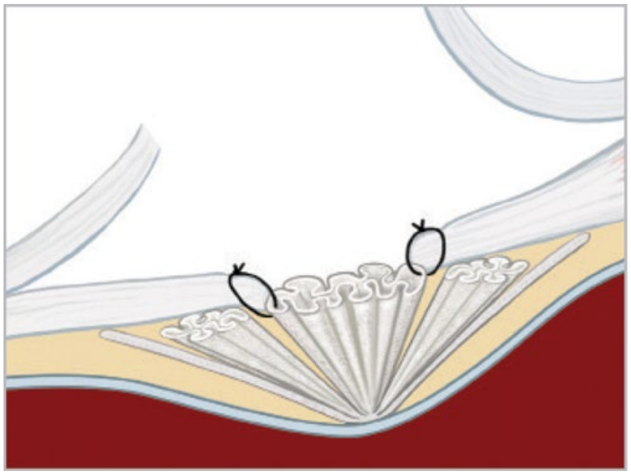

**Figure 113.12** Placement of plug through defect in transversalis fascia.

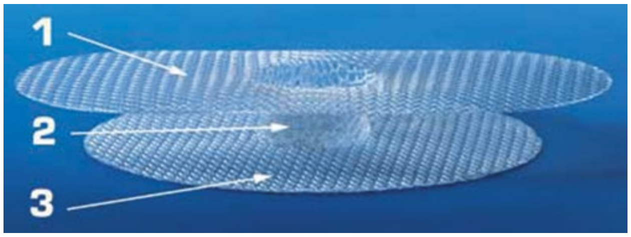

**Figure 113.13** Prolene hernia system: 1. Onlay patch, 2. connector, 3. sublay patch.

There are two popular types of laparoscopic repair currently in use. Total extraperitoneal (TEP) repair and transabdominal preperitoneal (TAP) repair both employ a mesh prosthetic placed in the preperitoneal space and therefore isolated from the viscera. A third technique involving intraperitoneal onlay mesh (IPOM) is also a viable technique, but somewhat less popular today.

For the TEP repair, the patient is given a general anesthetic, use of a Foley catheter is optional, although we have patients void just prior to entering the operating room. An incision is made in the infra-umbilical region and carried down to the anterior rectus fascia. On either side of the midline, an incision is made in the anterior fascia with elevation of the rectus muscles and exposure of the preperitoneal space. A balloon dilator is placed up to the pubis and inflated, thereby creating the working space for the repair (Figure 113.14). In general, two working ports are placed.

The hernia is identified (femoral, direct or indirect), reduced, and a mesh is then placed preperitoneally (Figure 113.15). The mesh is then fixed to the abdominal wall either with dissolving tacks or fibrin glue (Figure 113.16). With tack fixation, care is taken to avoid the triangle of doom and triangle of pain (Figure 113.17). At completion of the procedure, the pneumoperitoneum is evacuated with collapse of the preperitoneal space.

The TAP procedure is essentially similar to the TEP procedure and is only different in that access to the preperitoneal region is gained transabdominally. The peritoneum is incised over the myopectineal orifice, the mesh is placed and secured with closure of the peritoneal opening.

From the perspective of the endourologist, inguinal hernia will rarely complicate the genitourinary procedure being performed. Consideration may be given to simultaneous repair of the hernia at the time of the urologic surgery.

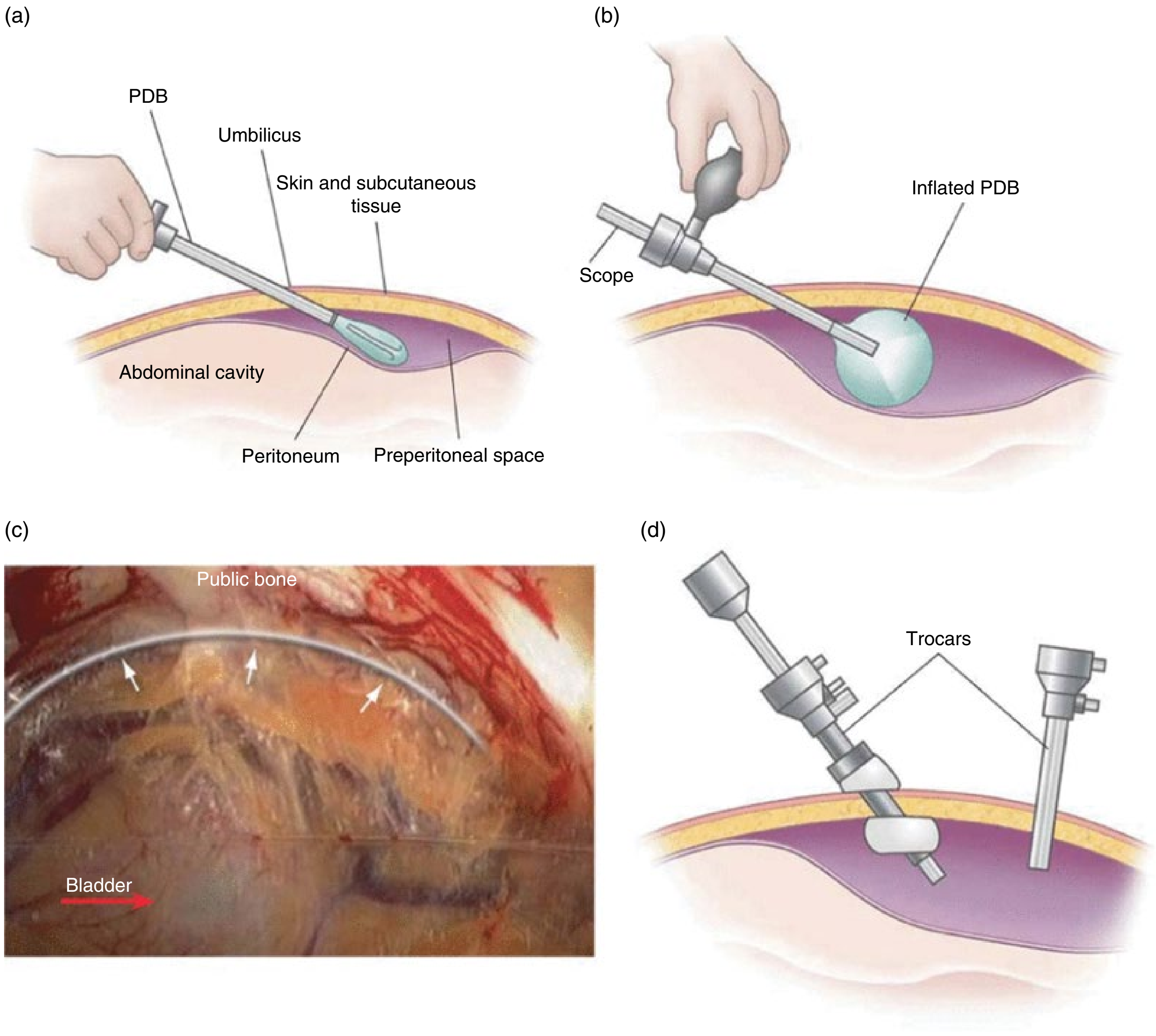

**Figure 113.14** Preperitoneal balloon dilator (PBD) and placement of working ports for total extraperitoneal (TEP) repair.

### Results of laparoscopic technique

With respect to repair of inguinal hernia, multiple series comparing laparoscopic to open techniques, and comparison of TEP and TAP repairs are reported. In general, series which compare open and laparoscopic techniques conclude that laparoscopic repairs have a slightly higher rate of recurrence. In 2012, a data analysis confirmed that there is a slightly higher recurrence rate in laparoscopic repairs compared to open repairs. In addition, TEP repairs were found to have a slightly higher recurrence rate than TAP repairs [13].

### Complications specific to laparoscopic repair

As in other minimally invasive procedures, there are complications unique to the laparoscopic approach. These are related both to mesh placement and the exposure necessary to complete the repair. Complications of laparoscopic inguinal herniorrhaphy occur in up to 13% of cases [14]. It is imperative that the surgeon has a full working knowledge of the preperitoneal anatomy of the groin. Injury to the femoral vein, iliac vein, and epigastric vessels have all been reported with potentially catastrophic consequences. In addition, injury to the femoral branch of the genitofemoral nerve, lateral femoral cutaneous nerve, and femoral nerve have all been reported. Small bowel obstruction after laparoscopic repair has been reported primarily due to two main factors: exposed mesh within the peritoneal cavity creating adhesions and entrapment of bowel within a peritoneal defect created at the time of the repair. As discussed previously, trocar site

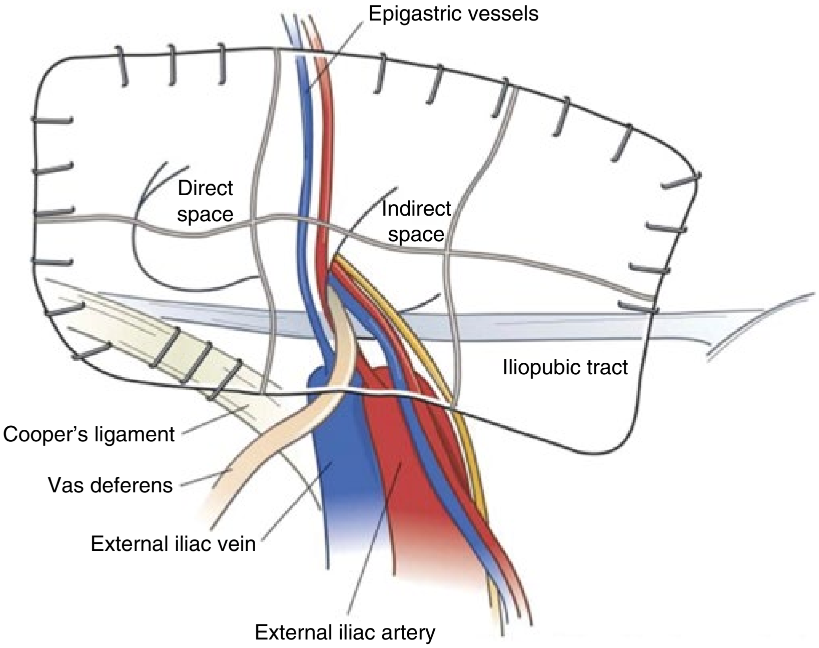

**Figure 113.15** Preperitoneal anatomy for total extraperitoneal (TEP) repair.

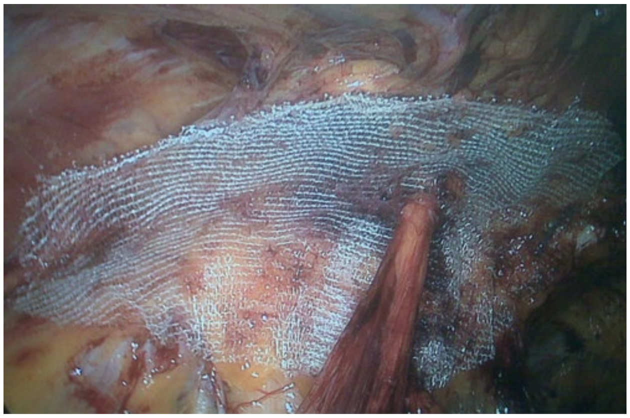

**Figure 113.16** Placement of mesh for total extraperitoneal (TEP) repair.

hernia can occur with 10 mm ports and rarely in 5 mm port sites. The use of cutting trocars with 10 mm fascial defects without closure are felt to be the primary cause of postop hernia. Many cases of Richter's type hernia in the trocar site can present with intestinal obstruction.

### Spermatic cord injury

Injuries to the testicular vessels leading to ischemic orchitis are well described in open inguinal hernia repair. These injuries occur much less frequently in the laparoscopic approach. Scrotal swelling and pain do occur as in open repairs and are related both to scrotal hematoma and irritation of the genital nerve. Hydrocele formation after laparoscopic repair is extremely rare and equals that found in open repair. Urinary retention also occurs with the same frequency as in open repair (2%).

Postoperative seroma and hematoma are relatively common in laparoscopic repair and most often resolve spontaneously. Regarding the use of mesh, infection after laparoscopic repair is extremely uncommon, as is erosion into surrounding structures. Infection and erosion of material requiring explantation and repair are rarely reported.

## Parastomal hernia

It is important for the endourologist to understand the causes and management of parastomal hernia. As with any iatrogenically created trephine, hernia complications are well described.

Parastomal hernia can lead to incarceration, poor fitting ostomy appliances with leakage, skin breakdown, and irritation (Figure 113.18). Parastomal hernias are reported to occur in as many as 50% of patients with a stoma [15] (Figure 113.19). Most often, these are elderly patients, considered high risk for surgical intervention who will end up living with a hernia without repair. In approximately 10–20% of patients, repair of parastomal hernia will become necessary secondary to symptoms of obstruction and poorly controlled stomal effluent. Of all surgically created ostomies, ileal conduit hernia carries an incidence of up to 6.5% [16]. Risk factors for the development of parastomal hernia are similar to those for incisional hernia. Elderly patients, high body mass index (BMI), respiratory comorbidity, cancer, and diabetes mellitus are all documented risk factors. Technical factors such as creating a small aperture size (less than 25 mm), stoma created through the rectus abdominis,

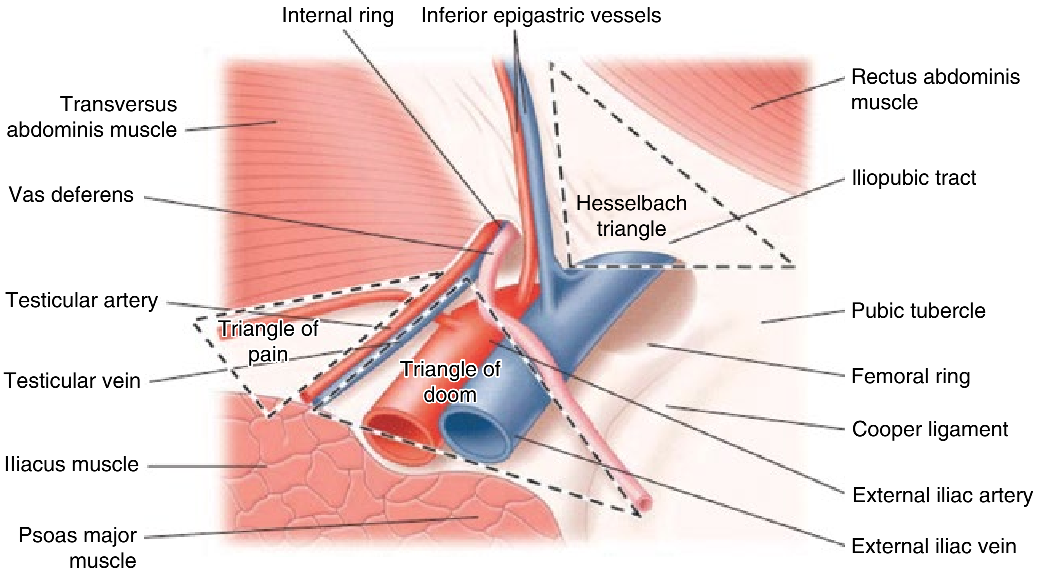
Internal ring
Inferior epigastric vessels
Transversus abdominis muscle
Vas deferens
Testicular artery
Triangle of pain
Testicular vein
Iliacus muscle
Psoas major muscle
Triangle of doom
Hesselbach triangle
Rectus abdominis muscle
Iliopubic tract
Pubic tubercle
Femoral ring
Cooper ligament
External iliac artery
External iliac vein

**Figure 113.17** Triangles of doom and pain.

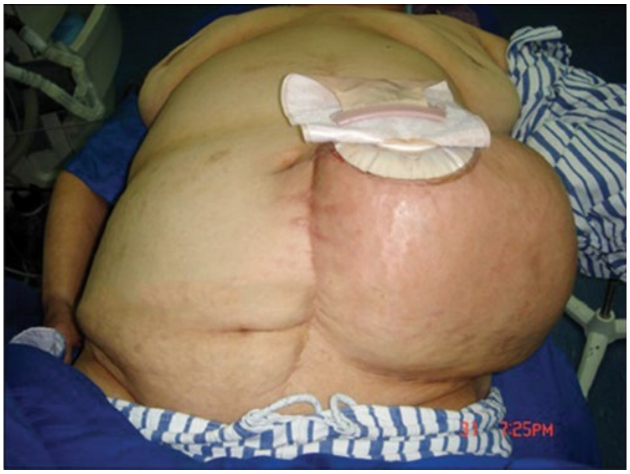

**Figure 113.18** Large parastomal hernia.

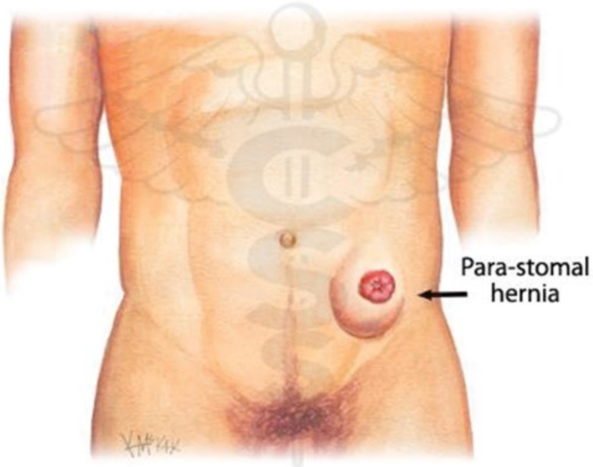
Para-stomal hernia

**Figure 113.19** Parastomal hernia.

and extraperitoneal stoma formation have all been studied and cited as important technical considerations. No randomized trials currently exist to evaluate these factors.

As stated, repair of parastomal hernia will only become necessary in a minority of patients. Symptoms of obstruction or incarceration are frequent indications for surgery, as is a poorly fitting ostomy appliance with chronic leakage. Initially, simple fascial closure of the defect around the existing stoma was used with poor results secondary to high rates of recurrence. This led to stoma relocation in which a laparotomy was necessary to close the existing defect and create a new stomal opening in the abdominal wall. Although still an alternative today, the magnitude of this approach carries higher attendant risk secondary to the laparotomy and potential for hernias at both the new and previous stoma sites.

As with incisional hernia repairs, the use of mesh in parastomal repair has gained acceptance. Both open and laparoscopic techniques are currently acceptable with mesh used to either bridge the defect or overlap the defect after closure. This can be accomplished as a mesh onlay or sublay with a keyhole cut around the bowel (Figure 113.20). Another technique, described by Sugarbaker, places mesh both around the defect and the stoma itself, with lateral egress of the bowel between the mesh and the abdominal wall at a distance of at least 5 cm from the stoma site [17] (Figure 113.21).

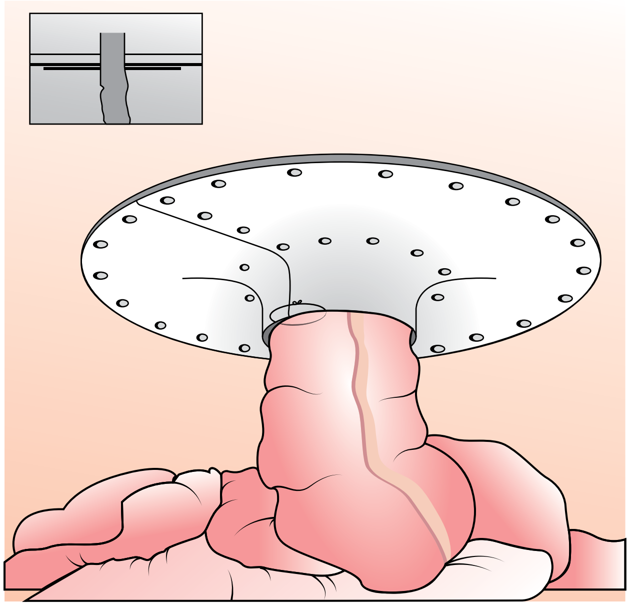

**Figure 113.20** Keyhole repair parastomal hernia.

Another technique, described by Berger and Bientzik, employs two layers of intraperitoneal mesh, one with a keyhole and a second to lateralize the stoma. The reported recurrence rate of this repair, initially performed in 47 patients, was 2.1% [18].

### Results

A meta-analysis by Hanson et al. in 2012 compared the results of parastomal hernia repair with respect to technique, mesh placement, keyhole, or Sugarbaker technique, and laparoscopic versus open repair. The analysis led to the following conclusions:

- Suture repair has a higher recurrence rate than mesh repair.
- Open and laparoscopic repair are comparable with equal rates of recurrence.
- The subgroup of laparoscopic repairs utilizing the Sugarbaker technique had a lower recurrence rate in the keyhole method [19].

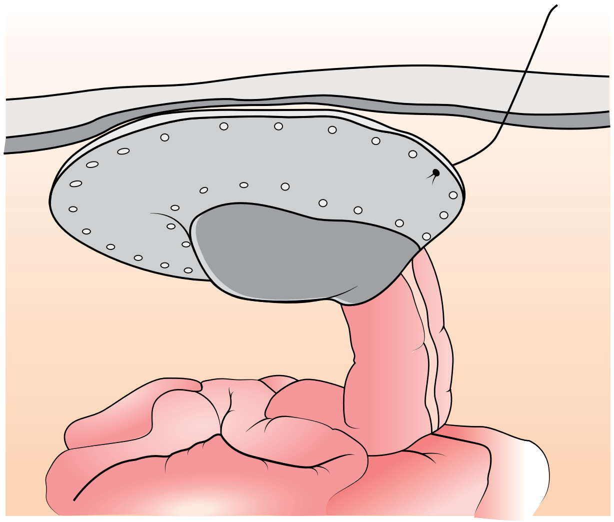

**Figure 113.21** Sugarbaker repair.

In more recent studies, the laparoscopic technique, as is true for other incisional hernias, shows a tendency towards shorter hospital stays and decreased surgical site infection [20]. Recent studies have also demonstrated that prophylactic mesh placed at the time of permanent stoma formation appears to decrease the incidence of parastomal hernia formation [21].

## Conclusions

A working knowledge of the current techniques employed in the repair of abdominal wall hernias is helpful for the practicing endourologist. With respect to technique, utilization of mesh prosthetics, and potential complications, any surgeon performing hernia repair should understand the potential outcomes and pitfalls. It should also be clear that a case can be made for either a laparoscopic or open approach depending on the clinical circumstances and experience of the operating surgeon.

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# 114

# Robot-Assisted Vasectomy Reversal

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## Introduction

Approximately 500 000 men in the United States undergo vasectomy every year. With a divorce rate of approximately 50% in the United States, up to 6% of men who have undergone vasectomy will elect to have the vasectomy reversed some time in their lifetime [1, 2]. Vasectomy reversal (VR) was described in the 1930s and the use of the operative microscope for magnification to assist in the anastomosis was applied in the 1970s with significantly improved patency rates [3–5].

For years, people have been dreaming of robots. Whether it has been for science fiction or for practical uses, the idea of robots mechanically assisting us with tasks has seemed appealing. We used to hear people say "some day robots will do surgery for us." This has not necessarily become the case, but robots are finding more utility in assisting us with surgery. The da Vinci® system began with uses for gross surgical procedures and has expanded its utility to microsurgery. In urology, this particularly lends itself to VR. Surgery that we initially tried with the naked eye advanced through multiple technologies including optical loupes, operative microscopes, and now the operative robot. The advantages of using robotics to assist with microsurgery include the ability of devices such as EndoWrists® to work with seven degrees of freedom, enabling movements that the human hand and wrist cannot make, an ergonomic design for the surgeon which is less fatiguing and that may enhance performance, the scalability of motion, and high-definition 3D optimal visualization of a microsurgical field. Once the learning curve for robotic microsurgery is mastered by microsurgeons it should improve operative times as well.

## Anatomy

Understanding the anatomy of the vas deferens and the epididymis is paramount to a successful outcome with VR and the same is true for robot-assisted vasectomy reversal (RAVR). The vas deferens is a tubular structure derived embryologically from the mesonephric (Wolffian) duct. It extends from the distal end of the cauda of the epididymis and the tortuous segment leaving the epididymis for the first 2–3 cm is known as the convoluted vas deferens. The vas deferens measures between 30 and 35 cm in length from the cauda epididymis to the ejaculatory duct, where it terminates. It travels behind the vessels in the spermatic cord, posteriorly. Depending on the segment, the lumen of the vas deferens ranges between 0.2 and 0.7 mm in diameter [6]. The deferential artery, a branch of the superior vesical artery, supplies the vas deferens [7]. The venous drainage of the scrotal vas deferens is via the deferential vein, which drains into the pampiniform plexus. The venous drainage of the pelvic vas deferens is via the pelvic venous plexus. The lymphatic drainage travels to the external and internal iliac nodes.

Sperm travel through the epididymis from the testis to reach the vas deferens. If uncoiled, the tightly coiled tubular epididymis would stretch to 3.5–4.5 m long. The three regions of the epididymis are characterized as the caput (head), the corpus (body), and the cauda (tail). The caput epididymis comprises 8–12 ductuli efferentes from the testis. The most distal portion of the cauda epididymis is continuous with vas deferens. The arterial supply of the caput and corpus epididymis is from a branch of the testicular artery, which further divides to

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supply the superior and inferior epididymal branches [8]. Branches from the deferential artery provide vascular supply to the cauda epididymis. Venous drainage of the corpus and cauda epididymis are via the vena marginalis of Haberer, draining into the pampiniform plexus via the vena marginalis of the testis, or through cremasteric or deferential veins [8]. Lymphatic drainage of the caput and corpus epididymis is through channels that travel with the internal spermatic vein, draining to the preaortic nodes. Lymphatic channels from the cauda epididymis join those leaving the vas deferens to drain into the external iliac nodes.

## Preoperative evaluation/physical examination

Prior to undergoing RAVR, the level of spermatogenesis in the patient should be assessed. A history of fertility from prior to the vasectomy is typically considered sufficient. A full physical examination should be performed prior to RAVR with special attention to the genital examination. Testicular volumes and consistency should be assessed. Firm, normal-volume testicles are indicators of good spermatogenesis, whereas small or soft testes may indicate some spermatogenic deficiency. It is not uncommon for the epididymis to feel dilated on examination in men who have undergone vasectomy. Epididymal induration may indicate the need for robot-assisted vasoepididymostomy (RAVE). When a large vasectomy defect or gap can be palpated, this should prompt counseling for a more extensive dissection to perform a tension-free anastomosis. When a sperm granuloma is palpated at the testicular end of the vas deferens, this indicates leaking of sperm as a result of a pop-off valve-like mechanism to decrease intraepididymal pressures. Sperm granuloma are associated with better outcomes with VRs, suggesting that the epididymis has protected itself by decreasing intraluminal pressures [9]. When physical examination reveals a very long vasectomy defect, a segment that has been removed, the surgeon should consider a nonstandard incision approach [10].

As more men are being diagnosed with hypogonadism and are being treated with testosterone replacement therapy, adversely impacting the level of spermatogenesis, medical management must be considered prior to performing RAVR in these men. Testosterone replacement should be discontinued, testicular salvage therapy with clomiphene citrate or human chorionic gonadotropin (hCG) should be implemented for approximately three months, and then RAVR can be performed with acceptable outcomes [11].

The obstructive interval since the vasectomy has a significant impact on the type of RAVR required, whether robot-assisted vasovasostomy (RAVV) or RAVE. This has been shown to affect patency rates in many studies on VR; in general, the longer the interval since vasectomy, the more challenging the candidate is considered to be for VR [12, 13]. However, in the hands of a surgeon who is proficient in both RAVV and RAVE, RAVR should still be offered to men with longer obstructive intervals. In technically skilled hands, success rates remain high regardless of the type of VR performed in men with obstructive intervals over 10 years [14].

Multiple nomograms have been constructed to predict the type of VR required and patency rates. Factors evaluated to assess these outcomes include patient age, testicular volume, the presence of sperm granuloma, and obstructive interval [15, 16]. There is a question over the accuracy of the nomograms and their utility with inconsistent data [17, 18]. As it is not typically possible to predict preoperatively if vasoepididymostomy will be required, VR should only be performed by surgeons skilled in both vasovasostomy and vasoepididymostomy [19, 20].

Before a man undergoes RAVR, his female partner should undergo a fertility evaluation, with counseling on female age and ovarian reserve impact on the couple's fertility potential [10].

## Preoperative laboratory testing

Semen analysis with a centrifuged evaluation of the pellet may be performed prior to VR. Ten percent of these centrifuged pellets will reveal whole sperm, suggesting good outcomes and indicating that sperm will be found in the vas deferens at least unilaterally at the time of VR [21]. When the semen analysis reveals low semen volume, transrectal ultrasound should be performed to rule out the possibility of a concomitant ejaculatory duct obstruction.

When the physical examination indicates potential spermatogenic deficiency with findings such as small, soft testicles, a serum follicle-stimulating hormone (FSH) should be obtained. An elevated FSH indicates spermatogenic failure, a potentially poor outcome with VR, and may be a predictor of the need for higher levels of assisted reproduction care [22]. Serum antisperm antibody (ASA) testing is not recommended as a routine preoperative test prior to VR. Approximately 60% of men develop circulating ASAs after bilateral vasectomy [23]. Preoperative ASA testing is of unproven value, and the high postoperative conception rate after VR questions the impact of circulating ASAs on fecundability [24–31].

## Anesthesia

RAVR may be performed with local, regional, or general anesthesia [10]. As meticulous robot-assisted microsurgical technique and tissue handling is mandated for superior outcomes, general anesthesia is the anesthesia of choice to minimize patient movement and to optimize patient comfort. Although RAVR can be performed with local anesthesia with sedation, this tends to result in more motion, which makes a challenging operation even more challenging. If a RAVE or a more difficult anastomosis is required, it may require lengthy operative times which can be difficult for the patient under local anesthesia or sedation.

## Patient positioning

The patient is placed in the supine position. After induction of general anesthesia, all pressure points are padded and the scrotum is shaved, prepared, and draped. Once the vasa are prepared and ready for the anastomosis, the operative robot is brought in from the patient's right side at a 90° angle with the 0° camera placed directly over the operative field of the scrotal incision, perpendicular to the floor (Figure 114.1).

## Incision approaches

The scrotal incision provides the most direct access to the vasectomy defect to isolate the ends of the vas deferens for anastomosis. In scenarios with high vasectomy defects or long vasectomy defects, the incision may be extended toward the external inguinal ring. The testis may be delivered in cases with a very low vasectomy defect or when a RAVE is deemed necessary. Mini-incision VR using no-scalpel vasectomy principles has been evaluated and found to have comparable patency rates with less postoperative pain and faster functional recovery [32, 33]. Mini-incision RAVR is the author's approach of choice, using an incision less than 1 cm.

In men who have previously undergone varicocele repair or inguinal hernia repair, the surgical approach to RAVR will vary. If a man has undergone varicocele repair for orchialgia or for hypogonadism with a concomitant vasectomy, the RAVR should be approached through the prior subinguinal incision after confirming that the vasectomy was performed subinguinally by previous operative report. In men who have suspected vas deferens obstruction from previous inguinal herniorrhaphy, approaching the RAVR through the previous scar will lead to the site of the vas deferens obstruction. RAVR following herniorrhaphy has also been performed intra-abdominally with robot assistance. This is a prime example of the robotic platform's ability to improve access to a difficult vas deferens repair [34, 35].

## Preparing the vas deferens

Once the vasectomy defect is isolated through the incision, the abdominal and testicular ends of the vasa may be isolated with the use of vessel loops. Care should

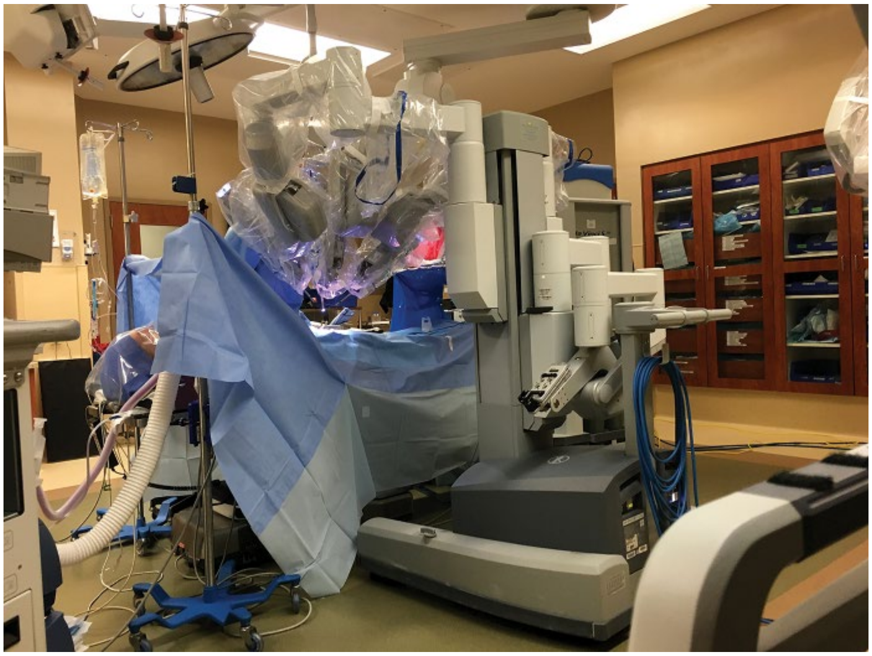

**Figure 114.1** The robotic system is positioned at a 90° angle to the patient with the camera positioned directly above the operative field (view from console).

be taken to not strip the vas deferens of the perivasal adventitia to maintain the microvasculature supply to the vas deferens. The abdominal and testicular ends of the vas deferens are adequately mobilized, with its adventitia intact, to allow for a tension-free anastomosis. The obstructed segment of the vas deferens at the vasectomy defect site may be excised or excluded. Care should be taken to preserve the deferential artery during this maneuver. After the testicular and abdominal ends of the vas deferens are isolated, the testicular end of the vas deferens is sharply divided at an exact 90°. The divided end of the vas deferens should have the muscularis and the mucosa inspected to confirm that there is a healthy surface to anastomose without fibrosis or scar.

Fluid from the testicular lumen of the vas deferens is then applied to a glass slide, diluted with a drop of saline, and examined under the light microscope (Figure 114.2). The quality of the fluid from the testicular end of the vas deferens and the microscopic findings dictate whether a RAVV or a RAVE should be performed. If microscopic examination of the vasal fluid reveals whole sperm with tails (Figure 114.3) or when there is copious, clear fluid from the vas deferens but no sperm are found in the fluid, RAVV should be performed. If fluid is not present, a 24 gauge angiocatheter sheath is cannulated into the lumen of the testicular end of the vas deferens and barbotage is performed with 0.1 ml of saline, which is then microscopically examined. If there is no significant vasal fluid or sperm identified after this maneuver, a RAVE should be performed. When the vasal fluid appears thick and toothpaste-like in quality, sperm are typically not found on microscopic examination of the fluid, and RAVE is indicated.

Over 90% of VRs will be successful when sperm fragments (sperm heads and/or short tails) are found in the vasal fluid intraoperatively, regardless of the fluid quality. This success rate surpasses the expected success rate with vasoepididymostomy [36, 37]. Sperm quality has been categorized in five grades to describe the findings in the vasal fluid. Grade 1 reveals mainly normal motile sperm, grade 2 mainly normal nonmotile sperm, grade 3 mainly sperm heads, grade 4 only sperm heads, and grade 5 no sperm [38, 39].

The abdominal end of the vas deferens is divided in a similar manner. The lumen is gently cannulated with a 24 gauge angiocatheter sheath and saline is injected into the lumen to demonstrate patency (Figure 114.4). Once abdominal vasal patency has been demonstrated, the ends of the testicular and abdominal vas deferens are approximated with the use of a Microspike approximating clamp, or with carefully placed 6-0 polypropylene adventitial sutures to approximate the ends with the help of an assistant. A Penrose drain covered metal ruler or tongue blade is then placed beneath the approximated

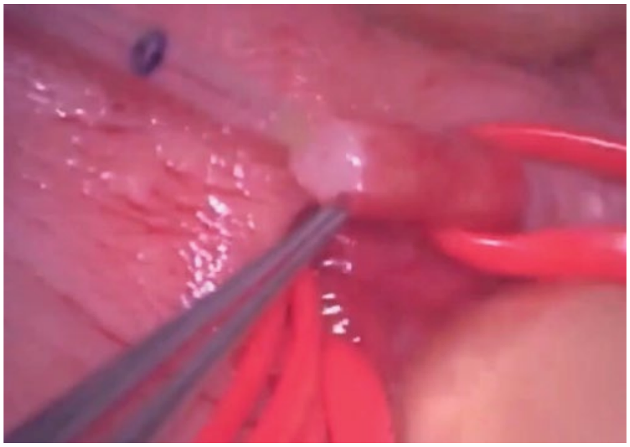

**Figure 114.2** Obtaining vasal fluid from the testicular end of the vas deferens to evaluate under the microscope.

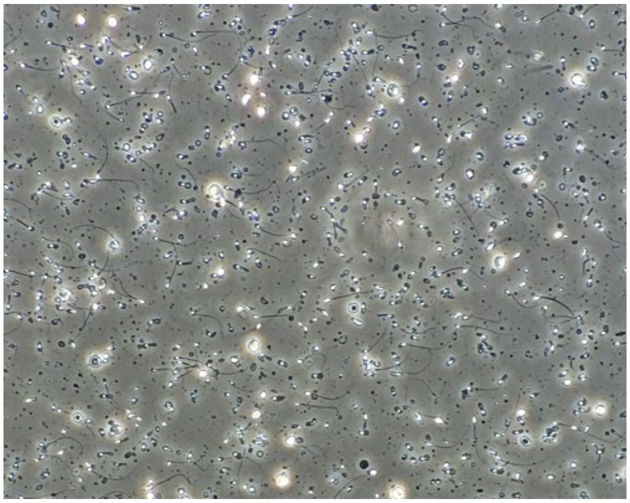

**Figure 114.3** Whole sperm visualized under the light microscope in the vasal fluid.

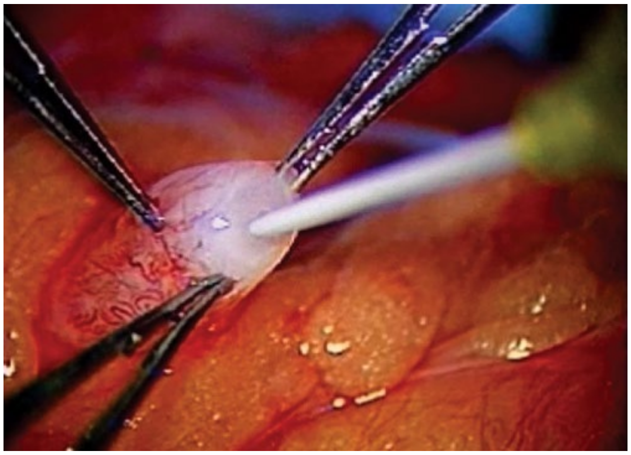

**Figure 114.4** Injection of saline through the abdominal end of the vas deferens to demonstrate downstream patency.

ends to provide a template for the anastomosis. If when saline is injected into the lumen of the abdominal end of the vas deferens the saline does not easily flow and there is high pressure, it suggests that there is no patency and that there is another obstruction further downstream in the abdominal end of the vas deferens. A 2-0 polypropylene suture is carefully passed through the lumen of the abdominal vas deferens to encounter the site of distal obstruction. If this obstruction is isolated within 5 cm of the initial vasectomy site, the abdominal end of the vas deferens may be dissected to the obstruction site and excised to perform one anastomosis after further mobilization of both ends to allow for a tension-free anastomosis. This may require extension of the incision. Performing multiple anastomoses on the vas deferens increases the risk of devascularization and failure.

## Anastomosis pearls

A high level of robotic microsurgical expertise is required for optimal RAVR outcomes. Prognostic advantages are gained by strict surgical principles during the anastomosis. The luminal mucosa of the abdominal and testicular ends of the vas deferens should be approximated meticulously. The anastomosis should be watertight as sperm are antigenic and will stimulate an inflammatory response which can lead to fibrosis and obstruction of the anastomosis if they leak at the anastomosis [40]. A tension-free anastomosis is crucial for long-term success. Mobilizing the abdominal and testicular ends of the vas deferens and placing reinforcing muscularis sutures to minimize tension on the anastomosis will improve long-term patency rates. A minimal touch technique, with as little manipulation as possible of the vasal ends for anastomosis is paramount to a successful outcome, as is maintaining microvascular supply to the vas deferens by maintaining the vasal adventitia and not stripping the vas deferens.

## Robot-assisted vasectomy reversal

VR has traditional been performed with magnification through the use of the operative microscope. Recently, da Vinci® robot assistance has been applied to VR. Robotic assistance was first utilized *ex vivo* on human vas deferens to perform RAVV, and it was found that it eliminated physiological tremor and gave comparable patency rates, suggesting that the operative robot may be used as an alternative to the operative microscope [41]. RAVV and RAVE were then performed in the rat model. The findings were improved stability and motion reduction during suturing of the anastomosis [42]. A multilayered RAVV was performed in an *in vivo* rabbit model with comparable patency rates, reinforcing the suggested role of robotics in microsurgery [43]. RAVR was performed in humans and resulted in shorter operative times and higher sperm counts in early postoperative semen analyses when compared to microsurgical VR [44]. A validating human study on RAVR compared to microsurgical VR demonstrated comparable patency rates, operative times, and early postoperative sperm concentrations and total motile counts. Although the mean anastomosis time in the RAVV group was statistically significantly longer in the early robotic experience than in the microsurgical group, this equated to a 10-minute longer mean anastomosis time clinically in the RAVR group [45].

The suggested advantages of the use of the operative robot for RAVR include: elimination of physiologic tremor, improved stability, surgeon ergonomics/decreased surgeon fatigue, scalability of motion, 3D high-definition visualization, the ability of the surgeon to manipulate three surgical instruments and the camera simultaneously, not requiring a specialty skilled microsurgical assistant, and the potential of improving operative times [45]. This early data show promise, but large-scale prospective, randomized controlled trials are needed to validate the broader adoption of robot assistance for VR.

The robotic platform provides advantages for more challenging scenarios such as intra-abdominal VR following laparoscopic vasectomy or in men with vasal obstruction due to inguinal hernia repair with mesh [34, 35].

## Robot-assisted microsurgical vasovasostomy

The same microsurgical tissue-handling principles that are used during microsurgical VR are applied to RAVR. The robotic microsurgical Black Diamond forceps are utilized in both the right and left robotic arms. The 0° camera is utilized and the 4× setting is selected. Scalability of motion is set at 3:1. RAVV may be performed by a modified one-layer anastomosis, placing 4–8 interrupted 9-0 Nylon sutures through the full thickness of each end of the vas deferens lumens (Figure 114.5). The same microsurgical principles of needle and suture handling that are used with microsurgical instruments should be applied to the robotic Black Diamond forceps in order to not bend needles or break sutures. Following the placement of these sutures, interrupted 9-0 Nylon sutures are placed between these full-thickness sutures in the muscular layer (Figure 114.6) [46]. Once completed, the anastomosis should be watertight and the vasal adventitia should be maintained to decrease the risk of stricture from microdevascularization (Figure 114.7).

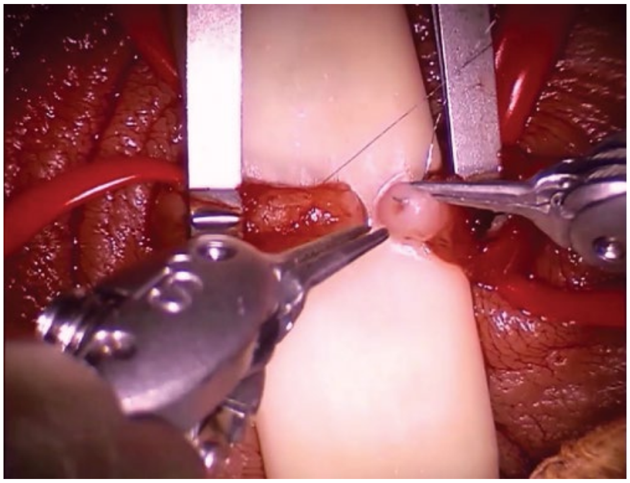

**Figure 114.5** Placement of a transluminal anastomotic suture with robot assistance.

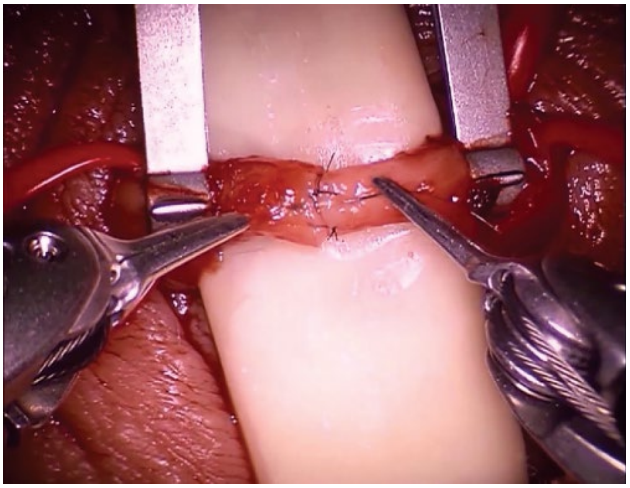

**Figure 114.6** Placement of interrupted suture in the seromuscular layer of the vas deferens between the transluminal anastomotic sutures with robot assistance.

Some surgeons prefer a two-layer anastomosis, which is performed by placing 5–8 10-0 Nylon interrupted sutures to approximate the inner mucosal edges of the ends of the vas deferens. Following the placement of these mucosal sutures, 7–10 outer muscular layer interrupted sutures of 9-0 Nylon are placed [39]. Experienced robotic microsurgeons compensate for the discrepancy in luminal diameters between the abdominal and testicular ends of the vas deferens during the anastomosis. Some place microdots with a microtip marking pen to preplan suture placement prior to performing the anastomosis [47]. This technique utilizes interrupted 10-0 monofilament Nylon sutures for mucosal approximation and interrupted 9-0 monofilament Nylon sutures deep in the muscularis in between the already placed mucosal sutures.

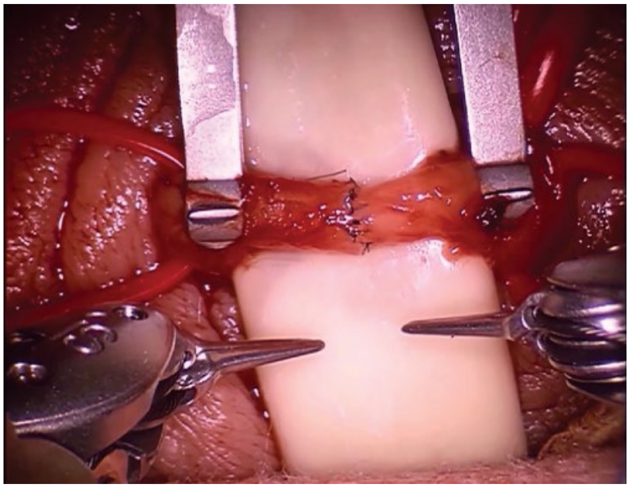

**Figure 114.7** The appearance of a watertight anastomosis with the vasal adventitia intact upon completion of a robot-assisted vasovasostomy.

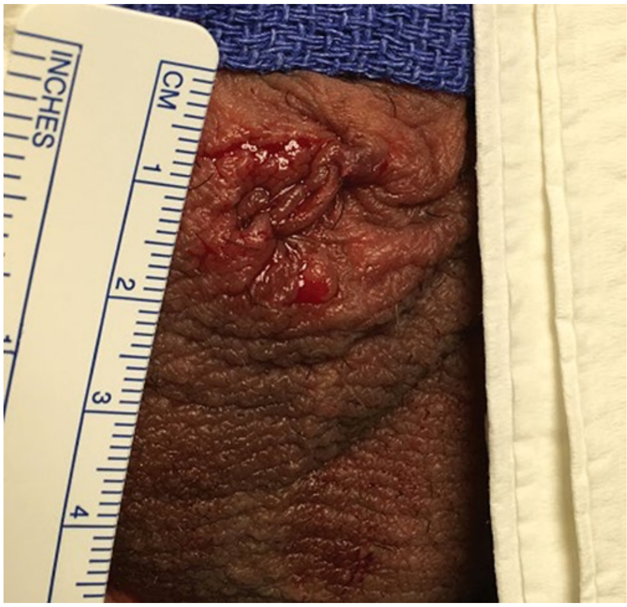

**Figure 114.8** Demonstration of a single <1 cm incision after closure following bilateral robot-assisted vasovasostomies.

When vasovasostomy is performed in the convoluted vas deferens, meticulous technique is mandated for a successful outcome. Although this anastomosis is more technically demanding, patency rates are comparable to anastomosis in the straight portion of the vas deferens when performed by skilled microsurgeons [48, 49]. The majority of RAVVs may be performed through one small incision, typically less than 1 cm in length, which assists with recovery and leaves a very small cosmetic incision with absorbable skin sutures (Figure 114.8).

A useful maneuver in difficult circumstances is the trans-scrotal crossed vasovasostomy. This technique allows for anastomosis of one testicular end of the vas deferens to the contralateral abdominal end of the vas deferens. It is used when there is unilateral inguinal vas deferens obstruction associated with an atrophic testis on the contralateral side, or obstruction of an inguinal vas deferens and epididymal obstruction on the contralateral side [1, 39, 50, 51]. Repeat VR is a valid option for men who failed an initial VR. The decision to perform a repeat VR should be based on the obstructive interval, the original VR, and the experience of the surgeon[52, 53].

When vasovasostomies are performed after sperm is found in the vasal fluid of at least one side, postoperative patency is demonstrated by the presence of sperm in the ejaculate in up to 99.5% of men [47]. One-layer vasovasostomy and two-layer vasovasostomy have been shown to have similar patency rates [54, 55]. Pregnancy rates within 2 years of VR of 52% have been achieved and up to 63% with exclusion of female factor and when based on female partner age and the time since vasectomy [9, 56–60]. Postoperative semen quality and female factors and age of the female partner determine the rates of spontaneous conception in couples after VR [54, 61].

## Robot-assisted microsurgical vasoepididymostomy

RAVE is a highly technically demanding operation and should only be performed by robotic microsurgeons with appropriate training and experience in this operation who perform it frequently. When the decision to perform a vasoepididymostomy is made, anastomoses are less technically challenging and more likely to succeed in the distal regions of the epididymis, as the epididymal wall thickens more distally with more smooth muscle cells. As the corpus and cauda of the epididymis is a single microscopic tubule, obstruction at any point will lead to a complete blockage of sperm from entering the vas deferens. The use of magnification significantly improves vasoepididymostomy patency rates [62, 63].

Multiple techniques have been employed to perform vasoepididymostomy. It may be performed by end-to-end or end-to-side anastomosis [19, 20], but the end-to-end anastomosis has fallen out of favor for the most part. The end-to-side vasoepididymostomy is performed by identifying the presence of markedly dilated epididymal tubules and approximating the muscularis and adventitia of the vas deferens to a specific opening in the tuinca of the epididymis. This is a relatively bloodless and atraumatic technique [20, 63–67]. The testis is delivered through a scrotal incision. The vas deferens is isolated with a vessel loop at the junction of the straight and convoluted vas deferens. The vas deferens is transected sharply and is prepared as previously described above. The tunica vaginalis is incised and the epididymis is inspected under magnification. The anastomotic site on the epididymis is identified where tubules are dilated, proximal to the suspected obstruction. A 3–4 mm incision is made in the tunica with the tip of the robotic micro-Potts scissors overlying the dilated tubules. The epididymal tubules are gently dissected and exposed.

The end of a 10-0 Nylon needle is used to puncture the selected epididymal tubule and the fluid is examined microscopically to identify sperm. The vas deferens is secured to the epididymal tunica with 3 or 4 interrupted 6-0 polypropylene sutures with positioning allowing the vasal lumen to reach the opening of the epididymal tunica without tension. Under high magnification, interrupted 10-0 monofilament Nylon sutures double armed with fishhook-tapered needles are used to approximate the posterior mucosal edge of the epididymal tubule to the posterior vasal mucosa. Two to four additional 10-0 sutures are used for the anterior mucosal anastomosis. Six to ten additional interrupted 9-0 sutures are used to approximate the outer muscularis and adventitia of the vas deferens to the incised edge of the epididymal tuinca. The robotic system is undocked and the testis and epididymis are carefully placed back in the tunica vaginalis and the scrotum is closed in layers.

The authors preferred technique for RAVE is the two-stitch intussusceptions technique. Two parallel needles of double-armed 10-0 Nylon sutures are placed in the dilated epididymal tubule longitudinally without pulling them through to avoid leakage of tubular fluid and collapse of the dilated tubule. The end of a 10-0 Nylon needle or the tips of the robotic microsurgical Potts scissors are used to make an opening longitudinally in the tubule between the parallel placed sutures. The fluid is examined microscopically for the presence of sperm. The needles of the pre-placed 10-0 Nylons are then passed inside out the vas deferens mucosa to perform the intussuscepted anastomosis (Figure 114.9) [63, 67–69]. The muscularis and adventitia are anchored to the epididymal tunica as described above.

In the hands of experienced, skilled microsurgeons, vasoepididymostomy patency rates are reported between 50% and 85% [68, 70]. Men who underwent the classic end-to-side or older, less commonly performed end-to-end anastomosis will have respective patency and pregnancy rates of approximately 70% and 43% [62, 71]. For the intussuscepted techniques, patency rates range between 70% and 90% [63, 67, 72].

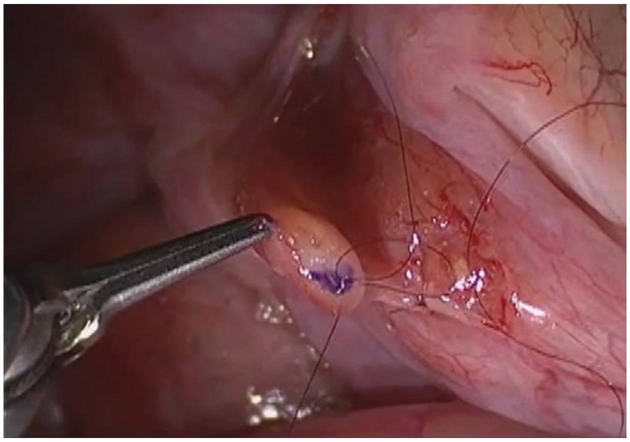

**Figure 114.9** Performing the anastomosis of a robot-assisted vasoepididymostomy with a two-suture intussuscepted technique.

## Postoperative care

Immediately following RAVR, the patient should be placed in a tight-fitting scrotal supporter with fluff gauze. Postoperative antibiotics are not indicated. Analgesics may be given. Most men return to work three days postoperatively as long as they do not partake in heavy or physical activity at work. No intercourse, ejaculation, exercise, or strenuous activity is allowed for three weeks after surgery. Semen analysis is obtained at six weeks, three months, and six months postoperatively and every six months thereafter until the couple achieves a pregnancy or further assistance is required. If azoospermia persists at six months postoperatively, this indicates a failure of the procedure.

## Complications

Hematoma and infection are rare complications of RAVR. Late stricture and obstruction are represented by progressive loss of sperm motility followed by decreasing sperm counts and eventually azoospermia in some men. Late obstruction has been reported to range between 5% and 12% at 18 months following VR [72, 73]. As a precaution, it is recommended that men cryopreserve sperm once motile sperm are identified in the ejaculate after RAVR as a safety backup.

See accompanying Video 114.1 .

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# Part 6 Laparoscopy/Robotics in Children

## 115

## Laparoscopic Considerations in Children

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### Introduction

Laparoscopy in pediatric urology began in 1976, when Cortesi et al. reported diagnostic laparoscopy to evaluate nonpalpable testes [1]. Since then, laparoscopy in children has gained widespread popularity. It has become a safe and effective approach for several different pediatric urologic procedures.

In 1991, Bloom introduced laparoscopic ligation of testicular vessels for first-stage Fowler–Stephens [2]. A year later, Jordan and Winslow described the first laparoscopic orchiopexy [3]. Work by these early pioneers led to diagnostic laparoscopy becoming the gold standard approach to evaluating nonpalpable testes. More importantly, laparoscopic orchiopexy, whether single or staged, has become an advantageous approach to treating high intra-abdominal testes [4, 5].

In its infancy, laparoscopy was adopted slowly by pediatric urologists. The instruments were cumbersome and limited, making the procedures technically challenging laparoscopically, while open surgery had very high success rates. Today, with the advancements of minimally invasive tools for pediatric patients, new technology, and increase in surgeon experience, laparoscopy has found a niche in pediatric urology as a safe, effective, and well-established alternative to many pediatric urologic procedures beyond orchiopexy, including nephrectomy, partial nephrectomy, pyeloplasty, hernia repair, varicocelectomy, bladder reconstruction, and antireflux surgery [6, 7]. The first pediatric laparoscopic nephrectomy was described by Koyle et al. in 1993 [8].

In July 2000, the US Food and Drug Administration approved the use of the da Vinci™ Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA). Robotic surgery has now replaced several of these laparoscopic procedures, but laparoscopy still has a role to play.

### Safety and efficacy

Initial criticism towards laparoscopy included the longer operative times and high success rates with open procedures through small incisions that obviated the need for a minimally invasive approach. In the hands of skilled surgeons, the benefits of pediatric laparoscopy are similar to those in adults: it offers decreased incisional pain, shorter recovery times, and enhanced cosmesis [9, 10].

Complications rates are relatively low. Laparoscopic orchiopexy is still the most common laparoscopic procedure performed by pediatric urologists, and success rates are as high as 90% with complications rates less than 3.0% [11]. Peters reported a complication rate of 5.4% in 5400 pediatric urologic laparoscopic cases. This number decreased to 1.2% once preperitoneal insufflation was excluded. This same study found that surgeon experience was the strongest predictor of complication rates [12]. In a recent systematic review, Kim et al. reported a complication rate of 3.5% in transperitoneal laparoscopic renal surgery [13]. In a prospective study by Penn et al., laparoscopic pyeloplasty was found to be a safe and effective alternative to open approach, providing shorter hospital stays and similar postoperative outcomes [14].

### Indications

As mentioned above, laparoscopy has become the gold standard for evaluating nonpalpable testes. It provides a quick assessment of intra-abdominal space through a small incision at the umbilicus (Figure 115.1). If an intra-abdominal testis is discovered, the size and location

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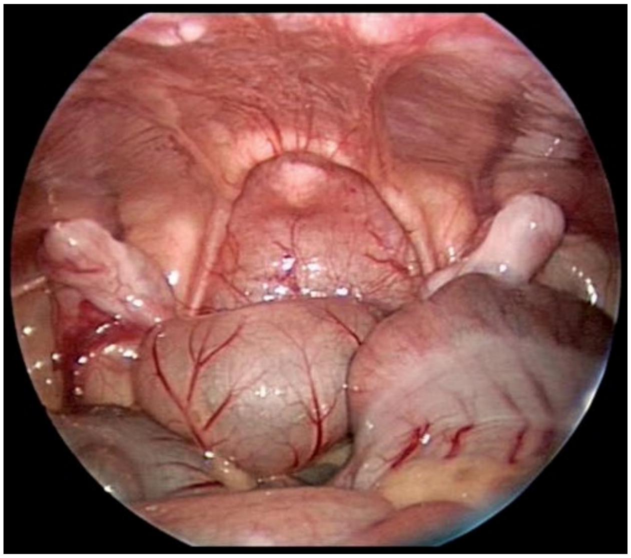

**Figure 115.1** Diagnostic laparoscopy aids in locating the position of intra-abdominal testicle. Depending on its position, the decision can be made to perform a single or staged laparoscopic orchiopexy, or an open inguinal orchiopexy.

are noted and the decision to proceed with laparoscopic single or staged orchiopexy can be made. If blind-ending vessels are noted in the rare case of vanishing testes, then no further action is needed and the patient spared an extrainguinal incision for exploration [4, 15].

Laparoscopic nephrectomy is usually indicated for removal of nonfunctioning kidneys secondary to obstruction, ureteral ectopia, or vesicoureteral reflux. The approach can be transperitoneal or retroperitoneal, with the former affording lower complication rates [13]. Laparoscopic nephroureterectomy and partial nephrectomy is performed to remove upper or lower pole moieties that are obstructed and nonfunctioning. Many authors argue that visualization of the renal vessels and moieties in a duplex system is much clearer laparoscopically than in open, helping to decrease the potential risk of vascular injury [15].

Laparoscopic pyeloplasty was first introduced by Peters in 1995 for treatment of ureteropelvic junction obstruction [16]. The procedure is technically challenging, but has good surgical outcome in high-volume centers [14]. This procedure has been replaced by a robot-assisted approach, but at several institutions around the world where robotics are unavailable, laparoscopic pyeloplasties are still being performed.

Other uses for laparoscopy include ureteral reimplantation, ligation of spermatic vessels for varicoceles, and reconstructive cases. Laparoscopic continence antegrade enemas and appendicovesicostomies have high success rates, decreased postoperative wound issues, and shorter convalescence times than the more morbid open procedures. Laparoscopic approach allows access to both upper and lower parts of the abdomen without having to make a large midline incision [17, 18].

## Anatomical and physiologic considerations

When considering a minimally invasive approach in children, one must be cognizant of the anatomic and physiologic differences between pediatric and adult populations. Pneumoperitoneum can produce significant changes to cardiac, respiratory, and autonomic physiology that must be recognized by both surgeons and anesthesia team.

Pneumoperitoneum can decrease ventricular preload, and although in children with normal cardiac function the changes are well compensated and the effects are negligible, in patients with congenital heart defects the result can be deleterious [19]. Moreover, abdominal distention can spark increased vagal tone and subsequent bradycardia, which can further decrease cardiac output in patients with cardiac insufficiency [20]. Temporary desufflation and reinsufflation at lower intra-abdominal pressures may be necessary. Patients with known cardiac issues will need preoperative consultation with cardiology and even cardiac anesthesia at the time of surgery.

In children, chest wall compliance is increased while functional reserve capacity (FRC) is decreased. Pneumoperitoneum can cause increases in mean airway pressure and end-tidal $CO_2$, which further decreases FRC and lowers oxygen saturation [19]. Hypercapnia can also result due to the increased absorption of insufflated $CO_2$ gas across the peritoneum into the bloodstream. With these changes, alterations to minute ventilation may be required to restore normal end-tidal $CO_2$ levels. It is imperative for the anesthesia team to be aware of these slight physiologic changes and to make the appropriate adjustments in a rapid, timely fashion [21].

Increase intra-abdominal pressure in children reduces urine output, but this effect is transient and does not result in permanent renal damage [22]. Temperature regulation is another concern in the pediatric population. Children lose heat more rapidly than adults because of their greater ratio of surface area to body mass, and appropriate warming devices and temperature monitoring should be utilized by anesthesia throughout the case [23].

Abdominal wall compliance is increased in children, but the intraperitoneal space is comparatively small. Lower insufflation pressures at 4–12 mmHg (vs. 15 mmHg in adults) and decreased gas flow rates 1–3 l/min (vs. 40 l/min in adults) are necessary to avoid overdistention of the intra-abdominal cavity and severe physiologic changes. The pliability of the abdominal wall helps to maintain lower intra-abdominal pressures while achieving adequate insufflation volumes in an otherwise small cavity, allowing sufficient intra-abdominal working space for surgeons.

Given that the cavity is small, visceral organs and major vessels are in close proximity to one another, increasing the risk of injury upon initial entry into the abdomen. The pediatric abdominal wall requires less force for entry but is extremely pliable and thus once must take extreme caution when placing trocars (Figure 115.2a,b). The smaller abdominal area in the pediatric patient also means care must be taken when placing ports to ensure there is enough distance between the ports so that there is freedom of movement.

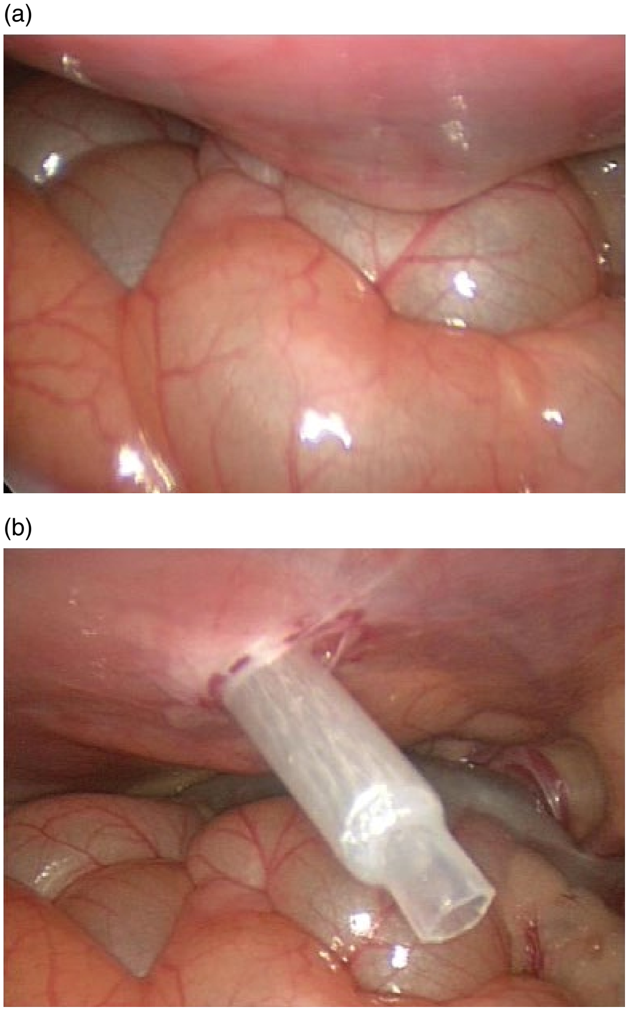

**Figure 115.2** (a) Note the abdominal wall compliance during entry of the port. (b) Placement of the step trocar.

## Instrumentation

The development of pediatric size-appropriate trocars and instruments has allowed laparoscopy to be more feasible and safer in the hands of experienced surgeon. Access is obtained using a Veress needle technique or an open technique. The Veress needle is a spring-loaded needle and punctures through the abdominal wall and then retracts once in the cavity to prevent visceral injury. Insufflation of the abdomen occurs though the Veress needle and then the initial trocar placement is performed blindly through the distended abdominal wall. Open techniques include box-stitch technique, Hasson cannula system, or radially dilating trocar, all of which involve an incision through fascia and ports placed while directly visualizing the viscera below. Direct open access through the umbilicus at its urachal attachment has gained popularity.

Pediatric trocars are smaller in diameter and shorter than their adult counterparts. Trocar diameters range from 3 mm to 5 mm in size. The 3 mm and 4 mm ports are metal and reusable, whereas the 5 mm ports are disposable and a step system can be used to prevent accidental dislodging of the port when removing instruments from the cannula. The camera port is usually 5 mm to accommodate the laparoscope. Instruments vary from 3 mm to 5 mm in size to accommodate the respective ports and are also shorter in length.

Endoscopic staplers now come in pediatric sizes that range from 2.5 mm to 12 mm to accommodate any size trocar that is being used. Pediatric LigaSure™ devices, electrocautery instruments, and clip appliers are also available. One must be careful with use of monopolar cautery as the tips get hot and may cause injury to nearby structures with direct contact. Moreover, because it is so small, the intra-abdominal cavity can overheat with excessive use of cautery.

## General complications

Laparoscopy introduces its own set of complications, including failure of instruments, camera failure, or problems with the insufflation. Complications can extend operative time, in particular time under anesthesia, which is especially important in the pediatric patient. Surgeons, nurses, and scrub technicians should be trained to troubleshoot these problems intraoperatively.

At the start of the case, patients are positioned and padded securely to prevent shifting or positional related injuries. During certain laparoscopic renal cases, patients are positioned in modified flank positioning, which

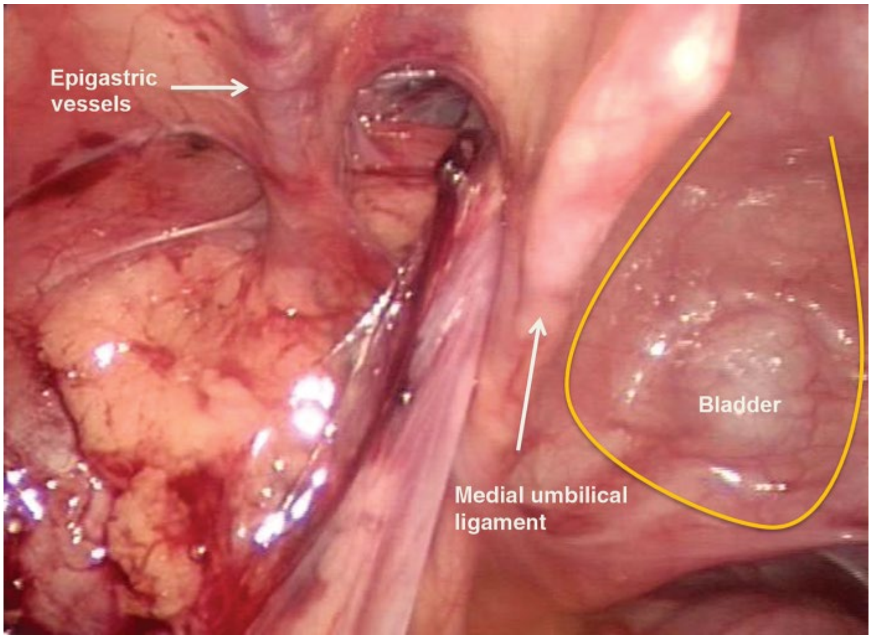

**Figure 115.3** Bladder injury during creation of neohiatus for a laparoscopic orchiopexy is of great concern given the close anatomic location to areas of interest during this procedure.

places stress on certain dependent portions of the body. Proper positioning is an important step to reduce neuromuscular injuries and decrease the chance of rhabdomyolysis. This step should not be ignored.

Complications in pediatric laparoscopic urologic surgery are similar to those in the adult: access or trocar injury, bleeding, hypercapnia, instrument failure, gas embolism, bowel or bladder injury, and thermal injury. In the literature, most complications do not require conversion to open. Esposito et al. reported a 0.85% conversion rate to open to repair complications [24]. Due to the smaller anteroposterior diameter of the pediatric patient, care must be taken in particular during access and trocar placement as previously mentioned. Open peritoneal access has been associated with lower complication rates than with Veress needle, with a 0.4% reported rate of epigastric and iliac vessel injury, and 0.1% rate of small bowel injury [25]. Bowel injury is a concern during laparoscopy during trocar placement, instrument passage, and use of cautery. Small injuries can be repaired laparoscopically, but larger injuries may require laparotomy and possible intraoperative consultation with a pediatric general surgeon.

Port-site herniation is a rare complication in pediatric population, but has been reported. Omental and bowel herniation rates have been reported 0.15%. Typically, 5 mm ports are left open in adults, but the fascia should be closed in children to prevent this complication [12, 26]. In contrast, 3 mm port sites are not typically closed, but there has been a reported omental herniation [27].

Bladder injury can be seen in laparoscopic orchiopexy and typically occurs at the time of neohiatus creation, with instrument passage to/from the scrotum (Figure 115.3). Reported rates in the literature are 0.03–0.17% [12, 28]. Steps to reduce risk of bladder injury include placing a urethral catheter during the case to empty the bladder, and adequate knowledge of pelvic anatomy and landmarks during creation of the neohiatus [28].

## Conclusion

This chapter covers a multitude of urologic applications of laparoscopy in children with high success rates and low complications. Surgeons and anesthesia teams alike need to understand the physiologic changes that occur in pediatric patients with pneumoperitoneum. With time and experience, surgeons have learned how to combat the challenges that laparoscopy presents intraoperatively. Good surgical technique, awareness of differences in the anatomy and physiology of the pediatric patient, and respect of the working space can help minimize complications overall. As the technology continues to evolve, laparoscopic instrumentation will become safer and easier to use, providing the surgeon with an an armamentarium of tools to perfect his or her laparoscopic technique.

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# Laparoscopic and Robotic Pyeloplasty in Children

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## Introduction

Traditionally, open pyeloplasty (OP) has been the gold standard for treating ureteropelvic junction (UPJ) obstruction in children, with a success rate of 97% in the reported literature. However, with continued advances in conventional laparoscopic and robotic surgical technology, as well as a general shift in patients' and families' mentality towards favoring minimally invasive interventions, these approaches play a growing role in pediatric pyeloplasty. In the past, conventional laparoscopic pyeloplasty (C-LP) has been demonstrated to be equivalent to open surgeries in terms of preservation of differential renal function [1]. The technical challenges in C-LP largely lies in the need for intracorporeal suturing, which has been subsequently rectified by improved dexterity offered by robot-assisted laparoscopic pyeloplasty (RA-LP). The superiority of the laparoscopic approach over the open approach, with or without robotic assistance, is believed to lie in its decreased morbidities in terms of length of stay and pain medication requirement [2, 3]. This chapter reviews the strategies, techniques, and outcomes of laparoscopic and robotic pyeloplasty in children, as well as providing literature updates from the past 10 years, given that there has been a dramatic increase in relevant studies since the last edition of this chapter was published in 2012.

## Background

In 1993, laparoscopic pyeloplasty was first described in adult patients concurrently by two groups [4, 5]. Two years later, in 1995, its pediatric application was first described by Peters et al. in a 7-year-old boy with right UPJ obstruction, using the classic Anderson–Hynes dismembered technique, interrupted sutures, a nephrostomy tube as drainage, and 5 hours of total operative time [6]. More than a decade later in 2007, Olsen et al. reported their favorable 5-year experience with robot-assisted retroperitoneoscopic pyeloplasty (RA-RP) in treating UPJ obstruction in 67 children, demonstrating shorter operative times and comparable complication rates compared to other approaches.

Minimally invasive surgery has unique benefits in the pediatric population with respect to cosmetic outcomes, as well as psychological and social impact on the caregivers. It has been demonstrated that up to 83% of parents believe the scar size for pyeloplasty is important [7], and a validated questionnaire showed higher parental satisfaction rates for RA-LP over OP with regard to size of the incision scar, burden of postoperative follow-up, and overall life [8]. In addition, shorter length of stay (LOS) associated with RA-LP was correlated to an average saving of US$90.01 in parental wage loss and US$612.80 in hospital expenses [9].

However, these financial considerations must be weighed against the cost of purchasing and maintaining a robotic platform and instruments. Although Liu et al. did not find any differences in overall costs between minimally invasive pyeloplasty and OP, Bennett et al. reported that robotic cases were more expensive by US$3991, with operating room charges and anesthesia charges dominating the cost difference [10, 11]. Some centers have been successful in overcoming the higher costs associated with RA-LP by high surgical volumes, as Sorensen et al. observed that operative times for RA-LP were initially longer than those for OP, but became equivalent after 15–20 cases [12]. Having a dedicated robotic team in the operating team also improves efficiency and minimizes cost while maximizing safety.

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With RA-LP rapidly showing signs of becoming the new gold standard for treating UPJ obstruction in children, it cannot be stressed enough that ultimately the decision-making regarding which surgical approach to take should be based on availability of equipment, family preference, and surgeon skillset and comfort.

## Indications

The indications for minimally invasive pyeloplasty are identical to those for OP, and include decreasing split renal function, increasing hydronephrosis, urinary tract infections or pyelonephritis, symptoms such as intermittent flank pain, nausea, or vomiting, and presence of nephrolithiasis [13].

There have been encouraging reports of expanding the application of RA-LP to include younger children and infants. The largest series of such nature was a multicenter retrospective review from Avery et al., examining the outcomes of 60 infants with a mean age of 7.3 months. It found 91% of the children with improved or resolved hydronephrosis, while 3.3% (2 patients) required reoperation due to recurrent obstruction [14]. Boysen and Gundeti detailed their suggestions for successful infant pyeloplasty from a technical standpoint, including positioning, port placement, lens degrees, and insufflation pressure [15].

However, overall, infant RA-LP remains in its early stages and it is standard practice at our institution to perform infant pyeloplasty cases via an open dorsal lumbotomy or flank approach. Interestingly, a recent crowd-sourced survey showed that the majority of patients would prefer the dorsal lumbotomy scar over flank and laparoscopic incisions, if given as an option [16]. We reserve minimally invasive pyeloplasty for older children and teenagers, with RA-LP being our first choice, and rarely C-LP if operating at an affiliated hospital without the robotic equipment.

## Patient preparation and operative setup

Here we describe the steps for a routine RA-LP performed at our institution. The steps for a routine C-LP are identical.

### Bowel preparation

Although some authors advocate for a liquid diet for 24 hours prior to laparoscopic surgeries and a single rectal suppository of oral bowel stimulant to clear the colon, we have not found routine preoperative bowel preparation to be necessary.

### Retrograde pyelogram and stent placement

As indicated above, our standard approach for infant pyeloplasty is via an open dorsal lumbotomy incision. As such, we routinely perform a preoperative retrograde pyelogram to assess possible kidney rotation, concomitant ureteral obstruction, and length of ureteral narrowing. Narayanan et al. reported that preoperative retrograde pyelogram can provide additional information in up to 19% of cases [17]. Following this practice, we also perform a routine retrograde pyelogram before our minimally invasive pyeloplasty cases.

However, there is variation among our partners regarding stent placement. For some, an internalized double-J ureteral stent is always placed in a retrograde fashion at the end of the retrograde pyelogram. They cite confirmation of distal curl in bladder by direct cystoscopic vision and not having to negotiate the ureterovesical junction (UVJ) blindly as major advantages over an antegrade stent placement approach. In this case, the bladder would be left full by clamping the urethral Foley catheter so that the renal pelvis can remain distended to facilitate dissection.

For others, an antegrade stent placement approach is preferred due to the added difficulty in intracorporeal suturing by the proximal curl of the stent interfering with visualization of the surgical field. This is the preferred approach by this author and will be discussed in more details in later sections. A Foley catheter is placed per urethra at the end of the retrograde pyelogram.

### Positioning

The patient is placed in the lateral decubitus position with the operative side up and rotated approximately 30° from the vertical plane. This position is maintained with one or two large gel rolls behind the patient. In order to maximize the movement range for the robotic arms, it is beneficial to have the front side of the patient as close to the edge of the operating room table as possible. Sequential compression devices are placed on bilateral lower extremities. The bottom leg is bent while the upper leg is straight, with a pillow in between them. The contralateral arm is extended and secured to a padded arm board, while the ipsilateral arm is folded across the chest. Care is taken to ensure that all bony prominences are well padded and protected. The patient is then secured to the table using folded blue towels and silk tape at three levels, across the chest, across the hip, and across the legs. The security of strapping is then tested by rolling the patient prior to draping. It is important to work closely with the anesthesia team, as the head may also need to be secured. An orogastric tube is placed for left-sided procedures. The patient is prepped over the entire abdomen from xyphoid to pubis.

### Access and port placement

For patients without prior abdominal surgeries, entry into the peritoneum is obtained via a Veress needle after making an incision at the base of the umbilicus with an 11 blade. Countertension is provided by a pair of symmetrically placed perforating towel clamps. For patients with history of prior abdominal surgeries, an open Hasson technique is the preferred method, given its inherent safety. Successful entry is confirmed by a satisfactory "saline drop" test, no bloody or bilious return on aspiration, and symmetric, four-quadrant insufflation with low starting pressure. Typically, a 5 mm port is first placed through the self-dilating sheath at the umbilicus and a 0° or 30° laparoscope is used through this port to facilitate placements of the two 8 mm robotic ports under vision, one cranial to the umbilical port in the midline and a second equidistant from the umbilical port in a caudal direction approximately 30° off the midline. Care is taken to ensure that there is at least a 6–8 cm distance between ports to maximize robotic arm movements. An additional 5 mm assistant port can be placed as needed to allow for passing of sutures, suctioning, and/or liver retraction for right-sided cases. At this point, the laparoscope is switched to one of the working ports looking back at the umbilicus, and the previously placed temporary 5 mm port is then upsized to a 12 mm robotic camera port under vision.

## Procedure in detail

Following port placement, the robot is docked, and the procedure begins with identifying the dilated renal pelvis. For dissection, this author prefers monopolar scissors in the right hand and bipolar grasping forceps in the left. For left-sided cases, a transmesenteric approach is preferred if possible. Otherwise, a retrocolic approach would be appropriate if a dilated pelvis is not readily visible through the colonic mesentery. The colon is mobilized by incision of the white line of Toldt and reflected medially. The hepatic flexure and the duodenum may need to be mobilized for right-sided cases, and the splenic flexure may need to be mobilized for left-sided cases in order to reveal the UPJ.

After the UPJ is successfully identified, dissection is carried out carefully while maintaining the ureteral blood supply. In our experience, a hitch stitch with 3-0 Prolene is very useful at this time to permit lifting, exposure, and stabilization of the UPJ and proximal ureter. This is placed percutaneously through the abdominal wall using either a straight Keith needle or a straightened needle through the renal pelvis and back through the abdominal wall. Tension can be adjusted by placing a pair of clamps on the extracorporeal ends of the suture at different levels. This maneuver also lefts the anastomotic area away from any potential pools of urine and blood.

The next step is to perform a pyelotomy. The cut into the pelvis is in a diamond shape, similar to OP. Posteriorly, the cut should be as close to the ureter as possible without cutting into it, as this would create a dependent lower vertex of the pelvis that will be sewn to the inferior aspect of the ureteral spatulation. The portion of the lower pelvis and the actual UPJ is now attached to the ureter and can be used as a handle for manipulation, in an effort to minimizing touching the anastomotic site. The ureters is spatulated laterally, away from the vascular supply, until the normal ureter is encountered. Again, preoperative retrograde pyelogram can provide added information regarding the length of the diseased segment.

The anastomosis begins at the inferior aspect of the spatulation and the inferior-most aspect of the renal pelvis using a 5-0 Vicryl suture cut to 12 cm in a running fashion. The posterior wall is usually closed first. After the back wall is completed, an antegrade stent is placed. This is accomplished by passing a 14-gauge angiocatheter through the abdominal wall and passing a guidewire with preloaded stent through the angiocatheter. The length of the stent selected is based on the formula (age in years + 10) or premeasured during retrograde pyelogram. The guidewire is advanced down the ureter as the stent follows behind. Proper positioning of the stent is confirmed by tactile feedback, as there should not be any resistance. Further confirmation that the distal end of the stent has reached the bladder can be obtained by filling the bladder, instilling blue dye in the bladder, clamping the Foley catheter, and observing reflux of blue urine through the stent. Following stent placement, the opposite wall of the anastomosis is completed using a second suture, also in a running fashion.

The decision whether or not to leave a wound drain is at the discretion of the operating surgeon. In this author's experience, a rounded Blake drain is preferred over a flat Jackson–Pratt drain or a Penrose drain because this still allows closure of fascial defect in excess of the drain without making drain removal difficult, thereby decreases the risk of port-site hernia.

The fascia at the umbilicus is typically closed with 2-0 Vicryl suture on an UR-6 needle in an interrupted fashion, while the fascia at the working port sites is closed using 3-0 Vicryl sutures.

## Application in variant renal anatomy

Although we have not had much experience in employing minimally invasive techniques in treating UPJ obstruction in pediatric patients with renal anomalies, success has been reported in pelvic kidneys as well as horseshoe kidneys [18–22].

## Other minimally invasive surgical techniques

A review of the literature demonstrated some novel adaptations to the standard surgical steps described in details above. Regarding access, laparoendoscopic single-site (LESS), as well as transumbilical multiport pyeloplasty cases have been reported before with outcomes comparable to those of C-LP in terms of success rates and complication rates [23–25].

Regarding port placement, Hong et al. reported that their hidden incision endoscopic surgery (HIdES) port placement for pediatric robotic pyeloplasty has outcomes comparable to those of traditional port placement in terms of operative times, narcotic administration, hospital stay, success rate, and complication rates [26]. In this innovative approach, the robotic camera port, a working port, and a 5 mm assistant port are placed below the line of a Pfannenstiel incision, while the second working port is placed at the umbilicus or infra-umbilically, thereby avoiding visible scars.

With regard to surgical steps,a vascular hitch procedure has been applied in pediatric pyeloplasty [27, 28] in cases of crossing vessels. In this approach, the aberrant vessel is wrapped in a sling of pelvic tissue which keeps the vessel above the UPJ. This shortens the procedure by avoiding dismemberment and suturing. However, many groups caution against this approach because the presence of a crossing vessel does not always rule out other concomitant intrinsic abnormalities of the ureter, such as polyps, stenosis, kinking, or high insertion.

In the non-dismembered category of surgical technique, a Heineke–Mikulicz repair has also been described, where the lateral aspect of the UPJ is incised longitudinally and then closed transversely [29].

## Postoperative follow-up

This author does not place children on routine prophylactic antibiotic after minimally invasive pyeloplasty, and this is in keeping with existing literature. In 2016, Ferroni et al. showed that the administration of extended prophylactic antibiotics after minimally invasive pyeloplasty with ureteral stent placement in children had no significant impact on the rate of urinary tract infection [30]. We typically obtain our first postoperative renal and bladder ultrasound about 4–6 weeks after the surgery while the stent is still in place. We find this study helpful in establishing the patient's new baseline renal appearance when drainage is maximized, which in turn assists with meaningful interpretation of stable but persistent hydronephrosis on subsequent ultrasound. If hydronephrosis is noticeably improved on this initial postoperative ultrasound, then the stent is removed via cystoscopy in the operating room. The second postoperative ultrasound is typically 6–8 weeks following stent removal, with the third ultrasound being another three months afterwards. In the event of consistently worsening hydronephrosis or persistent symptoms following pyeloplasty, a postoperative nuclear medicine renal scan is obtained to reassess the drainage pattern on the operative side.

## Complications

A review of the literature revealed that the rates for complications following a pediatric pyeloplasty is 10–15% overall, but only 2–3% if complication is defined as a need for repeat invasive intervention, comparable to Clavien III grading for adults.

### Persistent obstruction

This is considered the most significant complication of pyeloplasty and can be caused by edema or blood clot acutely in the perioperative period, or by stenosis or kinking of the repair more chronically. As stated in previous sections, consistently worsening hydronephrosis or persistent symptoms following pyeloplasty warrant evaluation for possible persistent or recurrent obstruction by way of a diuretic renogram. Alternatively, the patient can be taken back to the operating room 4–6 months after the initial procedure for retrograde pyelogram. At our institution, we typically attempt balloon dilation and double stent placement as the first-line intervention if a stricture is found on retrograde pyelogram. Post-balloon dilation follow-up timeline is similar to what was described earlier for initial pyeloplasty, with reoperative pyeloplasty as the next step should the endoscopic treatment fail.

### Urinary leak

If a wound drain is left in place at the end of the pyeloplasty, sometimes persistent urinary drainage can be present postoperatively. In this situation, maximal urinary drainage is of value. Ureteral stent or nephrostomy tube placement should be considered if the initial pyeloplasty was done without a stent. Occasionally, postoperative urinary retention can contribute to urine leak from the anastomosis due to backflow through the stent. In this situation, Foley catheter replacement is the next step, and it is usually left in place for 3–5 days. Repeat voiding trial can occur when narcotic is minimized and bowel regimen is optimized.

### Complications related to laparoscopy

Similar to other laparoscopic procedures, C-LP and RA-LP carry the risks of access-related complications, such as bowel injury, adjacent organ injury, port-site hernia, and port-site infection, as well as insufflation-related complications, such as hypercarbia, increased abdominal pressure affecting ventilation, and hypothermia. With improved optics and visibility during laparoscopy, the incidence of these complications is low. However, children do have higher risk of severe injury, owing to their size and physical characteristics [31].

## Comparative outcomes

Since the last version of this chapter was published in 2012, there have been many more studies systematically examining the success rates and complication rates of pyeloplasty in children using different surgical approaches. In 2015, Ekin et al. wrote a review paper providing an up-to-date overview of minimally invasive treatment methods in UPJ obstruction [32]. In 2017, Boysen and Gundeti reviewed the technique, outcomes, complications, and special considerations in infants with respect to RA-LP in the pediatric population [15]. The author summarizes the overall findings in the following sections and refers interested readers back to these two review articles for details of individual studies regarding publishing year, number of cases, and study design.

### Descriptive series

A review of pediatric C-LP case series revealed that average operative time ranges from 140 to 255 minutes, with follow-up period from 13 to 41 months and a success rate of 91–100% [32]. A similar review of pediatric RA-LP case series revealed that average operative time ranges from 105 to 198 minutes, with follow-up period from 12 to 31 months and a success rate of 94–97% [15].

### Conventional laparoscopic versus open pyeloplasty

In 2017 in a comparative, prospective, case–control study of C-LP versus OP in children with UPJ obstruction, Piaggio et al. found that C-LP was a longer procedure than OP, but that both procedures had the same efficacy and complication rates. Patients who underwent C-LP needed fewer narcotics and had a shorter hospital stay [33]. Also in 2017, Gatti et al. conducted a randomized, prospective, and controlled trial comparing C-LP versus OP in children. Their study demonstrated the same results of longer operative time and shorter hospital stay in the C-LP group [3].

### Robot-assisted laparoscopic versus open pyeloplasty

From 2006 to 2014, there were at least five comparative studies looking at the differences between RA-LP and OP. Overall, RA-LP takes longer than OP, but the difference starts to diminish after 20 cases and may not exist after 40 cases. RA-LP, when compared to OP, tends to have shorter LOS and decreased narcotic requirement.

### Conventional versus robot-assisted laparoscopic pyeloplasty

When comparing the two minimally invasive approaches, C-LP and RA-LP, RA-LP tends to have shorter operative time and no difference in LOS or narcotic requirement. However, in the study with the most patients, Silay et al. reported in 2016 that operative time was similar between RA-LP and C-LP [34]. This study presented results from the Pediatric Urology Expert Group of the European Association of Urology Young Academic Urologists, which may explain their proficiency in conventional laparoscopic suturing and may not necessarily be applicable to an average urologist without advanced conventional laparoscopic skills. In this group of practitioners, the dexterity and three-dimensional visualization offered by robotic assistance can conceivably be beneficial and may level the playing field.

### Three-way comparison between open, conventional laparoscopic, and robot-assisted laparoscopic pyeloplasty

In 2017, Song et al. retrospectively reviewed an age-matched cohort of 30 children who underwent OP, 30 who underwent laparoscopic-assisted extracorporeal pyeloplasty, and RA-LP [35]. They found that those who underwent RA-LP had a shorter LOS and decreased narcotic requirement; however, there was no difference in the success rates for OP, C-LP with extracorporeal suturing, and RA-LP. Interestingly, the presence of crossing vessel was a negative prognostic indicator for surgical outcomes regardless of surgical method.

Also in 2017, Chan et al. aimed to determine if surgical approach, age, case volume, or other factors influence perioperative outcomes of pediatric pyeloplasty at academic institutions in a large contemporary cohort of 2219 patients. They found the complication rates to be 2.1%, 2.2%, and 3% after OP, C-LP, and RA-LP, respectively [36]. This large multicenter analysis also demonstrated that patient comorbidity had the greatest impact on complication rates and LOS.

## Reoperative pyeloplasty

Indications for reoperative pyeloplasty are similar to those for initial pyeloplasty, and include decreased renal function, worsening hydronephrosis, and persistent symptoms. As mentioned in previous sections, retrograde pyelogram, balloon dilation, and double stent placement is usually the first-line intervention at our institution for those who show signs and symptoms of failed initial pyeloplasty for UPJ obstruction. Should the endoscopic intervention fail as well, then typically the surgical approach for reoperative pyeloplasty is open at our institution.

However, minimally invasive approaches have been described and studied in the pediatric population in the context of reoperative pyeloplasty. In 2017, Moscardi et al. compared their outcomes of reoperative C-LP to primary C-LP and found similar results regarding safety and effectiveness [37]. Transperitoneal laparoscopic approach following a failed open pyeloplasty has the benefits of entering a virginal surgical territory and avoiding scar tissue, as most likely the OP would have been done via a retroperitoneal approach [29].

## Conclusions

Traditionally, pediatric patients with UPJ obstruction are treated with open pyeloplasty. However, with the advancement in laparoscopic and robotic surgical technology, a minimally invasive surgical approach, particularly with robotic assistance, is rapidly becoming the new gold standard worldwide for this procedure in children. Since the last version of this chapter was published in 2012, there has been a raft of newer studies with improved follow-up, continuing to demonstrate that the safety and effectiveness of these approaches is comparable to the open approach. The benefits are also possibly extended to younger patients and even infants [36].

In conclusion, the author wishes to remind the readers that when interpreting outcome results it is important to clarify each study's definition of success and complication and to not automatically equate statistical significance with clinical significance. To have a successful RA-LP series, having a dedicated robotic operating room staff and appropriate mentoring are extremely important [38]. Ultimately, the approach to UPJ repair should be based on availability of equipment, family preference, and surgeon skillset and comfort, rather than classically objective outcomes measures.

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# 117

# Lower Ureteral Reconstruction: Robotic Surgery

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## Introduction

Obstruction of the lower ureter requiring reconstruction can take place from a variety of extrinsic and intrinsic causes, including both non-iatrogenic and iatrogenically induced strictures. In addition, diseases such as reflux and other bladder-related issues, such as diverticuli, might necessitate ureteral reimplantation. The treatment paradigm for distal ureteral obstruction evaluation and treatment should be well known to most practicing urologic surgeons. The evaluation of distal ureteral obstruction is often focused at attempting to delineate the causal events. Workup and evaluation of the various differential diagnoses are beyond the focus of this chapter.

Urologic surgeons may bring varied skills, including endourologic, laparoscopic, robotic, and open surgery, to bear on the complexities of distal ureteral obstruction. A standard underlying tenet of care is the appreciation and relief of complete or marked obstruction to prevent significant ongoing renal nephron functional loss. This may involve the use of temporizing endourologic and radiologic interventions such as ureteral stent placement or percutaneous nephrostomy tubes to relieve obstruction. Especially in cases where significant obstruction exists or there is evidence of longstanding hydronephrosis and parenchymal loss, the urologic surgeon should also employ selected radiologic studies such as computed tomography (CT) and nuclear scans to evaluate the overall functional status of the kidney prior to undertaking reconstructive surgery. In cases where the kidney is of minimal function, typically less than 15% with a normal contralateral kidney, nephrectomy should be considered in appropriate patients if symptoms or complications such as pain, infection, hematuria, or significant renal-based hypertension are found and necessitate intervention.

Specific cases such as bladder tumors causing local invasion and obstruction of the ureter as well as distal ureteral tumors are beyond the scope of this chapter and are managed according to standards of oncologic practice. In certain distal ureteral tumor scenarios, utilization of reconstructive efforts described in this chapter, such as either psoas hitch or Boari flap, follow the standard approach as noted below when oncologically appropriate [1, 2]. Techniques differ from benign stricture disease as the distal ureter is usually completely removed and surgeons are encouraged to utilize caution in the approach to distal ureteral tumors as implantation of tumor remains a risk for this often aggressive disease.

This chapter describes the robotic and laparoscopic options for managing common distal ureteral obstruction scenarios. Readers are encouraged to review other sources as to the etiology, diagnosis, and indications for management in specific disease processes. This chapter will concentrate on surgical technique for laparoscopic and robotic approaches to distal ureteral reconstruction.

## Diagnostic evaluation

The evaluation of distal ureteral stricture disease, especially if no causative factors are apparent, should include the process of ruling out the presence of intrinsic or extrinsic malignancy. Distal ureteral stricture disease is often related to stone disease. Although endoscopic treatments for stone disease have advanced, the presence of long duration impacted stones as well as iatrogenic damage to the ureter can still cause ureteral stricture. Additional causes of benign ureteral strictures are numerous and include pelvic radiation for a variety of malignant pelvic disease processes, infection, endometriosis,

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

trauma, and inflammatory disease, such as retroperitoneal fibrosis and pelvic lipomatosis.

Modern diagnostic studies typically include CT urogram as well as potentially retrograde or antegrade pyelography combined with endoscopic evaluation performed prior to definitive intervention. At the time of this endoscopic evaluation, the status of the bladder, especially in patients who have neurogenic bladder or other potential complicating factors such as radiation to the pelvis, should be assessed as to the bladder tissue's potential suitability as a ureteral substitute if necessary. In some selected scenarios, endoscopic intervention such as endoureterotomy can be employed for short strictures to avoid ureteral reimplantation or reconstruction. Endoscopic incision is typically only successful for strictures less than 2 cm without underlying tissue compromise by radiation. Use of endoureterotomy via both antegrade and retrograde approaches is discussed in other chapters within this text.

Some contraindications to procedures such as psoas hitch and/or a flap include the presence of significant bladder outlet obstruction, neurogenic dysfunction, or significant reduction in bladder capacity or tissue mobility. In these circumstances consideration of other repair methods such as ileal interposition, autotransplantation, or even urinary diversion may be warranted.

## Basics of surgical repair

A variety of techniques are available to reconstruct distal ureteral obstruction. Urologic surgeons should be familiar with each of these techniques and their potential use as well as indications and contraindications in different patterns of ureteral length loss. In most surgical situations the intrinsic involvement of the ureter has been assessed prior to surgical intervention with radiologic and endoscopic evaluation. The general tenets of open surgery that have existed for decades underlie the choice made for reconstructive efforts in distal ureteral obstruction and have been emulated in modern robotic and laparoscopic procedures. Preoperative assessment will often give clues to the length of ureter involved with the stricture process that will need to be bridged in some manner to reach the bladder or perform a primary anastomosis. Historically, most disease processes involving the distal ureter have been defined as the pelvic brim to the bladder. Most "distal" strictures have been approached with reimplantation of the ureter directly into the bladder via either mobilization of the bladder (psoas hitch) for use of a flap of bladder tissue (Boari flap) [3–5]. In rare cases, primary ureteroureterostomy might be feasible but is typically more employed for the upper or mid ureter. Lower ureteral stricture repair is best managed by reimplantation into the bladder when feasible.

The length of ureter involved by stricture and damage differentiates the various surgical techniques. Urologic surgeons should be knowledgeable about the typical length gained by employing these maneuvers. Surgical maneuvers and techniques such as ureteroureterostomy (length of ureteral involvement is 2–3 cm), ureteroneocystostomy (length 4–5 cm), psoas hitch (length 6–10 cm), and Boari flap (length 12–15 cm) are often employed. Typically, for distal strictures, reimplantation into the bladder is the preferred management paradigm. Additional techniques such as renal mobilization with nephropexy (renal descent) can provide an additional 5–8 cm of ureteral length, but this is typically mainly useful for mid-ureteral and upper ureteral strictures [6]. In certain cases renal mobilization with nephropexy can aid in the performance of an especially long Boari flap type repair. Additional procedures that can be employed for even more significant ureteral length loss such as transureteroureterostomy, ileal ureter, buccal ureteral graft, and autotransplantation are available and reviewed in multiple publications throughout the urologic literature [7, 8]. There has been some literature experience with performing these procedures with laparoscopic or robotic approaches but these have been relatively limited in number and experience to date [9–12].

## General concepts

### Surgical scenarios

In many of the surgical scenarios, the precise type of repair to be employed will not be completely understood until a full dissection of the surrounding structures and identification of the length of ureter involved with stricture and damage which needs bypassed or replaced is understood. Unfortunately at times the ureter may be more involved than originally anticipated. One of the key tenets of ureteral repair surgery is that, similar to urethral repair, diseased tissue is removed until good, viable, full-thickness tissue with blood supply is encountered. Even if this involves conversion to a more extensive repair procedure the success rate is highest when tissues with excellent blood supply make up both sides of the anastomosis site. Informed consent should be obtained for all potential procedures, including psoas hitch, Boari flap, ureteral replacement, and even possible autotransplantation. Certainly for extensive or long strictures the patient should be aware of the potential to need a larger or more complex procedure.

### Patient preparation

A patient's preparation is performed depending on the clinical scenario and follows the typical evaluation for major urologic surgery. We typically employ a mild preoperative bowel prep to aid with bowel decompression. In patients with history of extensive previous transabdominal surgery consideration should be given to full bowel prep if the potential of enterotomy is high and depending on institutional standards. In addition, if the stricture is long and the potential exists for ileal interposition, a more complete bowel preparation may be considered. Standard preoperative preparation is performed as per institutional and physician protocol.

### Preoperative presence of drains and tubes

In our practice, we typically remove the ureteral stent 4–6 weeks prior to the proposed repair if one is indwelling. If it is a more complete obstruction or the patient has significant obstructive pain then a percutaneous nephrostomy tube is placed ipsilateral. In our experience the ability to differentiate healthy ureteral tissue is enhanced by the removal of an indwelling stent several weeks prior to the proposed procedure, similar to the removal of transurethral catheters prior to urethroplasty surgery.

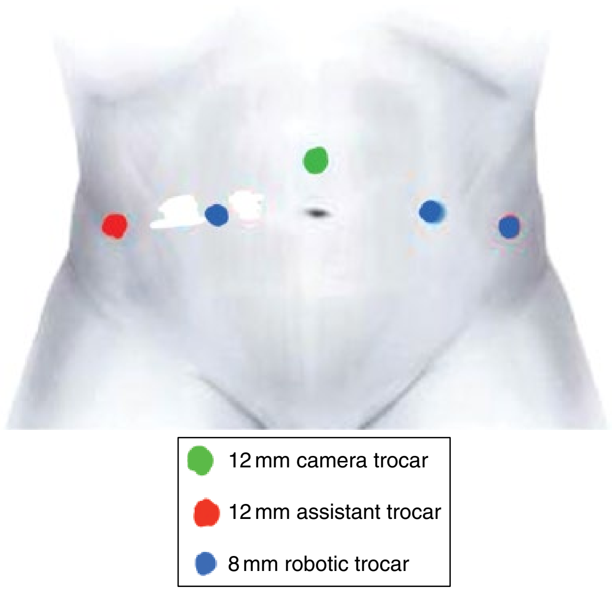

**Figure 117.1** The trocar arrangement is standard for pelvic surgery. The camera is docked through a 12 mm supra-umbilical midline port. We typically place the robotic fourth arm to the contralateral side from the strictured ureter to allow for use in providing traction on the bladder. For longer, more proximal strictures, such as those requiring extensive Boari flaps, the trocars can be moved cephalad.

## Intraoperative

### Position and preparation

Patient positioning for the majority of distal ureteral surgeries has the patient placed in a standard low lithotomy supine position similar to standard robotic pelvic surgery. Standard preparation for laparoscopic-based surgery includes an orogastic tube and a Foley catheter, which is placed transurethrally sterilely onto the field. In addition, if a nephrostomy tube is present we typically connect this to tubing extenders so that injection and irrigation are possible.

In some cases the complexity of the previous abdominal surgeries, operative field, or situation may necessitate the urologist perform a cystoscopy and place a retrograde ureteral stent and wire to aid in finding the ureter. This is possible only if the ureter is patent distally. For the majority of repairs, this is not necessary. In specialized procedures for distal ureteral tumors, the urologist may wish to perform cystoscopy to ensure that the bladder is free of any tumor or extensive progression of the distal ureteral tumor, depending on the oncologic scenario

### Entry and port placement

For both robotic and laparoscopic repairs, standard abdominal entry techniques and port placement geometry are employed. We currently perform the majority of these repairs robotically as it aids in suturing, especially for complex flap repairs etc. Although we have had extensive experience in performing these with pure laparoscopic techniques in the decade prior, there is no doubt in our opinion that the suturing, while feasible laparoscopically, is made easier to both perform and learn with the robot.

We typically employ all four arms of the robot. The fourth arm can be placed either ipsilateral or contralateral depending on surgeon preference. A 12 mm assistant port is placed opposite the fourth arm. Standard port configuration for pelvic surgery is employed, although typically the trocars are moved more cephalad (2–5 cm superior to the umbilicus), especially for more extensive flap type repairs (Figure 117.1). With the newer da Vinci™ Si and Xi platforms (Intuitive Surgical Inc., Sunnyvale, CA, USA) the ability to extensively move quadrants within the abdomen aids in performance of these procedures. Especially in reoperative or iatrogenically caused injuries, surgeons may be required to perform extensive adhesiolysis to gain exposure to the pelvis, ureter, bladder, and the site of injury. In some scenarios mobilization of the kidney may be necessary, making patient positioning and repositioning more complex. Conversion to open surgery may be required. All surgeons undertaking these types of reconstructive efforts should be well versed in laparoscopic, robotic, adhesiolysis, and versatile repair techniques.

## Basic surgical techniques

In most scenarios discussed in this chapter, the surgeon will enter with the plan of either performing a direct ureteroneocystostomy for short, very distal injury, a psoas hitch for a slightly longer distal injury, or a Boari flap combined with a psoas hitch in more severe and lengthy distal strictures. As stated previously, the surgeon should be prepared to perform more advanced procedures such as transureteroureterostomy, ileal ureter, or autotransplantation for extensive ureteral disease processes or loss and if the clinical situation requires.

Ureteral exposure is the initial step after any adhesiolysis. The surgeon should identify the ureter superior to the involved obstructed segment. We typically mobilize the ipsilateral colon superior to the external and common iliac vessels along the white line of Toldt. The fourth arm or the assistant can aid in retraction of the colon to allow dissection to proceed into the retroperitoneum. Mobilization of the colon superiorly and inferiorly along the white line of Toldt aids in full exposure. The surgeon should typically attempt to get the ureter at a level that is uninvolved superior to the disease process at this point. For the majority of repairs this will involve identifying the iliac vasculature and the ureter superior to or as it courses over the iliacs. During this dissection the surgeon should remain cautious of the gonadal vessels and, if feasible, preservation of these with lateralization is performed. In some scenarios the disease process does not allow preservation of the gonadal vessels and they should be hemostatically secured and divided only when absolutely necessary. We typically get circumferentially around the ureter superior to the iliac vessels once we have dissected and lateralized the gonadal vasculature. We often employ a vessel loop or Penrose drain to encircle the ureter for retraction, especially if it is involved in a severe amount of scar tissue or disease process as it approaches the iliac level. Using the fourth arm for assistance to gently retract the ureter superiorly using the vessel loop allows the surgeon to dissected caudally toward and over the iliacs (Figure 117.2). At this point the ureter should be dissected down circumferentially to the level where marked involvement in the obstructive disease process is noted. For benign processes the ureter can then be divided just superior to its involved segment. In malignant intrinsic ureteral tumors the dissection is carried completely to the bladder as per standard oncologic principles.

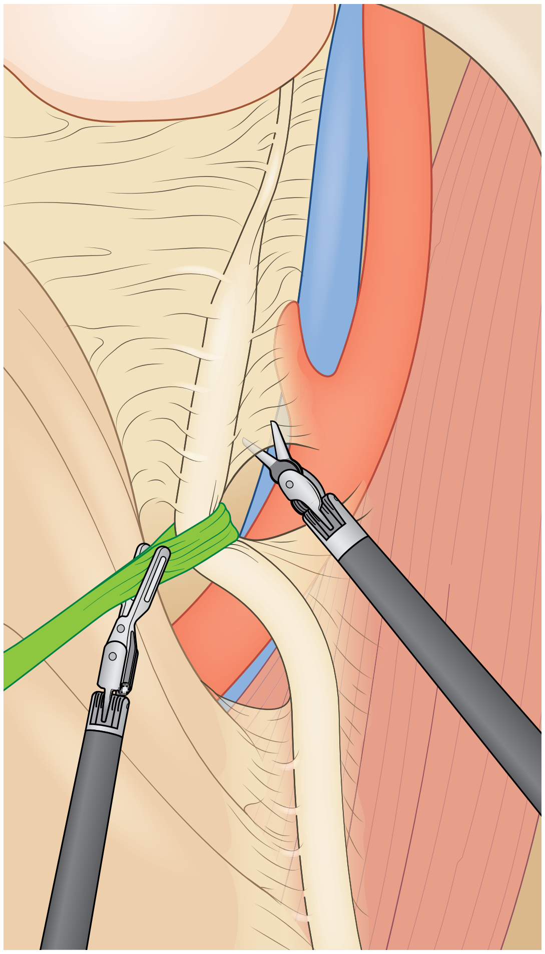

**Figure 117.2** The obstructed ureter is exposed and dissected superiorly about the external iliac vessels, with care taken to preserve adventitial blood supply. Once it is circumferentially dissected at a normal level, a vessel loop can be passed around it and the robotic grasper used to provide retraction as the surgeon works with either scissors or cautery to dissect caudally toward the stricture level and the bladder.

Once the ureter is divided, we typically remove our vessel loop or Penrose drain at this point and place a stay suture at the very distal end of the ureter as we prepare for the next steps of the operation. Although the ureter is typically spatulated later in the procedure, we typically avoid spatulation at this point until we have conceptualized how the repair will proceed in terms of eventual reimplantation. This decision impacts the orientation of the spatulation, which is typically anterior (hitch or flap) but can be posterior for a direct onlay dome reimplant (ureteroneocystotomy) such as a modified Lich–Gregoir. Handling of the delicate ureter especially at the level of where the eventual anastomosis will be performed is discouraged. Care is taken to preserve maximal vascularity and adventitia around the ureter during the exposure and dissection. Surgeons should avoid “stripping” the ureter, as this will often remove vital adventitia and blood supply, placing the distal ureter at risk for stenosis. During this dissection a cephalad portion of the ureter is typically mobilized which will avoid tension during the subsequent anastomosis.

At this point the various repair types diverge as to technique, depending on the necessity to make up longer distances of ureteral loss or removal. Each type of repair will be covered separately with technical nuances in the subsequent text of this chapter.

## Ureteroneocystotomy

Once the more caudal end of the ureter has been identified and the stricture level defined during full dissection the surgeon can appreciate the length of ureter which must bridge with the bladder. In some circumstances, when the ureter is strictured quite distally, mobilization of the bladder is not needed. In these scenarios a direct reimplantation onto the dome or posterior bladder can be performed. If a direct dome reimplantation is possible, techniques such as the direct onlay reimplantation where the ureter is spatulated posteriorly and directly anastomosed with a refluxing anastomosis onto the bladder dome is performed. Surgical standards include the performance of a direct mucosa-to-mucosa anastomosis with absorbable suture. In most circumstances an interrupted technique is employed, using 4-0 or 5-0 suture of either Vicryl or PDS. Care is taken to minimize manipulation and grasping of the distal ureter, especially the mucosa. Options to aid manipulation include a traction suture, leaving a small piece of strictured ureter attached to the distal ureter for grasping and mobility (subsequently excised), placing a segment of small ureteral catheter in the end of the ureter and grasping the catheter, or simply only grasping the seromuscular tissue cautiously. In the case of an ureteroneocystotomy, the bladder is incised with cautery through the seromuscular layers and then the incision in the mucosa is typically made with cold scissors. The incision should be approximately 1–2 cm.

The spatulated ureter and bladder are anastamosed with interrupted sutures of fine absorbable suture, typically 4-0 or 5-0 Vicryl or PDS, with care taken to get adequate mucosa and seromuscular tissue in each suture of each structure. We have observed some authors everting the mucosa of the bladder with fine absorbable sutures and then performing the mucosa-to-mucosa anastomosis. We also place a suture from the seromuscular layer of the bladder to the seromuscular layer of the ureter slightly away from the site of anastomosis to take any tension off during the anastomotic procedure. Prior to full closure of the anastomosis, a stent is placed into the ureter with the distal coil in the bladder. Stent placement techniques are discussed in a separate section later. Once anastomosis is complete, any residual vesicostomy is closed with running or interrupted suture. The bladder is irrigated to ensure a watertight closure. A standard closure of appropriate trocar sites along with a perivesical drain placement is performed. We typically leave the drain for 1–2 days or until minimal output and the Foley for 10–14 days. The Foley is removed at the time of clinic visit with a cystogram to ensure bladder closure, especially in cases of radiated or abnormal tissue healing potential.

## Psoas hitch and Boari flap

### Bladder mobilization

For both psoas hitch and Boari flap techniques, full mobilization of the bladder, including potential transection of the contralateral vesicle pedicle, can be performed to reduce tension on the anastomosis and allow for reconstruction tissue length from the bladder. Typically, we begin the process by filling the bladder with 150–200 ml of sterile fluid through the preplaced Foley catheter. We then mobilize the bladder from its anterior peritoneal attachments, similar to prostatectomy etc. In some cases with large bladders and psoas hitch approaches this is all of the mobilization needed, as the bladder's compliance and elasticity allow it to be pulled over to the ipsilateral psoas area for hitching. In other cases, a more thorough mobilization is necessary. This may even include division of the contralateral vesicle vascular pedicle to allow for full mobilization. During this mobilization, the posterior peritoneum is incised and the contralateral ureter should be identified thoroughly to ensure that there is no risk of damage to it during this pedicle mobilization process. A variety of technologies can be used to transect the pedicle contralaterally, including hemostatic vessel sealing, clips, or vascular staplers. Again, the urologic surgeon is cautioned to identify and prevent any damage to the contralateral ureter during this mobilization.

### Psoas hitch

For the standard psoas hitch procedure, the psoas minor tendon and fascia investing the iliopsoas is exposed superior to the common and external iliac artery. The bladder is grasped on its seromuscular surface and brought over to the iliopsoas where it is secured with 1–2 sutures that encompass the posterior seromuscular wall of the bladder without mucosa and the fascia investing the psoas. Often the psoas minor tendon can serve as a strong anchor point. Sutures are thrown through the psoas fascia and psoas minor tendon in a direction parallel to the muscle fibers to hopefully avoid nerve entrapment. Care is taken to only take superficial bites of the psoas

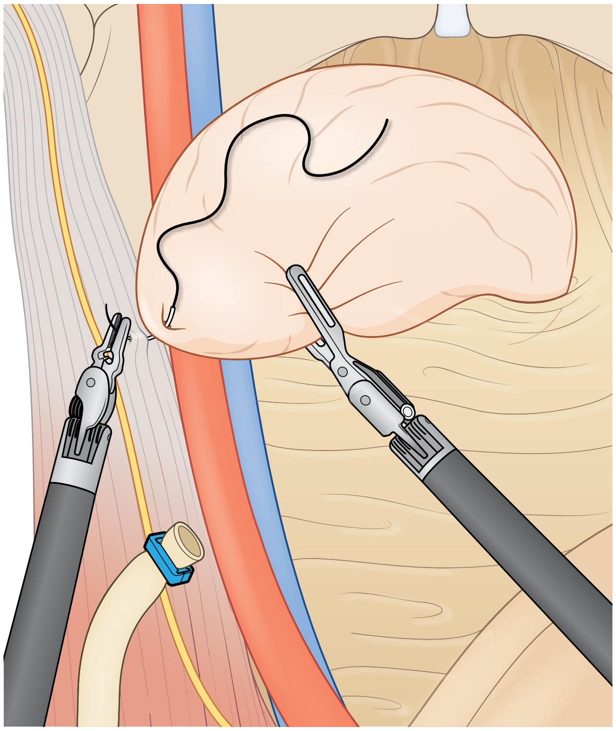

**Figure 117.3** Once the bladder is fully mobilized, it is retracted up to the psoas tendon above the external iliac vessel and sutured in place incorporating both the psoas tendon and the full-thickness musculature and adventitia of the posterior lateral dome of the bladder. We currently employ barbed sutures for anchoring fixation. Care should be taken to avoid entrapment of any nearby nerves.

fascia (Figure 117.3). Alternatively, if the bladder is not easily mobilized up to this position a horizontal cystotomy can be made in its anterior superior ipsilateral dome area and the contralateral fourth arm placed within the bladder and used to retract upward on the bladder to place it juxtaposed to the psoas fascia. This is similar to the open surgical maneuver where the surgeon places their fingers into the bladder to draw the dome superior onto the psoas fascia for securing. This does, however, create an additional cystotomy that will need to be sutured closed in layers.

Once the psoas hitch is in place, if the ureter reaches the dome easily the anastomosis type is at the discretion of the surgeon. One can either perform an onlay type anastomosis directly down onto the most superior portion of the bladder similar to that performed for direct dome ureteroneocystotomy (see Video 117.1) or, using a stay suture on the distal posterior aspect of the anteriorly spatulated ureter, the ureter can be drawn into the bladder through a posteriorly made opening above the psoas, securing with sutures and an intravesical mucosa-to-mucosa anastomosis performed in a "rosebud" fashion. The latter approach, however, does require the use of a more extended cystotomy to allow visualization of the posterior wall of the psoas hitch. We typically perform only refluxing anastomoses as there are no definitive data to suggest that a nonrefluxing anastomosis performs better.

Once the anastomosis is underway, an appropriately sized ureteral stent is brought in and placed up the ipsilateral ureter with the distal curl within the bladder. The surgeon should take into account the shorter distance up into the renal pelvis once the ureter vesicle junction has been moved far superiorly by the psoas hitch. We typically place a stent around 2 cm shorter than would have been standard for patient height. This sizing should minimize the amount of stent in the bladder, although postoperative stent irritation seems rare in these patients, probably due to the amount of mobilization and bladder surgery. Once the anastomosis is completed and the stent placed, any remaining cystotomy is closed with standard two-layer closure of absorbable suture.

In most cases, we prefer at this point to use a barbed absorbable suture for the bladder-to-psoas securing sutures. For the actual anastomosis we prefer either 4-0 or 5-0 interrupted Vicryl or PDS. Closure of the bladder, if a separate cystotomy is done, is performed in two running layers with absorbable suture with a mucosa and then a seromuscular layer running closure. A Foley catheter is left indwelling typically for 10–14 days in our practice, followed by a cystogram confirming bladder closure integrity prior to removal. The stent is left indwelling for 6–8 weeks and removed cystoscopically in the clinic setting.

## Boari flap

The technique for Boari flap formation to allow for replacement of significant distal ureteral loss or involvement with obstruction follows the principles of open surgical performance of this procedure [3]. In any case, where the potential need to bridge a longer distal defect to the level above the iliac vessels exists, this technique is a valuable adjunct. In these scenarios, the surgeon should avoid performance of any cystotomy or incision in the bladder before planning potential flap location and size.

Basic principles of tissue flap creation include using a well-vascularized flap of full-thickness bladder tissue with a broad base to allow for vascular supply to the flap tip, especially with long flaps. We typically perform a crude measurement from the filled bladder (volume of around 200–300 ml) lateral dome to the location of the most distal ureteral transected healthy end, using either a sterile measuring tape, suture, or a known instrument tip length. With the bladder still distended, the location, size, and geometry of the flap are then marked on the bladder with a broad-based area. Care should be taken to not make the tip of the flap too narrow. We typically aim for at least a 2 cm broad tip with a ratio of 1:3 tip-to-base width. In some scenarios, if an extremely long defect is to be reconstructed, a flap may be spiraled from the superior dome (flap base location) down and then across the bladder to create a large spiral flap. In some scenarios authors have even performed these types of flaps to reach all the way to the renal pelvis. Surgeons should be well versed in these operations prior to attempting such long flaps. Other types of approaches, including ileal ureteral substitution or autotransplantation, may also be considered for such extreme ureteral loss.

We typically mark the flap on the surface of the bladder either using a tip from a surgical marker grasped by the robotic instrument or simply marked using the cautery hook or scissors on the seromuscular surface of the bladder (Figure 117.4). We then typically incise the entire seromuscular tissue layer outlining the flap layout prior to dividing the mucosa using cold incision. Once the bladder starts to become decompressed, the surgeon will note extreme shrinkage of the flap. It is therefore essential that the borders of the previous markings be followed as the flap will appear much smaller once the bladder is emptied. Once the flap is formed, the ipsilateral posterior dome area directly below the base of the flap is then anchored to the psoas fascia above the iliac artery similar to a psoas hitch procedure [5]. The flap is then manipulated into juxtaposition with the ureter. The surgeon can then choose the type of anastomosis that suits this situation and the appropriate spatulation direction of the distal ureter, which is commonly anterior. Options include a direct end of ureter onto the tip of the flap. Alternatively, the ureter can be spatulated anteriorly, a traction suture placed on the distal ureteral edge, and a small hiatus created vertically through the posterior superior portion near the tip of the flap. The traction suture is then used to bring the ureter in from posterior to the flap in a tunneled manner (Figure 117.5).

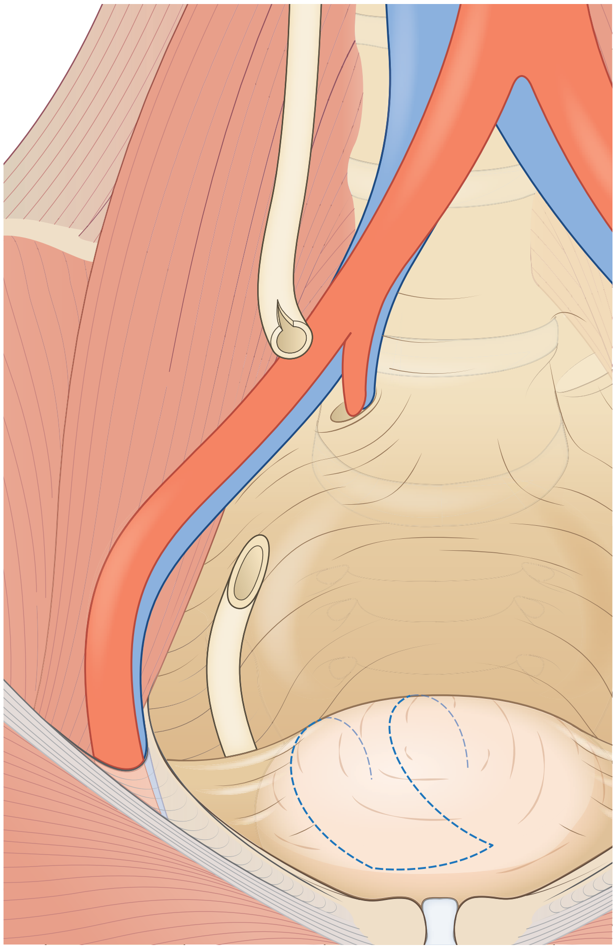

**Figure 117.4** Boari flap. The required flap is marked on the seromuscular surface of the bladder using either a marking pen or cautery. Care should be taken to give the flap a broad-based blood supply. The tip of the flap should be at least 2 cm wide.

We do not attempt to create a non-refluxing submucosal tunnel, but this can be performed if desired, albeit with a slightly higher presumed risk of obstruction. Once the spatulated ureter is brought into the mucosal lumen part of the flap, it can then be "rosebudded," performing an excellent mucosa-to-mucosa anastomosis using interrupted absorbable suture. Prior to rolling the flap, a double-J stent is placed, utilizing the techniques described later. The flap is

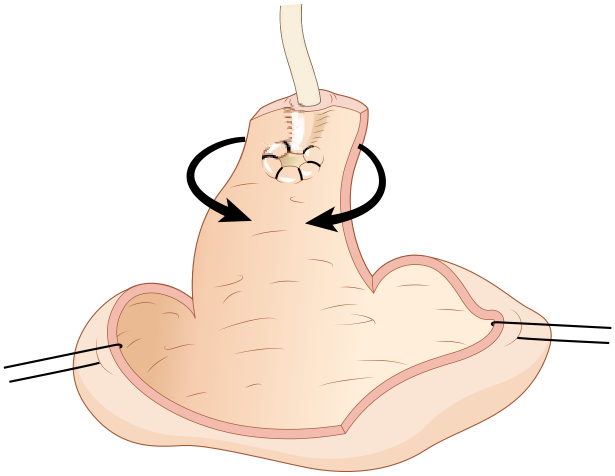

**Figure 117.5** Several methods for approximating the ureter to the flap are feasible. The end of the flap can be tubularized and directly anastamosed end-to-end to the spatulated ureter or, as illustrated here, the ureter is tunneled through the posterior wall of the flap and a "rosebud" type everted mucosa-to-mucosa anastomosis is performed. Once the anastomosis is completed, the flap is tubularized and the residual cystotomy is closed.

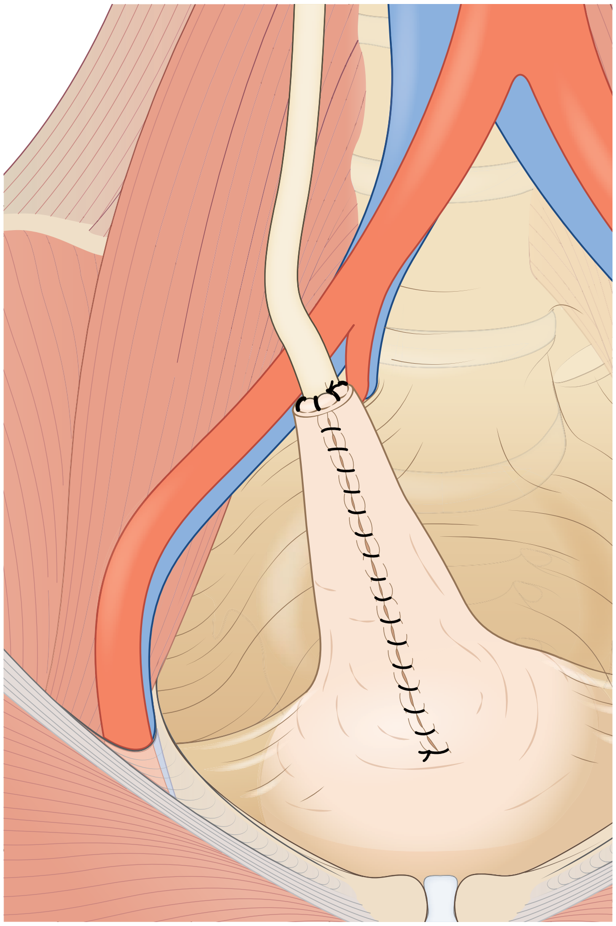

**Figure 117.6** The flap is rolled closed from proximal to distal over the indwelling stent. Following this, the remaining anterior cystotomy is closed in a running fashion. If adequate tissue is available, a two-layer closure can be performed, bringing further seromuscular tissue over the top of the closure suture line. The repair is then leak tested.

then tubularized over the stent that protrudes down into the bladder (Figure 117.6). A stent, typically shorter than the appropriate size stent, is used because the ureter in this scenario is now typically multiple centimeters shorter. The remaining bladder opening is then closed using a standard two-layer absorbable suture approach. The sutures can be run. We are now employing barbed suture for the seromuscular closure. After full closure, the bladder is gently irrigated through the Foley to check for leakage and the Foley is left indwelling. A drain is placed in the perivesical space. We typically leave the Foley for 10–14 days and check with a cystogram prior to removal. The drain is removed when drainage decreases appropriately. Stent remains indwelling for approximately six weeks and is removed cystoscopically in the outpatient setting.

## Stent placement during lower ureteral reconstruction

The majority of repairs use an indwelling ureteral stent placed prior to closure of the anastomosis. Many authors place this by advancing a standard endourology 0.035 guidewire through either one of their assistant trocars or through a small (<3 mm) trocar or stab incision just above the midline pubis. The wire tip is grasped by the robot arms and manipulated up the ureteral lumen. An appropriately sized stent (typically 2–3 cm shorter than for patient height) is then passed by the tableside assistant over the wire and aided into position by the robotic tools.

We employ a slightly different technique, placing a Councill tip Foley at the beginning of the case. At the time of stenting, the guidewire is placed through the Councill and out of the proximal intravesical lumen of the catheter. The wire is then steered via the robotic instrument needle drivers up the ureter. The stent is then placed over the wire and advanced until it can be grasped and manipulated up over the wire and into position. This technique results in the wire and stent having a typically "straight on" angle into the ureteral lumen and, in our estimation, makes passage far easier than fighting against the curves and risking the trauma often induced by coming in through the abdominal wall, which is usually superior and at an acute angle to the partially anastamosed ureter (see Video 117.1 ).

## Discussion

Open surgical ureteral reimplantation into the bladder for benign distal ureteral strictures has been a gold standard with high success rates. These procedures possess the standard postoperative morbidities of a significant abdominal incision, despite being a nonextirpative procedure. Endoscopic interventions expanded during the 1980s and 1990s with the growth of semirigid and flexible ureteroscopy, laser and incisional technologies, and the seminal work of many leaders in the field of endourology. Such endoureterotomy approaches are discussed in other chapters and are typically reserved for shorter strictures (<2 cm) in length.

The initial description of a laparoscopic ureteral reimplantation into the bladder in adults was by Reddy and Evans in 1994 [13]. Other groups then rapidly followed with small case series of laparoscopic distal ureteroneocystotomy [14, 15]. As would be expected with a minimally invasive techniques such as laparoscopy, the authors showed decreases in perioperative blood loss, hospital stay, and requirements needed for analgesia. In 2001, Fugita et al. published the first laparoscopic Boari flap series [16]. Other authors followed with published reports of successful series [15]. However, as with many complex laparoscopic procedures involving suturing and reconstruction, only a small group of highly skilled laparoscopic urologic surgeons were able to perform these procedures utilizing standard laparoscopic techniques. The challenges of learning advance suturing techniques and time-consuming nature of these reconstructive procedures limited more widespread application of laparoscopic reconstruction techniques.

With widespread adoption and market penetration of the Intuitive Surgical da Vinci robotic platform by urologists, multiple authors soon incorporated this advanced computer-assisted surgery into the performance of ureteral surgical reconstruction. Uberoi et al. described their technique of robotic psoas hitch procedure in 2007 [17]. Several multi-institutional consortium groups have subsequently published on larger patient cohorts of robotic ureteral reconstructions [18–20]. Success rates with radiologic follow-up in most series approach 100%.

In summary, the role of minimally invasive reconstruction of distal ureteral pathology using psoas hitch and Boari flap techniques continues to expand and has been aided in adoption by the development of robotic surgical technology. These advances, developed by visionary laparoscopic surgeons, have been further enabled by the increasing widespread use of robotics and are now standard at many institutions. New and even more advanced techniques, such as robotic ureteral buccal grafting, ileal ureteral substitution, and autotransplantation are now at the leading edge of technique advancement [9–12].

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# 118

# Laparoscopic Management of the Undescended Testicle

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## Introduction

An undescended testicle on physical examination is reported in between 2% and 5% of full-term and 30% of premature male infants [1]. There is increasing prevalence of cryptorchidism with low birth weight. Infants with birth weight under 2000 g were found to have undescended testicle in 7.7% of patients at three months of age, compared to 1.4% of infants with birth weight over 2500 g [2]. Cryptorchidism is more frequently a unilateral finding than bilateral finding, and approximately 20% of boys who present with cryptorchidism have at least one nonpalpable testis [3–5]. When identified in the newborn setting, standard of care is observation as spontaneous descent can be seen over time. Studies have reported rates of 45–75% of spontaneous descent when examined serially [6, 7]. In contrast, Wenzler et al. observed spontaneous descent in only 7% of undescended testicles presenting in infants when re-examined at 1 year of age, with all observations occurring in patients that presented less than six months of age [8].

However, surgical intervention is indicated when spontaneous descent does not occur as early surgical intervention confers growth advantage to the cryptorchid testicle compared to delayed surgery. When the undescended testicle is not palpable, the undescended testicle may be intra-abdominal or absent/atrophic. In one retrospective study of 447 nonpalpable testes, 40% were atrophic or absent, 20% were intra-abdominal, and 40% were found to be canalicular, scrotal, or ectopic testes at the time of surgery [5]. Historically, an open laparotomy was performed in patients with nonpalpable undescended testicles to address an intra-abdominal testicle if present. Cortesi et al. in 1976 were the first to describe laparoscopy for diagnostic purposes to determine whether a viable testicle was present [9]. Therapeutic laparoscopy for a nonpalpable undescended testicle was then described by several investigators soon after and this allowed minimally invasive therapeutic surgery to be applied to urology [10, 11]. This chapter reviews the diagnosis and management of the child with nonpalpable undescended testicle.

The combination of an undescended testicle and hypospadias merits specific mention due to its association with disorders of sexual development (DSDs). Kaefer et al. observed a significant increase in frequency of DSD conditions with more proximal location of the undescended testicle, with the highest observed association for a nonpalpable cryptorchid testicle and hypospadias [12]. Therefore, when cryptorchidism and hypospadias are identified in the same patient, whether palpable or nonpalpable, a karyotype is mandatory to rule out a DSD. Further diagnostic workup is beyond the scope of this chapter.

## Preoperative assessment

A thorough history is the initial part of any patient encounter. The pertinent aspects for the patient with an undescended testicle are a birth history (full term or premature), birth weight, a family history of cryptorchidism, the patient's own medical/surgical history and any genetic syndromes. Prior physical examination findings will be important information to know as well to gauge whether the condition is improving or not.

The physical examination is the most critical component of the diagnostic workup for the cryptorchid testicle. Ensuring that the patient is calm and cooperative, especially in the pediatric age group, allows for more confidence in the observed exam findings. The examiner's hands and fingers must be in the proper position for an

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

appropriate examination of the scrotum. Ideally, the index finger and/or middle finger of the examining hand are placed over the posterior aspect of the scrotum, with the thumb of that hand positioned over the anterior aspect of the scrotum.

If the testicle is not palpated in the scrotum, the inguinal canal should be examined for retained testicular tissue. For the right-handed individual, with the index and middle finger of the examiner's left hand positioned over the inguinal canal, the examiner should palpate the length of the canal while inferomedially sweeping in an attempt to trap the testicle along its projected line of normal descent and if possible express any retained testicular tissue into the scrotum. At the same time, the middle finger, index finger, and thumb of the right hand should be properly positioned to palpate the ipsilateral proximal scrotum for any testicular tissue entering from the inguinal canal. Reducing friction between the examiner's fingers and the inguinal canal by placing soap on the fingertips can increase the likelihood and sensitivity of palpating an undecended inguinal testicle. If the examiner has difficulty palpating scrotal testes in the older child, the patient should be placed in a sitting knee–chest position to help force the testes into a dependent position or, while seated leaning forward, in crossed-leg position ("tailor's position").

The decision regarding orchiopexy versus orchiectomy in a postpubertal male who presents with unilateral postpubertal cryptorchidism must be made on an individual basis and based upon the health of the contralateral testicle, competing medical comorbidities and fertility/paternity status of the man. The cryptorchid testicle should be saved if it is the only source of testosterone and/or sperm (i.e. if the contralateral testis is absent or abnormal). On the other hand, if the contralateral testis is normal, orchiectomy may be beneficial to avoid potential development of malignancy or torsion. A discussion with the patient about surgery while discussing risks and benefit of surgery is needed while accounting for risks of general anesthetic accounting for patient age and competing comorbidities when present. In certain instances when the crytorchid testicle is identified later in life the theoretical risks of an anesthetic complication may outweigh the risk of malignancy from the intra-abdominal testicle, making observation a third viable option [13].

## Laparoscopic surgical technique for the nonpalpable testicle

Following induction of anesthesia, repeat physical examination is performed to confirm a cryptorchid testicle and to determine whether it is palpable or nonpalpable. Surgical technique is modified accordingly to exam findings. Cisek et al. reported that a nonpalpable undescended testicle in clinic became palpable with exam under anesthesia in 40 patients of their 225 patient series [14]. A palpable undescended testicle will not benefit from laparoscopy and should receive an inguinal exploration. If the testicular examination demonstrates a nonpalpable testicle than proceeding with a diagnostic laparoscopy is indicated. Perioperative antibiotic prophylaxis is recommended and given prior to incision. Drainage of the bladder through urethral catheterization may help minimize bladder injury during the procedure. Although the use of laparoendoscopic single-site (LESS) surgery for orchiopexy utilizing a single access point for the camera and trocars has been described [15, 16], the surgical technique described in this chapter is standard multiport laparoscopic orchiopexy.

Pneumoperitoneum can be established via Veress needle placed through rectus fascia at the umbilicus or open Hassan technique. Each technique has their own advantages and disadvantages, as described elsewhere (Chapter 84). Following creation of pneumoperitoneum, the placement of the initial trocar through the umbilicus for the laparoscope permits visual inspection of the pelvis and both internal inguinal rings. Putting the patient in Trendelenburg position will allow for intestine to be displaced cranially while inspecting the pelvis. During the intraoperative inspection of the pelvic anatomy the surgeon should be focused on identifying the testicular blood vessels as this will dictate the proper sequence of events. Inspection of the normal contralateral side for a unilateral undescended testicle will assist in acquiring normal orientation under the assumption there is no contralateral occult pathology.

Most commonly, three possible scenarios are encountered for the nonpalpable undescended testicle upon diagnostic laparoscopy. The first is vessels leading to an intra-abdominal testicle that typically is found within a few centimeters of the internal ring (Figure 118.1a). The laparoscopic identification of an intra-abdominal testicle permits planning for the definitive procedure and additional trocar placement if laparoscopic orchidopexy or orchiectomy is pursued. The second situation is gonadal vessels that end blindly in the retroperitoneum, indicating that there is no testicle present (Figure 118.1b). Third, the vessels may lead to and exit through the internal inguinal ring into the inguinal canal (Figure 118.1c). Inguinal exploration is carried out if testicular vessels and vas deferens are visualized exiting the internal ring. In one review, 27 patients with 30 nonpalpable testes underwent laparoscopy after previous negative inguinal exploration with the findings of one-third of patients had blind-ending spermatic vessels, one-third had viable intra-abdominal or inguinal testes, and one-third had intra-abdominal remnants [17].

Further mobilization of the intra-abdominal testicle is accomplished with additional working trocars placed under direct vision with laparoscope. Three or five millimeter trocars can be placed, depending upon the size of the patient, surgeon preference, and whether introduction of a laparoscopic clip applier is anticipated. If the latter is expected then a 5 mm trocar is a better choice. The placement of the working trocars on the abdominal wall depends on whether a unilateral or bilateral procedure will be performed. Trocars placed in the midclavicular line at the level of the umbilicus on each side of the abdomen enable the surgeon to change sides when bilateral orchidopexy is indicated (Figure 118.2). Alternatively, simple incisions in the abdominal wall allow for passage of laparoscopic instruments without using ports [18].

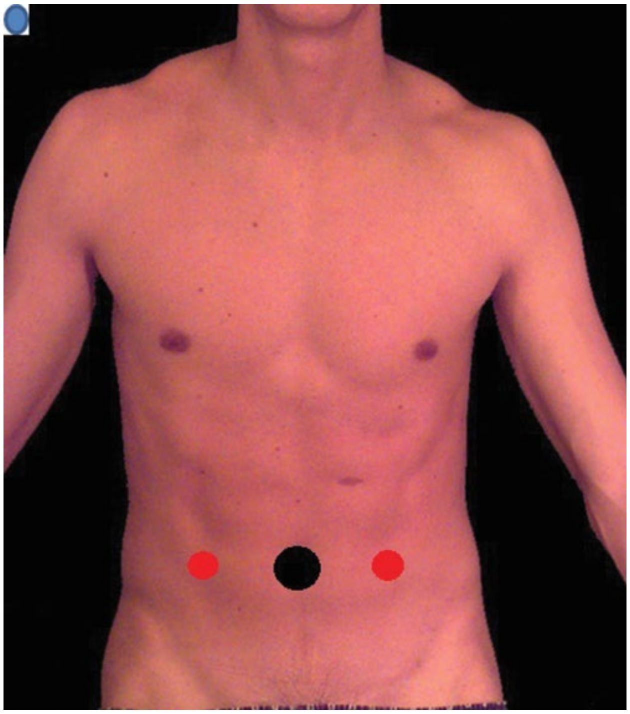

**Figure 118.2** Diagrams of trocar placement for laparoscopic orchiopexy. An umbilical trocar (black circle) allows for inspection of pelvic and abdominal structures. Trocars placed in the midclavicular line at the level of the umbilicus on each side (red circles) enable the surgeon to change between sides when bilateral orchidopexy is indicated.

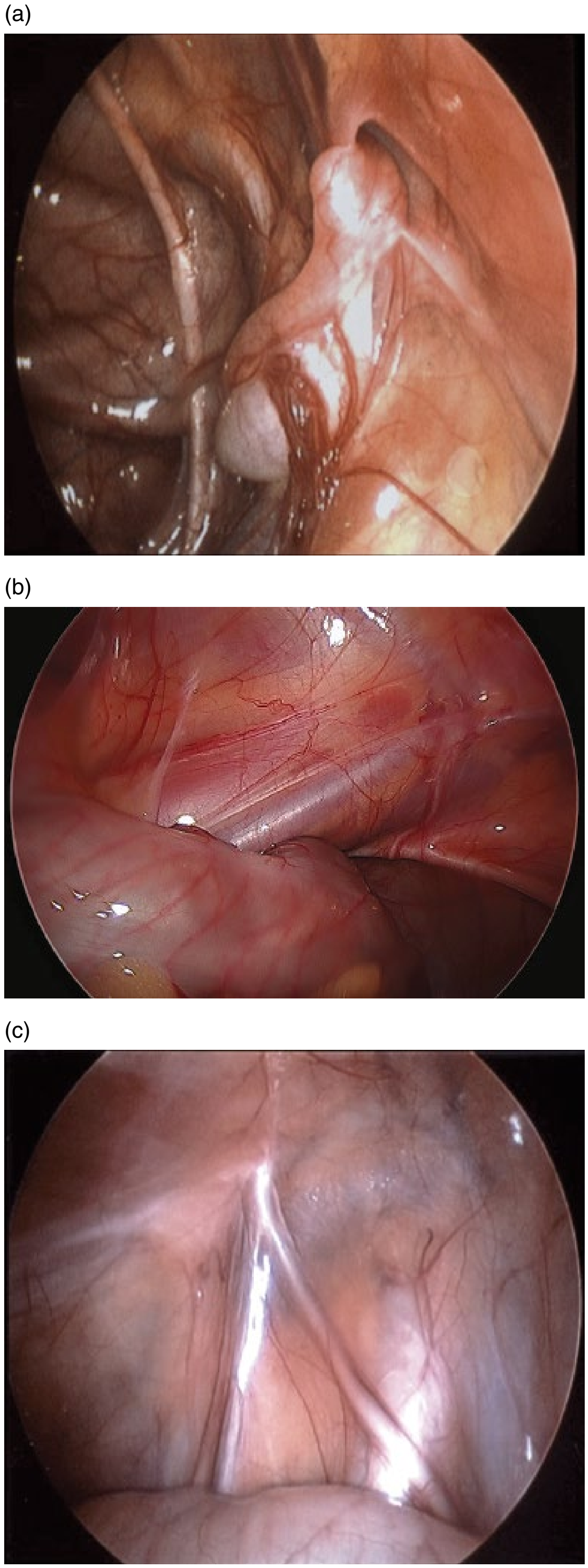

**Figure 118.1** (a) Intraoperative image of intra-abdominal testicle that typically is found within a few centimeters of the internal ring. (b) Intraoperative image of testicular vessels that end blindly in the retroperitoneum, indicating that there is no testicle present. (c) Intraoperative image of testicular vessels leading to the internal inguinal ring and exiting through the internal inguinal ring into the inguinal canal

This may lower operative costs, possibly improves cosmesis, and reduces the risk of port-site hernias.

The tunica albuginea of the testicle can be grasped using an atraumatic grasper to provide traction and more accurately ascertain its proximity to the internal ring. Grasping other structures such as epididymis or vas risks their injury given their delicate nature and should be avoided. Intuitively, the difficulty in placing the intra-abdominal testicle into the scrotum increases as the distance from the scrotum increases. The need to perform a Fowler–Stephens technique rises as the distance of the intra-abdominal testicle from the internal ring increases and this will be discussed more in depth later in the chapter. However, it is critical for the surgeon to integrate the information obtained during the diagnostic laparoscopic portion, such as size of testicle, distance of testicle from internal ring, and spermatic cord anatomy, in order to determine if a one-stage or two-stage laparoscopic orchiopexy is best for the patient.

## Laparoscopic orchiopexy technique (see Video 118.1)

Caudal to the intra-abdominal testicle the gubernacular attachments are closely examined as they enter the inguinal ring when present. The optical magnification of the laparoscope assists in differentiating between the gubernaculum and vas deferens; however the surgeon must be cognizant that risk of injury to the delicate Wolffian structures is always present during the dissection. Division of the gubernaculum is typically performed with the use of cautery, depending upon the surgeon's discretion. After the gubernaculum has been divided this can serve as a handle for elevating the tissue cranially during further dissection, which minimizes the need for manipulation of delicate Wolffian structures. Incision of the peritoneum lateral to the intra-abdominal testicle enters the retroperitoneum and further mobilization is facilitated with use of blunt dissection off the iliac vessels. The dissection is expanded cranially along the lateral border of the gonadal vessels. Incision of the peritoneum inferiorly in a plane parallel to the vas deferens from the internal ring towards the obliterated umbilical ligament occurs next. Additional dissection is carried out with the aim of maintaining a wide swathe of peritoneum in the shape of a triangle between the vessels and vas, with the testicle being the apex. The peritoneum over the proximal gonadal vessels can be divided, releasing any tension and at times affording additional length. This last maneuver can be accomplished after the testicle is moved out of the abdomen when the sites of tension on the cord are best appreciated.

There have been various techniques for moving the testicle out of the abdomen into the scrotum. One described technique involves bringing the testicle through the internal inguinal ring into the inguinal canal and scrotum, similar to standard inguinal orchiopexy. Another frequently employed technique is to create a neohiatus through the abdominal wall directly over the pubic tubercle into the ipsilateral scrotum. Directing the testis through this new, straighter path created above the pubic tubercle rather than following the longer course through the internal inguinal ring and inguinal canal can potentially add 1–2 cm of length, which makes the difference between a tensioned and tension-free testis placement in the scrotum. Pertinent anterior abdominal wall anatomical landmarks while making the neocanal are the inferior epigastric vessels, medial umbilical ligament, and bladder. Decompression of the bladder will help minimize its inadvertent injury when the neocanal is created between the lateral edge of the bladder and medial umbilical ligament. The canal can be created from inside the abdomen outwards or vice versa under direct laparoscopic view. An incision in the scrotum is made and a hemostat or Kelly clamp can be used to bluntly create a defect in the anterior abdominal wall anterior to the pubic tubercle through this incision. Upon entering the abdomen through this neohiatus, the clamp can be used to grasp the gubernacular attachments for pulling the testicle into the scrotum. Alternatively, a laparoscopic instrument can bluntly penetrate the anterior abdominal wall over the pubic tubercle and exit the scrotum. At this point a hemostat can be locked onto the laparoscopic instrument and fed through the abdominal wall defect to expand the diameter of the neocanal, allowing the testicle to exit through it. Opening the hemostat can widen the neohiatus enough to allow the testicle to pass through without injury. Instillation of saline into the bladder to fill it allows the surgeon to identify any injury to the bladder intraoperatively and repair it. Creation of the neocanal medial to the inferior epigastric vessels, but lateral to the medial umbilical ligament would likely minimize the risk of bladder injury.

A superficial dartos pouch for the testicle to reside in is created after incising the scrotal skin with the use of hemostat. After the testicle is brought into the scrotum and into the pouch it can be affixed to the scrotal skin, ideally without tension to minimize risk of postoperative ascent. The technique of scrotal testis fixation is important, especially when initially there is a high testis. The author prefers the use of nonabsorbable monofilament suture, passed superficially through the lateral and medial sides of the testis and sutured to dependent portion of dartos pouch. The use of an absorbable suture is reasonable as there is no evidence that nonabsorbable sutures are superior. Placement of these tunical fixation sutures transcutaneously through a gauze fixation pledget or sterile button over the scrotum has been utilized to assist in healing in a scrotal position when tension-free placement in the dartos pouch cannot be accomplished.

After the testicle is secured into its scrotal position the abdomen is surveyed one final time, searching for sites of bleeding from laparoscopic dissection. The ipsilateral open inguinal ring does not need to be closed as clinical inguinal hernias are not evident, despite the patency demonstrated on laparoscopy. Khairi et al. reviewed nearly 400 laparoscopic orchiopexy cases with near equal distribution of testicles passed through the internal inguinal ring into the scrotum or neohiatus medial to native internal ring [19]. After over 3 years follow-up for each technique there were no cases of inguinal hernia in any patient. The contralateral inguinal ring has been demonstrated to be patent in 9–33% of patients, with increasing rates in patients younger than 2 years [20, 21]. Concurrent laparoscopic repair of the patent processus has been reported [21].

Hemostasis is obtained as needed and each working trocar is removed under direct laparoscopic view. Although radial-dilating trocars that are 3–5 mm in diameter have been purported by manufacture not to result in abdominal wall defects that lead to hernias, the author routinely closes the trocar fascial defects under direct laparoscopic vision with suture ligature. The umbilical trocar and laparoscope are removed together and the trocar site closed. Skin incisions are closed according to surgeon's preference.

## Fowler–Stephens technique for inadequate testicular vessel length

A high intra-abdominal undescended testicle with short testicular vessels may require a Fowler–Stephens technique, either in a one-stage or two-stage approach to achieve a position within the scrotum after laparoscopic orchidopexy. The need to perform a Fowler–Stephens technique rises as the distance of the intra-abdominal testicle from the internal ring increases. A distance of greater than 2 cm was an indicator of inadequate testicular vessel length for primary laparoscopic orchidopexy in one study [22]. Another purported visual cue suggested to check for sufficiency of the testicular vessels to reach the scrotum is to grasp the testicle and seeing if it can be extended to the contralateral inguinal ring prior to any dissection [23]. The rationale behind this maneuver is that if the testicular vessel demonstrates that amount of laxity then there should be enough length to achieve scrotal position. Unfortunately, the testis will not reach the contralateral internal inguinal ring prior to dissection in most cases, so this cannot be used as the sole indication for Fowler–Stephens procedure in all cases. In fact Yucel et al. reviewed their outcomes of laparoscopic orchiopexy in 46 testicles, where only 20 testicles reached the lower scrotum and the remainder the upper scrotum, to identify any intraoperative predictors for successful lower scrotum outcome [24]. The authors found that patient age, location within 2 cm of the internal ring, or mobility of the testicle to the contralateral inguinal ring were not predictive factors to bring the testicle to the lower scrotum. Atrophy was identified during follow-up in six testicles (14%) and secondary procedure was performed for position at or above the upper margin of the scrotum in five patients (12%).

A recent single-surgeon series of an innovative technique has been described to lengthen the vessels prior to orchiopexy. Shehata et al. describe a staged laparoscopic traction orchiopexy entailing fixation of the testis to a point 1 inch (2.5 cm) above and medial to the contralateral anterior superior iliac spine on the anterior abdominal wall for 12 weeks [25]. The second stage involves division of the traction suture and delivery of the testicle out of the abdomen and into the scrotum with a subdartos orchiopexy. The technique has been applied to 140 testes in 124 boys with a scrotal position achieved in 84% of the patients (mean follow-up of 16 months). Distance of testicle from internal ring 0–2 cm achieved 93% (80/86) success, 2–4 cm achieved 78% (25/32) success, and very high intrabdominal testicles that were >4 cm from internal ring were unsuccessful in all cases 0% (0/7).

The Fowler–Stephens technique is predicated on the multiple arterial blood supply to the testicle. The testicle has three arterial sources: the testicular artery originating from the aorta, the cremasteric artery from the inferior epigastric artery, and the vasal artery from the superior vesical artery (Figure 118.3). Early decision for deliberate transection of the testicular vessels is essential before mobilization of this collateral blood supply that is derived from the pelvic collaterals.

A staged orchiopexy in which the testicular vessels are ligated to allow for sufficient testicular mobility was first described by Fowler and Stephens in 1959 [26]. Ligation of the testicular vessels is usually performed with a laparoscopic clip applier and typically performed cranial to the testicle well away from the critical collateral vessels arising inferior-medially to the testicle. Immediate further mobilization of the testicle with aforementioned surgical technique with an emphasis on wide mobilization of the testes and adjacent peritoneum can be performed for the one-stage Fowler–Stephens laparoscopic orchiopexy.

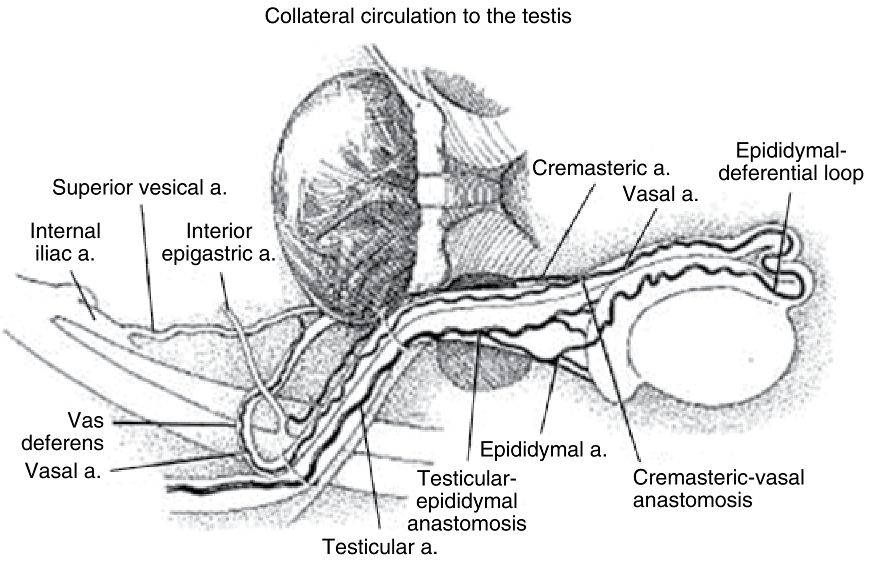

**Figure 118.3** The testicle has three arterial sources, the main being the testicular artery originating from the aorta. There is also the cremasteric artery that originates from the inferior epigastric artery and the vasal artery that originates from the superior vesical artery. *Source:* Hima F. *Atlas of Urosurgical Anatomy*, 497. London: Elsevier, 1993. Reproduced with permission of Elsevier.

Alternatively, ligation of the vessels and an intentional two-stage approach can be pursued, allowing for an increase in collateral blood flow over time now that the main arterial blood supply has been interrupted. This has been associated with lower rates of testicular atrophy than a single-stage technique. After approximately six months, the second stage laparoscopic orchiopexy is performed. Access is obtained through the previous laparoscopic trocar sites and the testicle inspected. If significant atrophy is noted then laparoscopic orchiectomy can be performed, as further mobilization of the testicle may not result in viable testicle following placement into the scrotum. Atrophy rates following division of testicular vessels has been reported and orchiectomy performed laparoscopically when this is encountered. Mobilization of the testicle with preservation of a wide swathe of peritoneum around the testicle and vas deferens is critical to avoid injury to the collateral blood vessels that now serve as sole blood supply to it. Regardless of whether a one-stage or two-stage approach is taken, the creation of the neocanal and scrotal fixation is performed according to the aforementioned techniques.

## Laparoscopic orchiopexy outcomes

There have been many published reports since the first description of laparoscopic orchiopexy by Jordan et al. [10]. Table 118.1 summarizes a few selected contemporary series [27–39]. Some series have compared historical open orchiopexy outcomes to pure laparoscopic technique. A systematic review of whether a staged Fowler–Stephens orchiopexy was more beneficial was reported by Elyas et al. [40]. Using electronic queries of published surgical series, the pooled estimate of success rates was 80% for single-stage Fowler–Stephens orchiopexy compared to 85% for two-stage Fowler–Stephens orchiopexy. Statistical analysis of the pooled odds ratio (OR) favored a two-stage Fowler–Stephens orchiopexy for adequate postoperative testicular size and scrotal position (OR 2.0, 95% confidence interval 1.1–3.9).

## Conclusions

The nonpalpable undescended testicle remains an important clinical situation for the treating physician. Identification of intra-abdominal testicle is critical to counseling patient and families regarding malignancy risk, and moving the testicle out of the abdomen and into the scrotum may preserve fertility. Laparoscopy offers an advantage over radiographic studies in that it has higher sensitivity and allows for therapeutic maneuvers at same setting. A minimally invasive approach confers a theoretical cosmetic and analgesic advantage over traditional open transabdominal orchiopexy. Several studies have demonstrated outcomes for laparoscopic orchiopexy equivalent to those of open orchiopexy for the intrabdominal testicle whether or not a Fowler–Stephens technique is applied. The widespread dissemination of laparoscopic surgical techniques and training with them during residency and fellowship programs make the laparoscopic management of nonpalpable undescended testicle increasingly first-line treatment when resources allow for its implementation.

**Table 118.1** A selection of contemporary series comparing orchiopexy outcomes.

| Author | Year | No. of testes | No. of testes with one-stage FSO | No. of testes with two-stage FSO | Success | Definition of success | No atrophic testis | Follow-up |
|---|---|---|---|---|---|---|---|---|
| Lindgren et al. [27] | 1999 | 44 | 13 | 5 | 89% | Not described in detail | 2/18 after FSO | Minimum 6 mo |
| Baker et al. [28] | 2001 | 310 | 27 | 58 | 97% LO alone<br>74% 1 stage FSO<br>88% 2 stage FSO | Scrotal position and testis size on exam | 4/178 LO alone<br>6/27 in 1 stage FSO<br>6/58 in 2 stage FSO | Range of mean: 7–20 mo |
| Radmayr et al. [29] | 2003 | 57 | None | 29 | 96.5% | Scrotal position and perfused by Doppler ultrasound | 2/29 | Mean 6 yr |
| Yucel et al. [30] | 2007 | 46 | 12 | None | 74% | Scrotal position and testis size on exam | 5/34 LO alone<br>1/12 FSO | Mean 7 mo |
| Kaye and Palmer [31] | 2008 | 42 | 2 | 2 | 91% | Scrotal position and testis size on exam | 1/38 LO alone<br>1/2 in 1 stage FSO | 1 yr |
| Esposito et al. [32] | 2009 | 12 | None | 12 | 83% | Scrotal position and perfused by Doppler ultrasound | 2/12 | Range 7–17 yr |
| Dave et al. [33] | 2009 | 61 | None | 61 | 75% | Scrotal position and perfused by Doppler ultrasound | 15/61 | Mean 13.5 mo |
| Stec et al. [34] | 2009 | 51 | 8 | 11 | 86% | Testis size and texture on exam | Not described | Mean 16 mo |
| Hvistendahl and Poulsen [35] | 2009 | 70 | None | 65 | 80% | Scrotal position and testis size on exam | 9/65 | Unknown |
| Moursy et al. [36] | 2011 | 76 | None | 43 | 100% LO alone<br>89% FSO | Scrotal position and testis size on exam | 2/36 (both in FSO) | Mean 34 mo |
| Bagga et al. [37] | 2012 | 28 | None | None | 56% | Scrotal position and perfused by Doppler ultrasound | 1/5 | Minimum 6 mo |
| Casanova et al. [38] | 2013 | 82 | None | 79 | 71% | Scrotal position and perfused by Doppler ultrasound | 14/82 | Median 3 yr |
| Alagaratnam et al. [39] | 2013 | 118 | None | 113 | 83% | Scrotal position and testis size on exam | 9/102 | Median 2 yr |

LO, laparoscopic orchiopexy; FSO, Fowler–Stephens orchiopexy.

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# 119

# Laparoscopic Varicocelectomy

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## Introduction

Varicoceles are abnormally dilated veins of the pampiniform plexus. They are primarily lateralized to the left side perhaps due to an anomalous valvular mechanism as the blood drains into the left renal vein. The prevalence of varicoceles increases through puberty from 8% to equal the prevalence of the adult population, approximately 15%, by the age of 15–19 years. Evaluating and treating varicoceles thereby comprises a significant proportion of problems presenting to the practicing pediatric urologist [1, 2]. In pediatric patients, varicoceles pose several intriguing conundrums: observe versus treat, if treat when to intervene, if treat what modality to use, and what is the evidence that treatment helps fertility, testicular volume, or symptoms? Significant correlation exists between testicular hypotrophy and altered semen parameters [3]. A body of evidence implies that a cohort of patients will demonstrate catch-up growth and spontaneous improvement of semen parameters and thus warrant observation only; yet, the parameters defining that group remain unclear [3–6]. Furthermore, there are conflicting data as to whether the testicular artery should be spared or not, as sparing may increase the risk of recurrence but has also been shown to improve semen parameters [7–9]. In addition, when specifically examining management approaches there are several to choose from: microsurgical subinguinal (Goldstein), inguinal (Ivanissevich), abdominal (Palomo, nonartery sparing), surgical antegrade sclerosis, radiographic retrograde embolization, and laparoscopic (complete ligation vs. artery/lymphatic-sparing). In a recent survey of pediatric urologists, there was no consensus as to the best surgical approach, with 38% of practitioners reporting the laparoscopic approach as their preferred method while 28% used subinguinal microsurgical, 14% inguinal, and 13% retroperitoneal (13%) [10]. This chapter focuses on the laparoscopic approach, which is the most frequently used method of treatment.

Laparoscopic varicocelectomy was first reported in 1988 with several technical refinements subsequently described [11–14]. The advantage of this approach is that magnification can improve the identification of the vessels and enhance the ability to spare lymphatics and/or the testicular artery. The disadvantages include a steep learning curve for physicians not exposed to laparoscopic techniques, as well as possible injury to the intra-abdominal organs. However, recent meta-analyses have deemed it a safe procedure in previously explored abdomens as well as effective in limiting hydrocele formation and varicocele recurrence [15, 16].

## Indications

Although clear indications exist for consideration for a varicocelectomy in adults, as outlined by the American Urologic Association (AUA) guidelines, which are mainly based on fertility testing, there is very little guidance for the pediatric patient aside from noting that varicocelectomy may be offered due to testicular size discrepancy [17]. However, these recommendations are nonspecific and are at variance with common clinical practice; when patients present with testicular asymmetry associated with a varicocele, 32% of practitioners intervene immediately despite data indicating that 85% of adolescent males presenting with greater than a 15% testicular size discrepancy will become normal after 2 years of observation [5, 6].

There are noteworthy differences between the pediatric and adult population; most adolescents present asymptomatically (the "bag of worms" finding on routine exam) and without a fertility question, whereas in the adult population fertility evaluations disclose varicoceles

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

in up to 35% of men found to be subfertile [18]. In addition, whereas assessing semen analysis is common in the adult population, only 13.1% of practitioners routinely obtain a semen analysis on adolescents with varicoceles. Furthermore, 48% of practitioners report discomfort discussing this issue with their adolescent patients and parents [19]. These differences highlight the difficulty in managing and knowing when to operate on a pediatric patient.

A closer examination of the question of surgical timing comes from a recent review by Kolon, who advocates for repair of the adolescent varicocele once the child is Tanner stage V and the total testicular volume is low, semen parameters are low, androgen laboratory results are abnormal, or the patient is symptomatic (rare) [2]. However, only 10% of pediatric urologists send semen for analysis at <17 years [5]. Although Kolon's review puts more weight on persistent abnormal semen analysis focusing on total motility counts (TMC) below 20 million and waiting until the patient reaches at least Tanner V maturity, others have used the testicular volume percent difference ($\text{TV}_{\text{diff}}$) as cut-off [2]. Diamond et al. found a correlation between a percent volume difference measured via ultrasound of >10% and lower TMC. However, at the 10% cut-off there would be a considerable number of patients with normal semen parameters. Hence some authors advocate for 20% $\text{TV}_{\text{diff}}$ as there was an inverse relationship between $\text{TV}_{\text{diff}}$ and TMC [3]. It is worth noting that Christman et al. followed 73 adolescent patients serially for a median of 2.7 years and was not able to reproduce the same finding [20]. They conclude that during adolescence there is too much variability to accurately assess future semen parameters; however, they do note that if the total testicular volume is low there is a significant correlation with low TMC.

Another parameter explored for indication for varicocelectomy is venous backflow. Van Batavia et al. reported that 50 of 53 adolescents with $\text{TV}_{\text{diff}}$ of >15% and peak retrograde flow greater than 38 cm/s failed to demonstrate catch-up growth after mean follow-up of 15.5 months [21]. These patients may be at risk for future fertility problems. Last, although rare in the adolescent population, pain is a consideration for varicocelectomy.

## Anatomy

Each variation of varicocelectomy takes into account the complex vasculature of the testis. Varicoceles develop when the pampiniform plexus experiences increased venous backflow and dilates due to elevated pressures. While the right internal spermatic vein drains directly into the inferior vena cava, the left internal spermatic vein connects to the left renal vein where backflow is higher. Hence, the majority of varicoceles are left sided. Consideration of a retroperitoneal mass or other pathology is indicated when there is a right-sided varicocele, and although pathology is rare we recommend retroperitoneal imaging when present [22]. Although the pampiniform plexus, eventually becoming the internal spermatic vein, is the main drainage of the testicle, the testicle and epididymis are also drained by the posterior spermatic plexus which flows into the external iliac vein and the cremasteric vein which drains into the pudendal vein. These collaterals allow for venous return following varicocelectomy.

The arterial blood supply to the testis is also complex, with blood coming from three arteries: (i) testicular artery from aorta; (ii) deferential artery from either the superior or inferior vesical artery off the internal iliac; and (iii) cremasteric artery from inferior epigastric artery. Thus, if the testicular artery is sacrificed, as in the Palomo repair, the testicle still receives adequate blood flow. Last, the primary lymphatics channels follow the testicular artery and hence can be confidently spared via a laparoscopic approach.

## Surgical procedure

The patient is brought into the operating suite after emptying his bladder. Following induction of general anesthesia, the patient remains in the supine position with his arms tucked. We prefer that both the surgeon and the assistant stand on the contralateral side from the varicocele. If desired, the patient may have a jell roll placed on the ipsilateral side of the varicocele to help keep the bowel away from the operative field (Figure 119.1; see Video 119.1). The required instruments are listed in Box 119.1.

Although this procedure has been reported using a single-site 20 mm port method, a three-port approach remains the most common [23, 24]. We place 5 mm trocars in the umbilicus, the right lateral rectus margin approximately 2 cm below the umbilicus and another port just superior to McBurney's point. This positioning and trocar placement can be mirrored for an isolated right-sided varicocele. For a bilateral varicocele repair, trocars are placed in the umbilicus, right and left lateral rectus margins approximately 2 cm below the umbilicus. An alternative trochar placement strategy is an umbilical port, one placed at the right lateral rectus margin about 2 cm from the umbilicus, and one placed midline approximately 8 cm below the umbilicus. In this case the camera is transferred from the umbilical trocar to the right lateral trocar when transitioning from operating on the left varicocele to the right side.

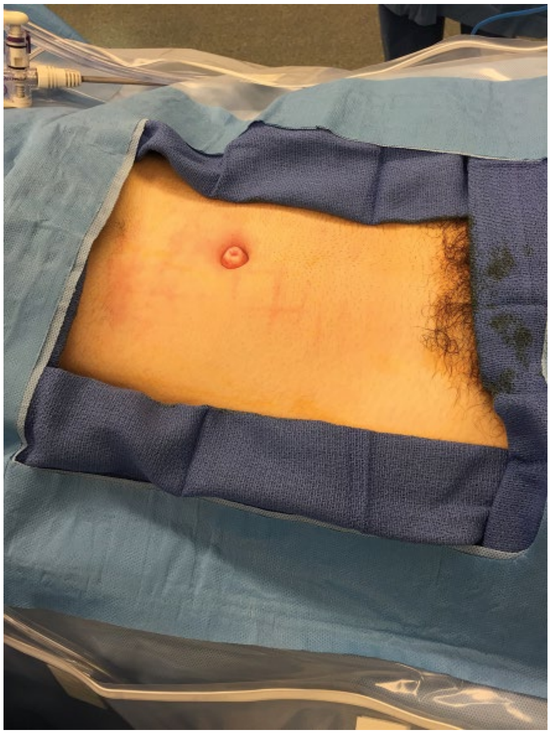

**Figure 119.1** Prepped and draped patient.

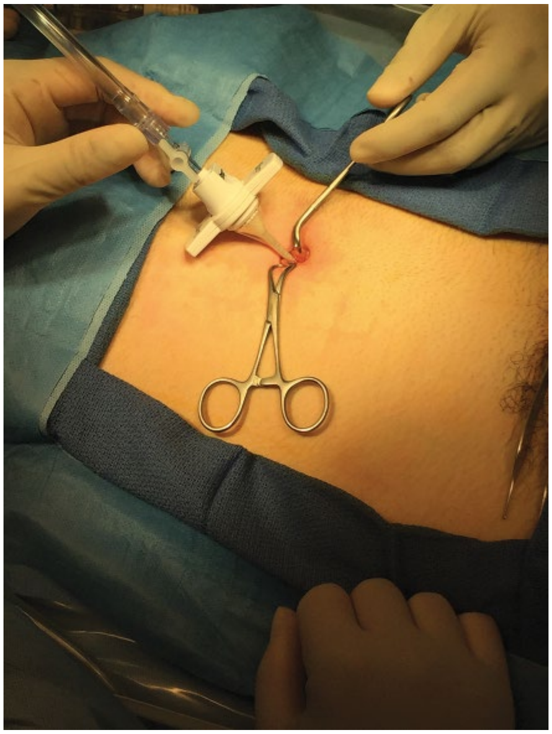

**Figure 119.2** Placement of 5 mm umbilical port: evert the umbilicus with towel clamps and make a 5 mm vertical incision using electrocautery down through to the fascia and place the Veress needle.

**Box 119.1 Instruments.**

- Electrocautery
- 15 Blade scalpel
- Towel clamp × 2
- 5 mm tocars × 2
- VeraStep™ 5 mm trocar
- 30° lens and camera
- 5 mm clip applier or LigaSure™
- 5 mm monopolar Endo Shears™
- Maryland grasping forceps
- Optional: laparoscopic Doppler

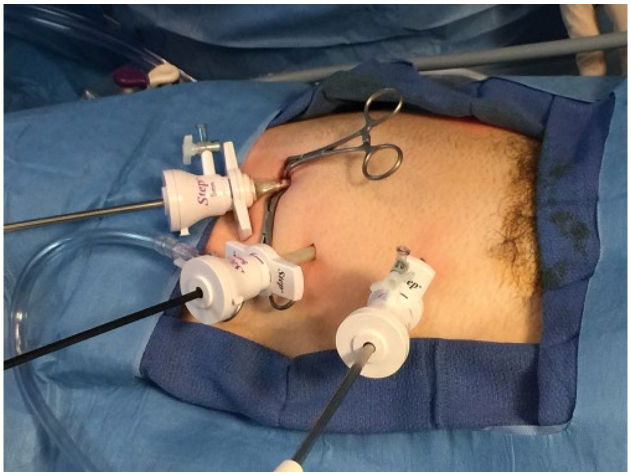

**Figure 119.3** Port placement for left-sided laparoscopic varicocelectomy.

Starting at the umbilical site, we evert the umbilicus and make a 5 mm vertical incision using electrocautery down through to the fascia (Figure 119.2). We use a 5 mm VeraStep Veress needle to insufflate with $CO_2$ at a rate of 3 l/min to a pressure of 10–15 mmHg, depending on the patient's body habitus. Once adequate pneumoperitoneum is achieved, the needle is exchanged for the 5 mm trocar in the nonslip sheath. A 30° lens is placed through the umbilical trocar and the other two 5 mm trocars are placed under direct vision with careful attention to avoid bowel and the inferior epigastric vessels (Figure 119.3). After inspection of all entry points and adjacent structures to ensure no damage, we look for closed internal rings bilaterally. Slight Trendelenburg position helps to allow the bowel to fall away from the cord. After identifying the spermatic cord and the vas deferens, a Maryland grasper is placed through the superior trocar and scissors in the inferior trocar and an incision is made in the posterior peritoneum over the spermatic cord vessels approximately 5 cm superior to the internal ring

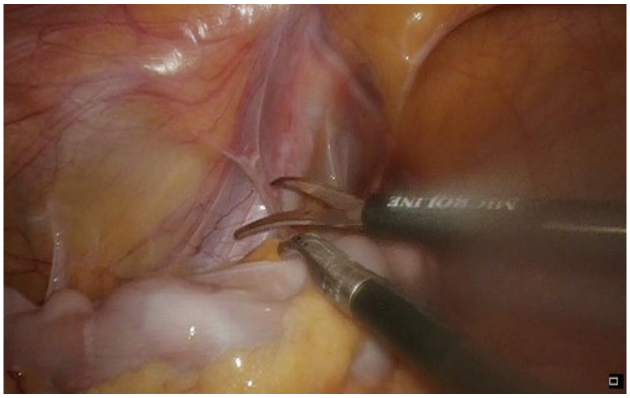

**Figure 119.4** Isolating the cord. Incise the posterior peritoneum over the spermatic cord vessels approximately 5 cm superior to the internal ring.

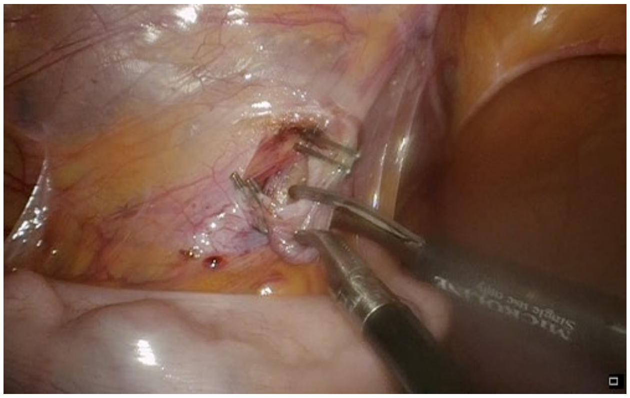

**Figure 119.5** Complete spermatic cord ligation. Place two 5 mm clips superior and two clips inferior and ligate the spermatic cord vessels when performing a complete ligation.

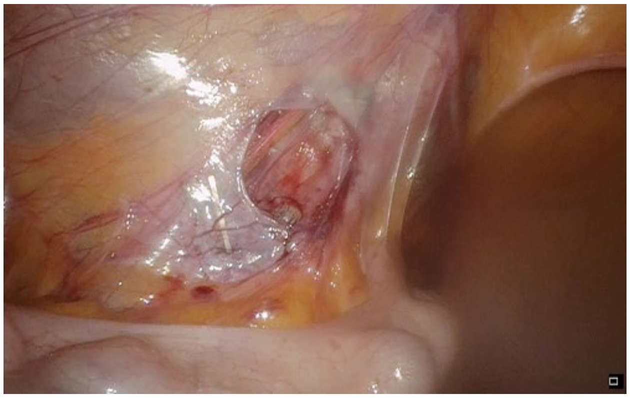

**Figure 119.6** Final inspection. Hemostasis is achieved and the clips are then tucked under the peritoneum to avoid contact with the bowel.

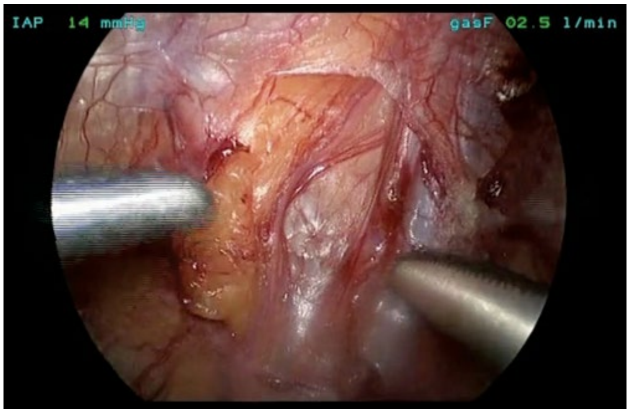

**Figure 119.7** Sparing the lymphatics. The lymphatic channels are small, translucent vessels lateral to the artery and vein.

(Figure 119.4). Once the cord is isolated for a distance, two 5 mm clips are placed superiorly and two clips inferiorly and the gondal veins is divided (Figure 119.5). In cases where the bundle is wider than the length of a clip, the clips are applied and the cord is partially transected and then another series of clips are applied to complete occlusion of the cord both proximally and distally and the cord severed. After inspecting for hemostasis the clips are then tucked under the peritoneum to avoid contact with the bowel (Figure 119.6). The ligation and transection of the vessels can be carried out using titanium or Weck clips and using scissors or a thermal device such as LigaSure™ or Harmonic scalpel.

The magnification offered by the laparoscopic approach assists in performing a lymphatic-sparing approach where the small translucent vessels are carefully dissected off the artery and vein and spared [25, 26]. This approach may limit hydrocele formation postoperatively (Figure 119.7). The injection of methylene blue into the subdartos tissue around the cord has been shown to help identify and isolate the lymphatics with good results [27]. In a series of 25 patients by Capolicchio et al. they had no postoperative hydroceles with a mean follow-up of 13 months. In addition, the use of a laparoscopic Doppler probe may be useful in sparing the testicular artery. This method may increase the recurrence of the varicocele but helps to improve semen parameters [9, 24].

The patient is then taken out of Trendelenburg and the surgical field is inspected. A laparoscopic aspirator may be used to suction any blood or irrigant that has pooled; however, we do not routinely open the device as its use is rarely necessary. The trocars are then removed under direct vision. With the use of 5 mm trocars it may not be necessary to close the fascia; however, it is our practice to routinely close the fascia with a 2-0 absorbable suture in figure-of-eight using a direct vision and groove director. The skin is closed with a 5-0 monofilament suture in a subcuticular fashion and Steri-Strips with collodion are applied (Figure 119.8). A weight-based dose of local anesthetic is injected at the end of the case.

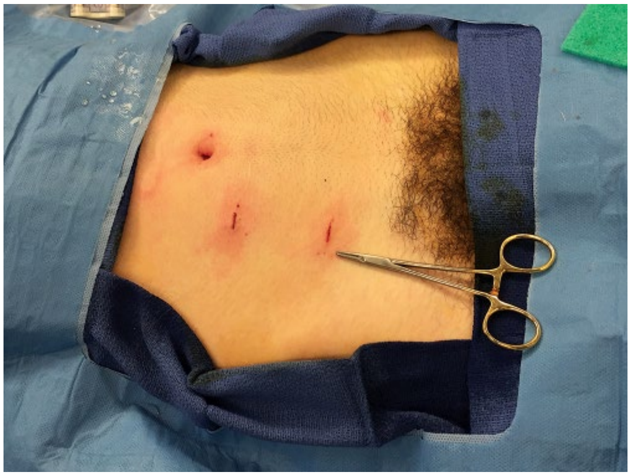

**Figure 119.8** The skin is closed with a 5-0 monofilament suture in a subcuticular fashion.

## Complications

Early complications include injury to adjacent organs, bleeding from insufficient spermatic vessel ligation, failure to ensure adequate hemostasis or injury to the inferior epigastric vessels. These complications are rare when using direct visualization and magnification. There is risk of bowel injury either through blind trocar placement, use of cautery and coupling, or through sharp dissection. By choosing plastic trocars and Trendelenburg these risks can be minimized. In a randomized controlled study of 654 pediatric patients comparing laparoscopic versus open varicocelectomy, Podkamenev et al. reported decreased testicular or scrotal edema rates of 3.9% versus 13.1%, wound complication rates of 0.23% versus 7.73%, and shorter operative times with 15 versus 26 minutes, respectively; however, there was no statistical difference between hydrocele rates of 0.23% versus 1.2% or recurrence rates of 1.84% versus 1.36% [28].

Late complications include hydroceles and recurrences. When comparing microsurgical, Palomo, embolization, inguinal, and laparoscopic approaches, postoperative hydroceles are reported as 0–1.6%, 4.6–9%, 0%, 4.3–17.5%, and 1.7–12.7%, while recurrences rates are 0.7–15.2%, 7.3–15.5%, 1.9–9.3%, 3.35–17%, and 4–26.5%, respectively [29, 30]. Hydroceles have been reported to occur on average up to 2 years (range 0.3–7.5 years) following the procedure [29]. Although hydroceles may occur following a mass ligation of the cord, Feber and Kass, reporting on adolescents undergoing an open Palomo approach, found that only 17% of the hydroceles required subsequent surgery [31]. We have found great success in managing recurrent varicocele using embolization. In our series of 60 patients undergoing salvage embolization, the presence of inguinal and retroperitoneal collaterals were significant independent prognosticators for recurrence and they were managed easily with this technique [32].

Borruto et al. in 2010 reported no difference between postoperative hydrocele or recurrence rates in a meta-analysis of 11 studies examining laparoscopic compared to open varicocelectomy [16]. In a large multicenter study of 1036 adolescents who underwent varicocelectomy either by open (39%), laparoscopic (51%), or percutaneous embolization (9.8%) Lurvey et al. reported significantly higher retreatment rates with embolization (1.5%, 3.4%, and 9.9%, respectively) while there was no statistical difference in hydrocele formation (4.9%, 8.1%, and 5%, respectively) [33]. Interestingly, they did note a higher hydrocele formation in younger patients with each year increase of age: there was 14% reduction in hydrocele formation with 1–5 years of follow-up. This finding may give more credence to observation in younger patients found to have an incident asymptomatic varicoceles.

## Outcomes

The goal of varicocelectomy in the pediatric population is to preserve future fertility while at the same time preventing morbidity. Direct evidence for preserving future fertility in pediatric population is lacking but many studies in the adult population demonstrate successful pregnancies in subfertile males. Pregnancy rates vary from 33.8–51.5% in a microsurgical subinguinal approach to 33–36% with a traditional Palomo approach to 13.1–40% utilizing laparoscopy, which is an improvement considering most adult studies involve treatment in subfertile males [3, 29].

Several studies have compared laparoscopic to open variocelectomy. Early comparisons demonstrated no superiority with respect to hospital stay, analgesic requirements, return to work, or operative times; however, over the past decade this has improved with refinement of the laparoscopic procedure [34]. In today's medical environment it is important to be cost-conscious. Al-Kandari et al. estimated costs of open, laparoscopic, and microscopic varicocelectomy at US$1800, US$2700, and US$2400 for unilateral and US$2100, US$3600, and US$3000 in bilateral procedures, respectively [35]. Robotic varicocelectomies have been reported to have outcomes similar to those of laparoscopy but have longer operative times when compared to laparoscopy (112 vs. 73 minutes) and significantly higher costs (US$15 000 vs. $8600) [36].

Recent studies have examined the different techniques utilized when performing a laparoscopic varicolectomy such as complete ligation versus lymphatic and/or testicular artery-sparing. Barroso et al. found no statistical difference in hydrocele or recurrence rates between the traditional open Palomo compared to laparoscopic approaches (9.7% vs. 6.9% and 2.9% vs. 4.4%, respectively) but reduced the hydrocele rate to 3.2% by sparing the testicular artery [37]. Kang et al. compared single-site laparoscopic variocelectomy with artery/lymphatic-sparing versus complete ligation of the cord and found a 0% hydrocele rate with a 2.9% recurrence rate in the sparing cohort while the complete ligation cohort experienced a 5.7% hydrocele rate and similar recurrence rate. Also, at three months follow-up there was improvement in both groups' semen parameters, with no difference between the groups [24]. Kim et al. compared complete ligation versus internal spermatic cord artery-sparing ligation and found a 5% versus 22% recurrence rate, respectively, but no hydrocele formation in the artery-sparing cohort compared to 4.7% in the complete ligation group [9]. When comparing specifically lymphatic-sparing to complete ligation Rizkala et al. noted a 4.5% hydrocele rate in the lymphatic-sparing laparoscopic approach versus 43% in the complete ligation group, with hydroceles forming much later in the complete ligation group (37 vs. 16 months) [26]. When the artery was not preserved in the lymphatic-sparing group the recurrence rate decreased from 6% to 1.3%. All of these studies showed adequate testicular catch-up growth regardless of the method used, and no hypotrophy, while reoperative rates for the hydroceles ranged from 0% to 31% and all recurrences were successfully managed with embolization. It is important to note that Zampieri et al. was able to demonstrate improvement of multiple semen parameters when the testicular artery was spared compared to it being ligated; however, in an adult population this did not necessarily translate to improved paternity [8, 35, 37, 38].

It has been noted that catch-up growth of the testicle improves with treatment as compared to observation, and that semen parameters, including total motility count, also improve with treatment [2, 38–41]. The degree of these improvements tends to parallel the grade of varicoceles; hence, physicians advocate for treatment of high-grade adolescent varicoceles in the absence of direct evidence that it improves fertility.

A more recent finding is that DNA fragmentation has been noted to lead to sperm damage and decreased pregnancy rates and has been found in patients with varicoceles [42]. A recent meta-analysis of adult patients with subfertility by Marmar et al. demonstrated an increased odds ratio of spontaneous pregnancy after varicocelectomy and other recent investigations have attributed this to a decrease in DNA fragmentation associated with a varicocelectomy [42, 43]. Lacerda et al. investigated DNA fragmentation in 21 adolescents between the ages of 14 and 19 and found improvements following varicocelectomy. In the future, DNA fragmentation may serve as a marker for those patients who could benefit from earlier intervention [44].

## Follow-up

Our patients return to the office 10–14 days following surgery to assess the trocar sites for good wound healing, signs of infection, hernias, etc. They follow-up again approximately 4–6 months later with a scrotal ultrasound to assess for recurrent varicoceles, hydrocele formation, and measurement of catch-up growth. If the patient had a preoperative semen analysis, we then request a follow-up semen analysis at this visit. Our last visit is scheduled at 2 years to assess the same parameters. If there is improvement in semen parameters, good catch-up growth, no hydrocele, and no recurrent varicocele we will have the patient return as needed.

## Conclusion

The adolescent varicocelectomy remains an evolving area of investigation. Many studies address issues of testicular growth, changes in semen parameters, complications, and timing of the procedure; however, without randomized prospective studies comparing treatment to observation, specifically examining paternity rates, there is a quintessential piece of data missing. This fact, combined with the current body of knowledge comprising varying degrees of evidence and very few being grade A, makes the issue of whether the benefits of varicocelectomy outweighs the harms a complex and unanswered question. However, when specifically examining the option of laparoscopy for treatment of the adolescent varicocele several conclusions can be made.

The laparoscopic approach to treating the adolescent varicocele with current technology and methods may rival or exceed success and complication rates when compared to the microsurgical approach and the traditional open Palomo procedure. Sparing the lymphatics reduces the risk of subsequent hydrocele formation; however, the need for intervention of these hydroceles is low and may bring into question the need for a lymphatic-sparing approach. In addition, we understand that sparing the artery will lead to higher recurrence rates but also to improvements in semen parameters. Last, with regard to catch-up growth, the ipsilateral testicle does improve with treatment; however, adolescents have asymmetrical growth during puberty and hence may warrant a longer period of observation.

In conclusion, laparoscopic varicocelectomy in the hands of an experienced surgeon can offer highly effective results with minimal complications. Future investigation should include randomized controlled studies of treatment versus observation and lab studies, such as DNA fragmentation, may in the future offer us further ability to identify those patients who would benefit from early intervention.

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# Part 7 Laparoscopy and Robotics: LESS and NOTES

## 120

## Laparoendoscopic Single-site Surgery: Ports, Access, and Instrumentation

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### Introduction

Since the first laparoscopic nephrectomy by Dr. Clayman in 1991 [1], advancements in minimally invasive surgery have led a push for even less invasive techniques. With reported benefits of improved cosmesis and less pain, Rane et al. presented the first single laparoscopic port procedure, called SLiPP, at the 2007 World Congress of Endourology [2]. Growing interest, varied surgical approaches, and differing language culminated in the formation of the Laparoendoscopic Single-Site Surgery Consortium for Assessment and Research (LESSCAR). A white paper was published in 2008 defining laparoendoscopic single-site (LESS) surgery as the umbrella term of this new technique [3]. Subsequent advancements in robotic surgery led to Kaouk et al. publishing the first urologic robotic LESS (R-LESS) series in 2009, reporting improved suturing and dissection compared to standard LESS surgery [4].

With increased adoption of both LESS and R-LESS over the following years, technology has broadened potential applications by improving ports, instrumentation, and optics. Herein, we discuss currently available products designed for LESS and R-LESS approaches.

### Ports

With the acceptance of LESS and R-LESS techniques, many new ports came to market. An analysis during the early adoption phase of LESS surgery (2007–2010) evaluated platform selection [5]. Of 1076 cases, 77% were performed with a single port (i.e. one skin and one fascial incision), while the remaining 23% were single-site with multiple trocars (i.e. one skin and multiple fascial incisions). The most popular single-port device at that time was homemade (46%), followed by TriPort™/QuadPort™ (29%), SILS™ Port (8%), GelPort®/GelPOINT® (7%), and X-Cone™/Endocone™ (5%). Although R-LESS was chosen in only 13% of cases, temporal trends noted increased utilization with a concurrent decrease in standard LESS surgery, which might explain the current selection of devices available [5]. This section focuses on currently available ports, and highlights described utilization for each in the literature.

#### Single-incision multiport

Single-incision multiport LESS surgery describes a single-skin incision with multiple standard low-profile laparoscopic trocars in separate fascial incisions (Figure 120.1a). Benefits include access to readily available products with potential downsides of external clashing. In 2007, Raman et al. described using this technique in a pig model, with subsequent successful completion in three humans [6]. Additional reports since that time have described this technique with transperitoneal LESS donor nephrectomy [7].

#### Homemade

Prior to the introduction of dedicated single-port devices, many clinicians created their own LESS ports. A popular method uses an Alexis® retractor and a surgical glove. Ports are placed through the fingers of the glove and secured with suture (Figure 120.1b) [8]. Benefits to using this system include flexibility in port placement, as well as the ability to use standard laparoscopic instruments given the potential wide range of motion [8]. Issues utilizing this type of system include lack of rigidity and port stability, as well as tearing of the glove requiring the need to stop the operation and redo the port [8–10].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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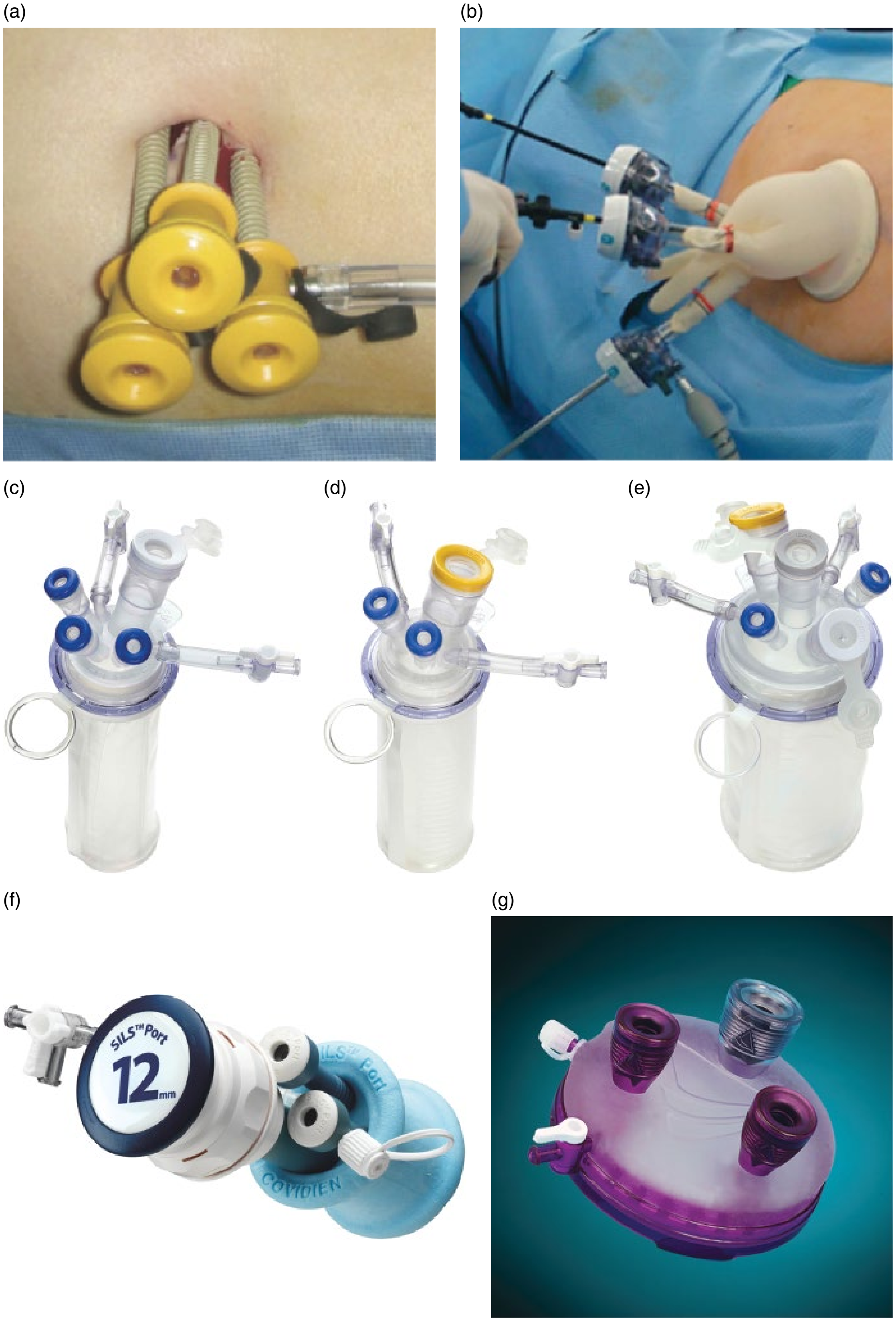
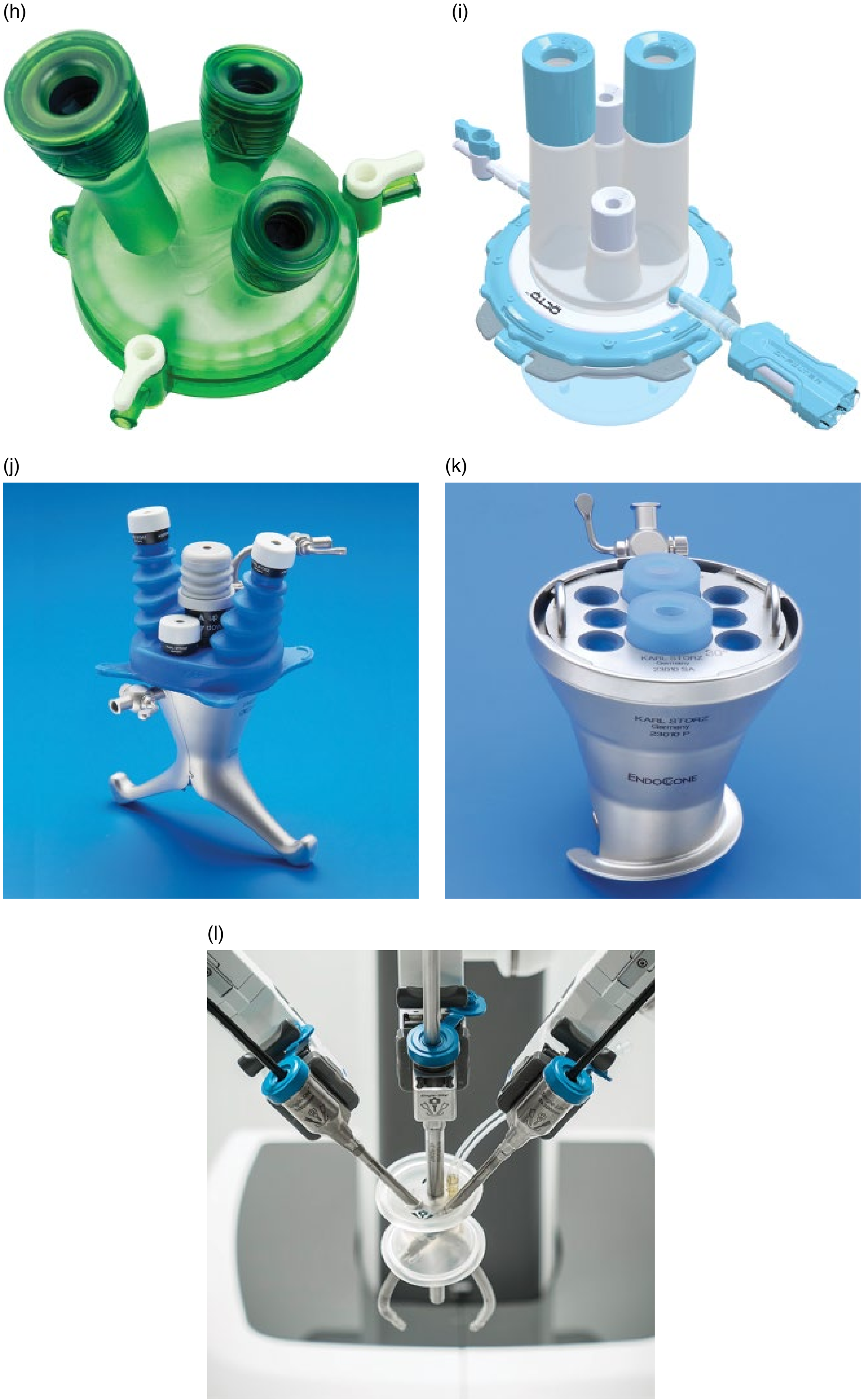


**Figure 120.1** Currently available laparoendoscopic single-site (LESS) and robotic laparoendoscopic single-site (R-LESS) ports. (a) Single-incision multiple-port LESS. (b) Homemade LESS. (c) TriPort+· (d) TriPort15. (e) QuadPort+. (f) SILS port. (g) GelPOINT. (h) GelPOINT Mini. (i) OCTO Port V2, four ports, configuration "A." (j) X-Cone. (k) Endocone. (l) Single-Site port. Sources: (a,b) Dr. Woong Khu Han, Yonsei University Hospital, Seoul, Korea. Reproduced with permission of Dr. Woong Khu Han. (c–e) Advanced Surgical Concepts, Bray, Ireland. Reproduced with permission of Advanced Surgical Concepts. (f) Medtronic, New Haven, USA. Reproduced with permission of Medtronic. (g,h) Applied Medical Resources Corporation, USA. Reproduced with permission of Applied Medical Resources, USA. (i) DalimSurgnet, Seoul, Korea. Reproduced with permission of DalimSurgnet. (j,k) Karl Storz Endoscopy-America, Inc., California, USA. Reproduced with permission of Karl Storz Endoscopy-America, Inc. (l) Intuitive Surgical Inc., California, USA. Reproduced with permission of Intuitive Surgical Inc.


(h)
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KARL STORZ
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**Figure 120.1** (Continued)

Reports describing the glove technique have included transperitoneal nephrectomy, partial nephrectomy, nephroureterectomy, adrenalectomy, partial cystectomy, ureterectomy, varicocelectomy, cyst decortication, ureterolithotomy, prostatic enucleation, and bladder rupture repair [8, 9]. This technique has also been utilized for R-LESS cases, including transperitoneal nephrectomy, partial nephrectomy, adrenalectomy, and nephroureterectomy [8, 10].

### TriPort+/TriPort15™/QuadPort+™ (Advanced Surgical Concepts, Bray, Ireland)

The first LESS port on the market, originally called the R-Port™ and subsequently the TriPort, was used in the first reported LESS nephrectomy [2] and the first R-LESS series [4]. Advanced Surgical Concepts now has three current configurations utilizing this technology: TriPort+, TriPort15, and QuadPort+. Models are currently distributed by Olympus (Tokyo, Japan). Each port has an internal anchoring ring that is placed through a Hasson incision with a blunt trocar and secures the device to the parietal peritoneum. An outer ring cinches down over a plastic sleeve to create a tight seal on the abdominal wall. The excess sleeve is excised prior to securing the port cap. The ports are built into the cap, and allow the passage of curved instruments due to their flexibility.

Both TriPort + and TriPort15 models are used with fascial incisions 12–25 mm and can accommodate abdominal walls up to 10 cm thick. They have two insufflation and/or ventilation ports, with the main difference being the working channels. The TriPort + has three 5 mm ports and one 5–10 mm port (Figure 120.1c) and the TriPort15 has two 5 mm ports and one 5–15 mm port (Figure 120.1d).

With the ability to accommodate the same abdominal wall thickness of 10 cm, the QuadPort + is for fascial incisions between 25 and 60 mm. It has two 5 mm ports, two 5–10 mm ports, and one 5–15 mm port, as well as two insufflation and/or ventilation ports (Figure 120.1e).

TriPort has shown broad utilization in the literature. In pediatric urology, it has been used for ochidopexy [11], varicocelectomy [12], simple nephrectomy [11, 13], and pyeloplasty [11, 13].

For adult transperitoneal LESS surgery, reports include partial nephrectomy [14, 15], radical nephrectomy [16], donor nephrectomy [17], adrenalectomy [18], vesicovaginal fistula repair [19], bladder diverticulectomy [20], and pyeloplasty [12]. Extraperitoneal LESS usage with TriPort has included cyst decortication [21], adrenalectomy [22], and radical prostatectomy [23]. More limited reports depict use of the TriPort to transvesically remove mesh [24, 25] and perform a bladder diverticulectomy [26].

Early R-LESS reports describe placing one robotic arm alongside the TriPort, but through the same skin incision, to limit instrument clashing. This technique has been utilized for radical prostatectomy, pyeloplasty, radical nephrectomy, and partial nephrectomy [4, 27].

### SILS port (Covidien, Dublin, Ireland)

The SILS port is a flexible foam port that is placed via Hasson technique through an approximate 2.0 cm fascial incision (Figure 120.1f). The low-profile design can mold to the incision tightly to limit gas leakage, but due to its relatively fixed size cannot accept a large range of fasical incision sizes or abdominal wall thicknesses. The three different models (SILSPT5TA, SILSPT12TA, and SILSPT15TA) each accommodate three trocars at a time, with the first two being 5 mm, and the last trocar either 5 mm, 5–12 mm, or 5–15 mm, respectively. There is also a separate insufflation/ventilation port, and one of the 5 mm ports has a side hole for additional insufflation/ventilation if needed.

Reports have described using the SILS port for pediatric cases [11], including simple nephrectomies [28]. In the adult literature, the SILS port has been utilized for transperitoneal LESS donor nephrectomy [7], varicocelectomy [29], and adrenalectomy [30], as well as retroperitoneal LESS adrenalectomy [31].

Because of its low-profile design and to prevent external clashing of instruments, adaptations to use the SILS port for R-LESS involve adjacently placed robotic ports through the same skin incision, essentially robotic single-site surgery [32]. This has been completed in patients undergoing robotic prostatectomy [33] and in select radical nephrectomy cases [34].

### GelPOINT/GelPOINT Mini (Applied Medical, Rancho Santa Margarita, CA, USA)

This system is based on an Alexis® wound retractor and is an evolution of the GelPort system. The device comes in two sizes, GelPOINT (incisions 1.5–7.0 cm, Figure 120.1 g) and GelPOINT Mini (incisions 1.5–3.0 cm, Figure 120.1 h). The retractor is placed through a Hasson incision and cinched to the abdominal wall. A GelSeal® cap is secured to the retractor, forming a tight seal and preventing gas leakage. Both systems incorporate three 5–10 mm sleeves and one 5–12 mm sleeve. The sleeves, which function as ports, are placed through the cap in a customizable configuration. In addition, two insufflation and/or venting ports are available on the cap. Benefits of these systems include the ability to move the ports in a number of configurations to prevent external and internal clashing. This has made this system ideal for R-LESS adoption, and is currently in use at the author’s institution.

To perform, robotic 5 mm flared trocars are predocked onto the robot arms and clutched through the sleeves.

Pediatric LESS reports using GelPOINT include transperitoneal nephrectomy, nephroureterectomy, partial nephrectomy, renal cyst decortication, gonadectomy, Malone antegrade continence enema, calyceal diverticulectomy, and ovarian detorsion with cystectomy [35]. Pediatric retroperitoneal LESS nephrectomy has also been reported [36].

Adult LESS procedures include transperitoneal nephrectomy [37] and donor nephrectomy [7, 38–41], and retroperitoneal nephrectomy [42], partial nephrectomy [43], and donor nephrectomy [44].

R-LESS procedures have included pyeloplasty [45], partial nephrectomy [45], and radical nephrectomy [34, 45]. In addition, GelPOINT Mini was used to perform the first R-LESS perineal prostatectomy [46].

## OCTO™ Port V2 (DalimSurgnet, Seoul, Korea)

The OCTO Port V2 is a two-piece device, consisting of a wound retractor and a port cap (Figure 120.1i). The wound retractor comes in three sizes: 1.5–3.0 cm, 3.5–5.0 cm, and a deeper 3.5–5.0 cm for thicker abdominal walls. An inner ring is placed through a Hasson incision, and secured by stretching the externalized silicone around the external ring. The port cap comes with either three (one 5 mm and two 5–12 mm) or four (two 5 mm and two 5–12 mm) built-in ports. In addition, each four-port cap can be in one of two configurations: (i) 5 mm ports on opposite sides and (ii) 5 mm ports on the same side, giving multiple different options depending on surgeon preference and the operation performed. The port caps are made of silicone, making them flexible during laparoscopy and allowing passage of curved instruments. After securing to the wound retractor, the port cap can rotate 360°, allowing for versatility in instrument position. There are also two smoke filtering systems and a separate insufflation port.

Notable OCTO Port use in the literature includes transperitoneal LESS radical nephrectomies in humans [47] and partial nephrectomies in a porcine model [48].

## X-Cone, Endocone, S-Port™ (Karl Storz, Tuttlingen, Germany)

The X-Cone is a reusable single-port device that consists of two metal halves that secure together to form a 2.5 cm cone (Figure 120.1j). A fascial incision of approximately 2.0 cm is used, and the two halves are inserted separately before securing in place. The silicone sealing assembly with built-in ports is secured on top of the cone. The port configuration is four 5 mm ports and one 5–12 mm port. There are two additional adapters for insufflation and/or venting.

The Endocone is a 3.4 cm multilumen reusable port with six 3–5 mm channels, one 5–12 mm channel, and one 5–15 mm channel (Figure 120.1k). It has a separate insufflation port, and is placed through a 3.0–5.0 cm fascial incision using the Hasson technique.

The S-Port consists of single-use wound retractors and an attachment cap that has an insufflation port. Once secured to the wound retractor, either the X-Cone or Endocone seal cap can be secured on top for variations in port placement.

Reports in pediatric urology have included transperitoneal LESS nephroureterectomy [49], nephrectomy, and orchidopexy [50].

Reports in adult urology have described using the X-Cone to perform transperitoneal LESS staging lymphadenectomy in patients with high-risk prostate cancer [51], varicocelectomy [52], radical nephrectomy, partial nephrectomy, pyeloplasty, and renal cyst ablation [53].

Greco et al. utilized the Endocone to perform LESS transperitoneal radical nephrectomy in 33 patients [54].

## Single-Site™ port (Intuitive Surgical Inc., Sunnyvale, CA, USA)

The Single-Site port is the first platform designed specifically for R-LESS with the da Vinci® Si Surgical System (Figure 120.1l). The flexible port is placed through a 1.5 cm fascial incision and has access for the 8.5 mm robotic endoscope, two 5 mm curved robotic cannulae, a 5–10 mm assistant port, and an insufflation port. The curved cannulae are designed to recreate triangulation and are used specifically with Intuitive semirigid instruments (described later).

R-LESS reports using this device have included pyeloplasty [55], radical nephrectomy [56], and partial nephrectomy [57].

## Comparison

The decision on which port or access system to use depends on multiple factors: whether the procedure is laparoscopic or robotic, trans- or extraperitoneal, pediatric or adult, and upper or lower tract, among others. However, multiple studies have attempted to compare the various devices in training simulation. Two independent investigators noted no benefit of access devices over single-incision multiport setups [58], including less instrument strain and shorter performance time with the latter [59]. Focusing on just the advanced device platforms, studies have shown the GelPOINT [60, 61] and the SILS port [61] to be the most consistent with regards to simulation completion.

For R-LESS, White et al. compared SILS port, GelPOINT, and TriPort, and preferred SILS port with adjacent robotic trocars for its durability, ability to exchange trocar sizes, and maximal range of motion [32, 34]. Ultimately, the port or access device used is a personal choice and we recommend trialing various models to determine what works best.

## Access

### Transperitoneal

Transperitoneal LESS access is typically obtained at the umbilicus to hide the surgical scar, although any abdominal entry site could be used based on patient or surgical factors. After making a skin incision, subcutaneous tissue is dissected to expose rectus fascia. If performing single-incision surgery, the fascia is typically retracted with Kocher clamps and a Veress needle placed to insufflate the abdomen [6]. Retractors are often used to stretch the skin in order to place the ports at the extent of the fascia. If performing single-port surgery, the Hasson technique is used to gain intraperitoneal access. After making a fascial incision of appropriate length based on the port chosen, the peritoneal cavity is accessed by sharply dividing preperitoneal fat and peritoneum. Before inserting the port, we recommend performing a finger sweep to ensure no adhesions are present where the port will be secured.

### Extraperitoneal

Both infra-umbilical and retroperitoneal LESS have been described and both utilize similar access techniques. For the former, an infra-umbilical skin incision of appropriate length, depending on the port to be used, is made and subcutaneous tissues are dissected, exposing anterior rectus fascia. An incision is made in the fascia and the rectus muscle is separated, exposing posterior rectus sheath. A finger is used to bluntly sweep anterior to the posterior rectus sheath in order to create a plane in the space of Retzius. A balloon dilating port can be used to develop this space prior to inserting the LESS port [23].

Retroperitoneal LESS surgery is typically performed off the 12th rib in the midaxillary line, although more inferior incisions have been described [22, 42, 43]. After dividing subcutaneous tissues, a Kelly clamp can be used to bluntly poke through lumbodorsal fascia into the retroperitoneal space. By inserting a finger into the space, a plane can be created, palpating the psoas muscle posteriorly and the lower pole of the kidney anteriorly. A balloon dilating port is again used under visualize guidance to enlarge this space, during which the psoas muscle should be kept horizontal to maintain orientation. Prior to inserting the LESS port, the fascial incision is often elongated, depending on the port used [42].

## Instrumentation

With adoption of LESS came advancements in instrumentation due to the loss of standard laparoscopic triangulation. Although any laparoscopic instrument could technically be used for LESS approaches [62], both prebent and articulating instruments are more frequently utilized [5]. Instruments sometimes require “chopstick” laparoscopy, where they cross at the fascial level, and the surgeon’s right and left hands control the intracorporeal left and right tip, respectively. In the following section we summarize currently available LESS and R-LESS instrumentation. Although literature regarding these instruments is less often highlighted, we cite the use when possible.

### HiQ LS handles and instruments (Olympus)

HiQ LS handles and instruments are 5 mm reusable instruments with a proximal curve to prevent external clashing, as well as distal double curves to restore triangulation without the surgeon having to cross instruments (Figure 120.2a). The rigid curves of these instruments limits their use to flexible ports such as TriPort+/TriPort15/QuadPort+. Graspers include Johann (atraumatic fenestrated), clinching (atraumatic), and a long multipurpose (atraumatic). Dissectors include a short Maryland, fine Maryland, and a right-angle Maryland. Electrocautery devices include a monopolar hook and Metzenbaum scissors, although both the monopolar handle and the deactivatable ratchet handle can be used with all instruments.

These instruments have been utilized for LESS vesicovaginal fistula repair [19], as well as donor nephrectomy [7].

### SILS hand instruments (Covidien)

This line of 5 mm single-use instruments can be used in a standard or “chopstick,” method. To recreate triangulation, the distal ends of the instruments articulate up to 85° in all directions by bending the handle externally. They also can rotate 360° (Figure 120.2b). Their straight design with articulated end allows these instruments to be used in any port. Instruments include a dissector, shears, and a hook, all with monopolar cautery, as well as a grasper.

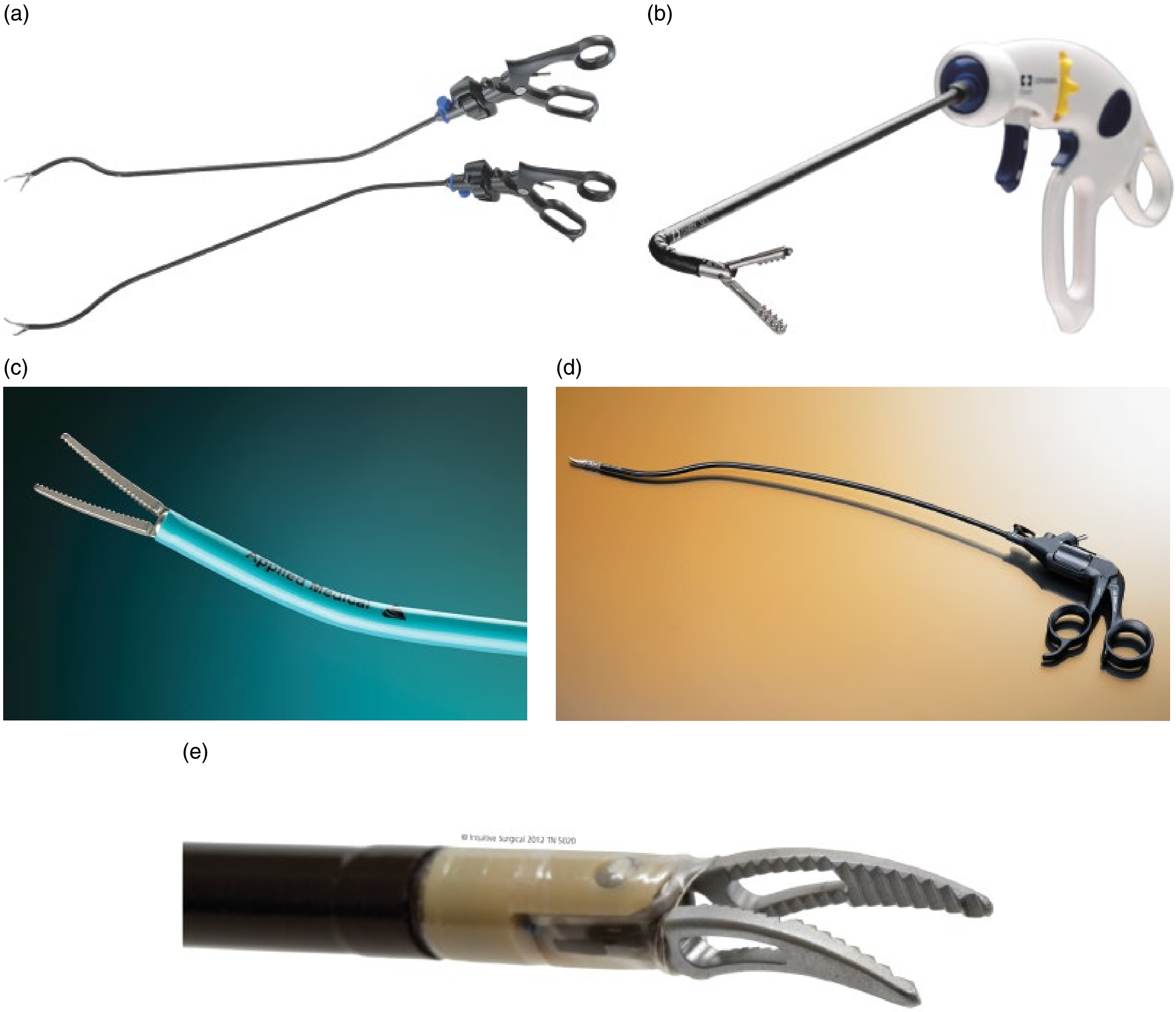

**Figure 120.2** Currently available laparoendoscopic single-site (LESS) instrumentation. (a) HiQ LS handles and instruments. (b) SILS hand instrument. (c) Epix inline angled dissector. (d) Rotatip CUSCHIERI D-CON. (e) Semirigid Maryland bipolar. *Sources:* (a) Olympus America Inc. Reproduced with permission of Olympus. (b) Medtronic, New Haven, USA. Reproduced with permission of Medtronic. (c) Applied Medical Resources Corporation, USA. Reproduced with permission of Applied Medical Resources, USA. (d) Karl Storz Endoscopy-America, Inc., California, USA. Reproduced with permission of Karl Storz Endoscopy-America, Inc. (e) Intuitive Surgical Inc., California, USA. Reproduced with permission of Intuitive Surgical Inc.

### Epix® inline angled dissector (Applied Medical, Rancho Santa Margarita, CA, USA)

Applied Medical has a line of 5 mm single-use laparoscopic instrumentation called Epix. Of the instruments, the angled dissector is the only one with a distal angle of 20°, which helps to facilitate triangulation during LESS surgery (Figure 120.2c). Although it is a fixed angle, the slight degree allows it to still be used in rigid ports similar to the GelPOINT system.

This instrument was used by Cherian et al. to perform retroperitoneal LESS nephrectomy [63].

### Rotatip® instruments (Karl Storz)

These 5 mm reusable curved instruments can be dismantled into three parts: handle, outer sheath, and working insert, and each insert can rotate independently of the outer sheath. There are four different sheath curves available, depending on the application: CARUS, CUSCHIERI O-CON, CUSCHIERI D-CON I, and LEROY. The CARUS sheath has a straight outer sheath and a double curved distal sheath to recreate triangulation. With the jaw offset at 45° to the axis of the outer sheath, the double distal curve allows a good view of the instrument. In contrast, the CUSCHIERI O-CON sheath has a straight outer sheath, and a single distal sheath curve. The CUSCHIERI D-CON I has a single curved outer sheath along with a double curved inner sheath (similar to the CARUS), to recreate triangulation and limit external clashing (Figure 120.2d). Lastly, the LEROY has a double curved outer sheath and a similar double curved inner sheath, to minimize external clashing and maximize triangulation. The handle and distal end of the LEROY sheath form a straight line, so movements can be more intuitive. Each sheath comes in Kelly forceps, atraumatic grasping forceps, and Metzebaum scissors.

### Semirigid instruments (Intuitive Surgical Inc.)

This selection of 5 mm R-LESS instruments are designed specifically for use in the curved cannulae of the Single-Site port. The cannulae cross in the midline similar to the "chopstick," method, but because the da Vinci Si Surgical System reconfigures the right and left hands to control opposite instruments, the result is more natural. Most of these instruments have a fixed wrist, unlike standard da Vinci instrumentation. The lone exception is the wristed needle driver, which can bend up to 45°. Other instruments include a cadiere forceps, crocodile grasper, fundus grasper, Maryland dissector, Maryland bipolar (Figure 120.2e), fenestrated bipolar, monopolar hook cautery, curved scissors, curved needle driver (not wristed), Hem-o-lok® clip applier, and suction irrigator. This system is currently only available with da Vinci Si Surgical System.

As before, these instruments have been used in pyeloplasty [55], radical nephrectomy [56], and partial nephrectomy [57].

### Comparison

A 2010 study by Stolzenburg and colleagues compared straight instruments in a standard laparoscopic port configuration to pre-bent and articulating instruments in a single-port dry model and porcine nephrectomy model. They noted no significant difference between the standard laparoscopic and pre-bent instruments, but significantly slower times with the articulating instruments [64]. As with ports and access devices, we recommend trialing multiple instruments to determine what works best.

## Camera/lenses

Given the tight external working space with LESS surgery, camera adaptations to improve movement and visualization have been developed. It is important to note that articulating laparoscopes have a digital chip in their tip, and are covered with a plastic casing that can degrade over time [65].

We describe three different cameras that have been designed specifically for LESS.

### ENDOEYE FLEX (Olympus)

The ENDOEYE FLEX is a 5 mm high-definition laparoscope that can articulate up to 100° in all directions and rotate 360° degrees (Figure 120.3a). It has a digital chip at the distal end, with built-in camera and light cord. The design allows maneuverability to minimize external clashing while still obtaining appropriate viewing angles.

### IDEAL EYES HD (Stryker, Kalamazoo, MI, USA)

The IDEAL EYES HD is a 5 mm high-definition laparascope that can articulate 100° in all directions and rotate 360° degrees. It has a digital chip at the distal end, the handle is angled 15° for improved ergonomics, and the camera and light are in an integrated cable.

### EndoCAMeleon (Karl Storz)

The EndoCAMeleon is a 10 mm telescope with a viewing angle that adjusts from 0 to 120° by rotating a knob near the light port (Figure 120.3b). The digital chip in the end rotates within the scope, so there is no plastic casing that might degrade [65]. Therefore, it is potentially more durable.

## Other products

### AirSeal® (CONMED, Utica, NY, USA)

The AirSeal system consists of an intelligent flow system (iFS), along with proprietary tubing and ports. This unique device can operate in three different modes: AirSeal, smoke evacuation, and continuous insufflation. In AirSeal mode, the port recirculates $CO_2$ with high-pressure nozzles in the cannula to create an air barrier and stable pneumoperitoneum without valves, regardless of the amount of suction used. Continuous air circulation also constantly evacuates intra-abdominal smoke, which can be a problem with LESS and R-LESS due to the close proximity of working instruments and the camera. Access ports are available in 5 mm, 8 mm, and 12 mm

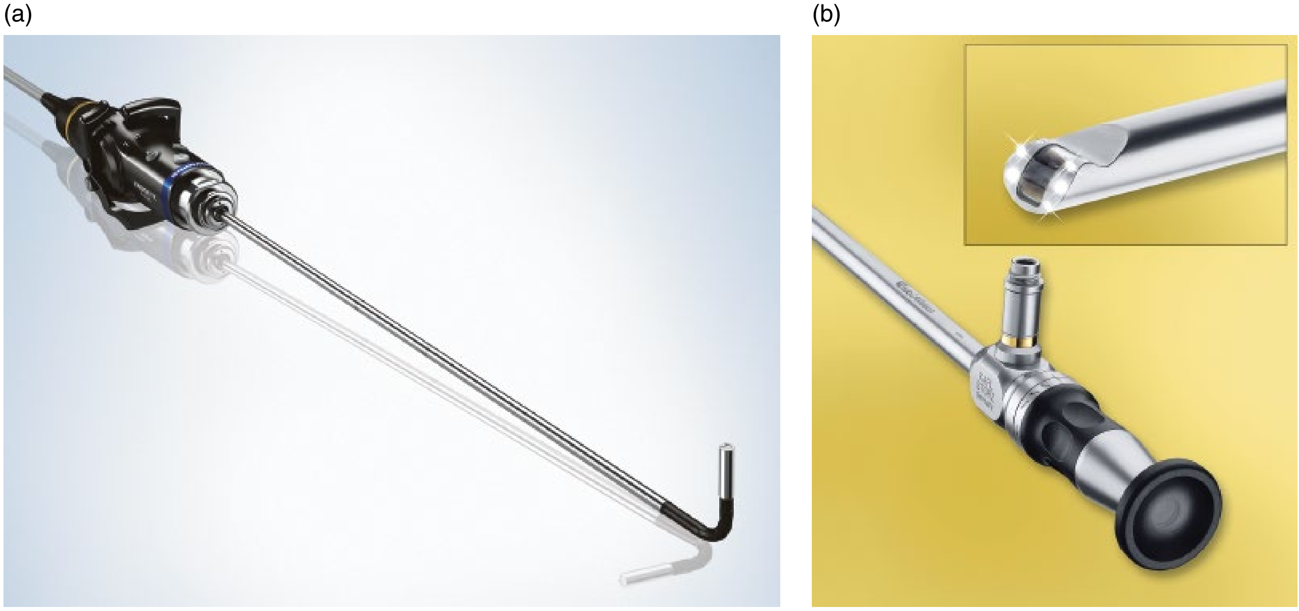

**Figure 120.3** Currently available laparoendoscopic single-site (LESS) cameras/lenses. (a) ENDOEYE FLEX. (b) EndoCAMeleon. Sources: (a) Olympus America Inc. Reproduced with permission of Olympus. (b) Karl Storz Endoscopy-America, Inc., California, USA. Reproduced with permission of Karl Storz Endoscopy-America, Inc.

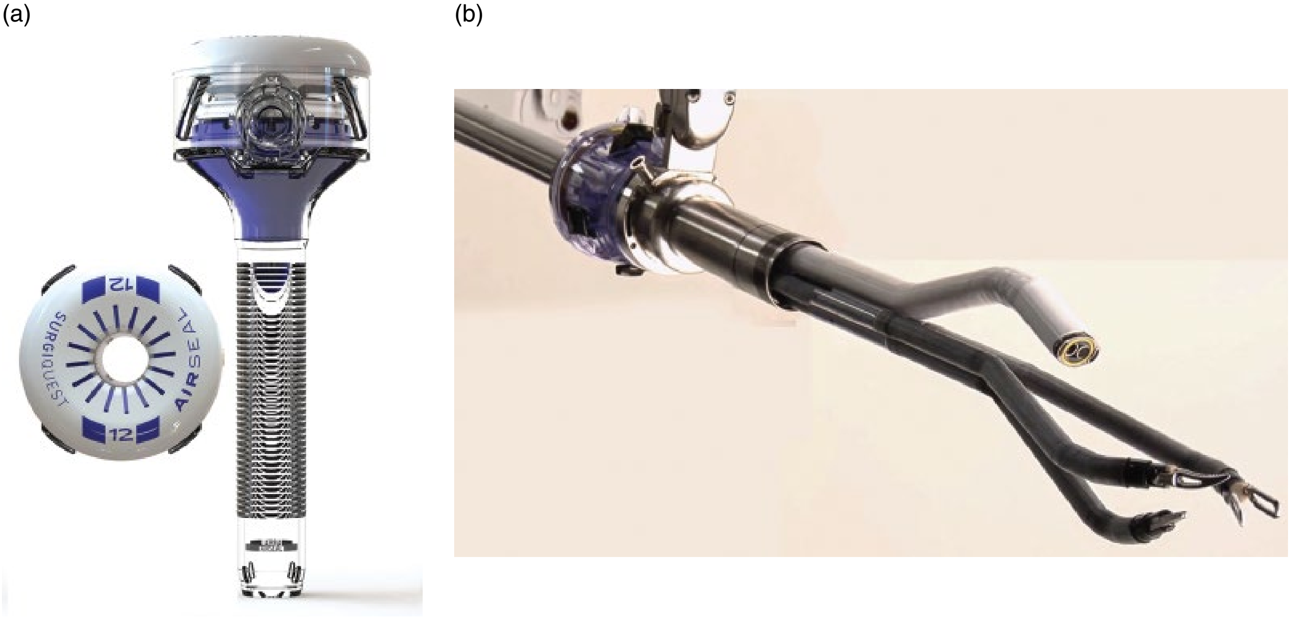

**Figure 120.4** Other laparoendoscopic single-site (LESS) products. (a) AirSeal. (b) da Vinci Sp Surgical System. *Source:* (a) CONMED Corporation, New York, USA. Reproduced with permission of CONMED Corporation. (b) Intuitive Surgical Inc., California, USA. Reproduced with permission of Intuitive Surgical Inc.

sizes (Figure 120.4a). Because of the need for specialized ports, AirSeal ports are only compatible with devices similar to the SILS port and GelPOINT. In smoke evacuation mode, proprietary dual-lumen insufflation tubing is connected to the iFS and two conventional ports. This can be used with any LESS port setup as long as two access points are available. For continuous insufflation mode, standard laparoscopic insufflation tubing can be connected from the iFS to a single conventional port to provide high-flow insufflation.

## Other systems

### da Vinci SP Surgical System (Intuitive Surgical Inc.)

This R-LESS system is not yet on the market, although it received US Food and Drug Administration (FDA) 510 k clearance in April 2014. It is designed to be used with the da Vinci Xi Surgical System. The SP platform is a separate patient-side cart which uses the Xi surgeon console and vision cart with a new software and foot pedal to allow for new control modes.

The port is a 2.5 cm cannula, with a 3D articulating high-definition 6 mm camera and three fully articulating 6 mm instruments (Figure 120.4b). Each instrument has EndoWrist® at the distal joint, in comparison to the semi-rigid single-site surgery instruments, as well as a proximal articulating joint to allow for triangulation [66].

Kaouk et al. performed 11 radical prostatectomies and 8 radical nephrectomies utilizing a previous platform, SP999 [67]. The newer platform is model SP1098.

See accompanying Video 120.1.

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# 121

# Laparoendoscopic Single-site Upper Tract Surgery

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## Introduction

Since 1991, when the first laparoscopic nephrectomy was reported, laparoscopy has flourished in urology for the treatment of both benign and malignant conditions. Techniques and instrumentation have evolved to address more complex cases and pathology. New trocars, optics, instruments, and robotic devices have all been developed in a collective effort to improve efficacy, minimize patient morbidity, and reach for superior cosmetic results.

Laparoendoscopic single-site (LESS) surgery is one example of how new technology and new techniques have converged to allow for the performance of complex surgery through fewer incisions. In a short time span, nearly the entire gamut of urologic procedures has been performed via a LESS approach [1, 2]. Moreover, the diffusion of LESS has been fairly rapid across the globe. The goal of LESS surgery is to provide equivalent surgical outcomes with improved cosmetic results. Ongoing research is aimed at clarifying what, if any, perioperative or convalescence-related benefits may be offered by minimizing the number of incisions and cumulative incision length used compared to conventional laparoscopy [3]. In addition, the role of robotics in LESS surgeries continues to be explored as a viable modality, the hope being that the shorter learning curve associated with robotic assistance may allow dissemination of LESS surgery to a greater number of patients.

Of the cases reported in the literature to date, the largest experience of urologic LESS surgery has been in the upper urinary tract, specifically renal procedures [1]. Upper tract urologic LESS surgery consists of both extirpative and reconstructive procedures of the kidneys, adrenal glands, and ureters. There is potential for high surgical volume of LESS procedures for renal and adrenal pathology, but challenges remain to its diffusion into widespread practice [4].

Although LESS surgery is a direct and natural extension of multiport, or “conventional,” laparoscopy, there are several unique aspects to LESS. Access is most commonly through the umbilicus as the “single site,” however, other locations can be utilized, such as a suprapubic or “mini-Pfannenstiel” approach, a transabdominal or retroperitoneal flank approach, or even a Gibson incision–retroperitoneal approach [5–7]. Access can be via a specialized port, or clustered conventional ports. A wide variety of purpose-built instrumentation and various options for imaging (e.g. rigid vs. flexible endoscopy) are available. For each LESS operation, although modifications in technique and maneuvers are often made, conventional laparoscopic techniques are largely followed. It is likely that advances in technology and, in particular, robotics will allow single-site access to be commonplace with expanding indications and outcomes data to support its use. This chapter will discuss these interesting facets of urologic LESS surgery of the upper tract.

## Trocar/port-site placement

### Umbilical and periumbilical

The majority of urologic upper tract LESS surgery is approached via an umbilical single-site access. Published reports of LESS have used all of the wide variety of access modalities available, both commercially manufactured and “homemade” designs created by surgeons using already available devices [1, 5, 8, 9] (Table 121.1). The umbilical trocar site is most often employed as it provides the opportunity to conceal incisions/scars. Multiport

*Smith’s Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 121.1** Laparoendoscopic single-site surgery access modalities.

| Device | Features |
|---|---|
| Triport 15 (Advanced Surgical Concepts, Dublin, Ireland) | Two 5 mm ports, one 15 mm port reducible to 5 mm<br>Incision required: 1.2–2.5 cm<br>Disposable |
| TriPort + (Advanced Surgical Concepts) | Three 5 mm ports, one 10 mm port reducible to 5 mm<br>Incision required: 1.2–2.5 cm<br>Disposable |
| QuadPort + (Advanced Surgical Concepts) | Two 5 mm ports, two 10–12 mm ports reducible to 5 mm, one 15 mm port reducible to 5 mm<br>Incision required: 2.5–6.0 cm<br>Disposable |
| Endocone (Karl Storz, Tuttlingen, Germany) | One 10 mm port, one 10–15 mm port, six 3–5 mm ports<br>Incision required: 3.0–3.5 cm<br>Reusable |
| GelPoint Advanced (Applied Medical, Rancho Santa Margarita, CA, USA) | Three 10 mm ports. One 12 mm port. Accepts multiple conventional trocars or direct insertion of instruments<br>Incision required: 1.5–7.0 cm<br>Disposable |
| SILS Port (Covidien,Minneapolis, MN, USA) | Three foam insertion sites for passage of low-profile trocars<br>Incision required: 2.0 cm<br>Disposable |
| AnchorPort (ConMed, Utica, NY, USA) | Uses recirculating $CO_2$ to create seal, may pass multiple instruments through ports of varying calibers<br>Incision required: 1.5–2.5 cm<br>Disposable |

trocars, GelPort™/GelPoint Advanced™ devices (Applied Medical, Rancho Santa Margarita, CA, USA), or a clustered series of low-profile trocars can be employed within the umbilicus. Multiport trocar placement at the umbilicus requires a single incision, ranging from 2 to 5 cm to accommodate the chosen trocar (Figure 121.1). Use of separate low-profile trocars allows for more independent mobility and use of reusable devices, also using an incision ranging from 2 to 3 cm at the umbilicus (Figure 121.2).

Compared with conventional laparoscopy, during LESS surgery the laparoscope and working instruments are in much closer proximity to one another due to the nature of single-site access. This can necessitate the use of flexible scopes and/or instruments to avoid clashing and to allow for triangulation. The umbilical port site allows for adequate access to the upper tract urologic organs with the use of regular length instrumentation, in most cases.

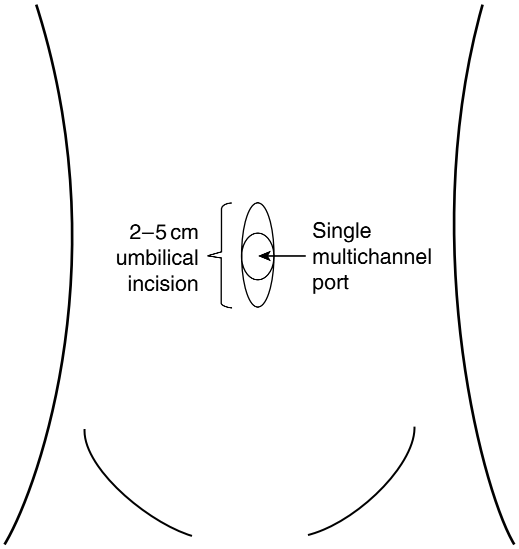

**Figure 121.1** Insertion of a multiport trocar at the umbilicus.

When treating obese patients, lateralization of the centrally located single incision toward the side of intended surgery may be necessary to offset length limitations of the operating instruments. The surgeon must consider whether this lateralized incision, no longer “hidden” within the umbilicus, still offers potential cosmetic advantages to the patient on a case-by-case basis. Alternatively, a retroperitoneoscopic LESS approach can be employed. Lateralization of the single site of access is akin to the lateralization of trocars employed during conventional laparoscopy in this patient population. Typically, this maintains the midpoint of the incision at the craniocaudal level of the umbilicus, but simply shifts it laterally toward the targeted kidney or adrenal gland, providing improved visualization with the laparoscope and simpler reach with the working instruments. Considerations when employing this modification in trocar placement include: the risk of developing incisional hernias, anatomic approach to traversing versus splitting muscle layers, as well as postoperative pain and cosmesis.

## Operative approach

A suprapubic approach has been reported for LESS simple, radical, and donor nephrectomy, as well as LESS nephroureterectomy. In selected patients, a cosmetic advantage may be obtained by concealing the single incision below the waistline. A small, or “mini-Pfannenstiel,” incision is employed that ranges between 5 and 8 cm in size. The size of the incision should allow for specimen extraction, but be as small as possible to optimize cosmesis. Access can be gained with a multiport device

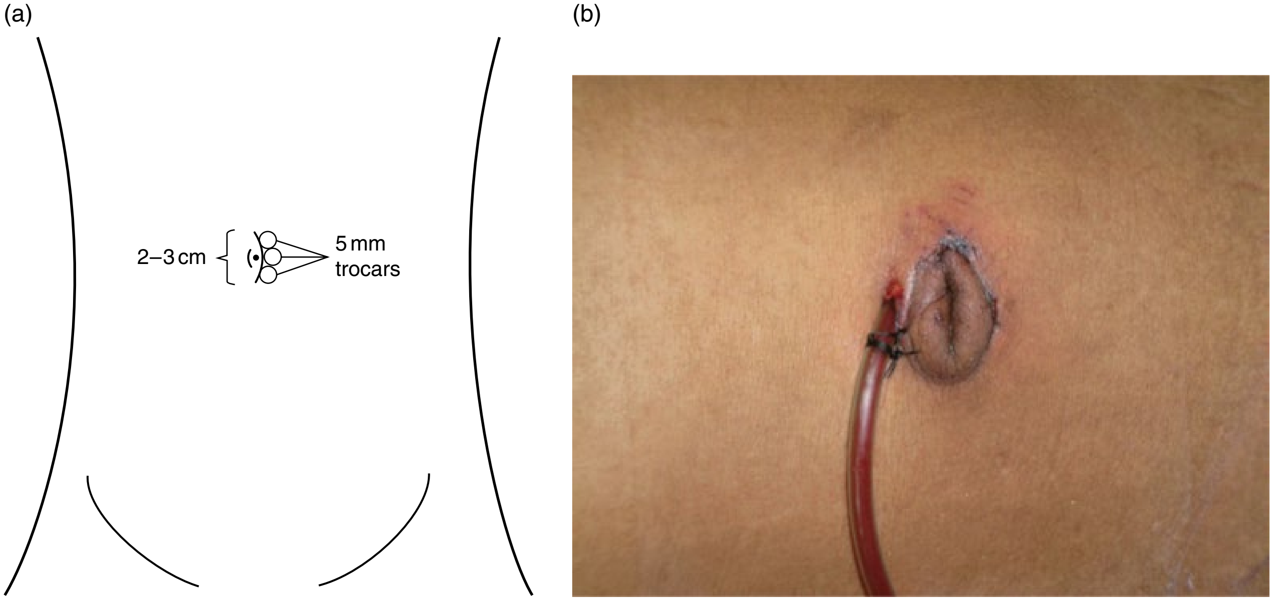

**Figure 121.2** (a) Insertion of three 5 mm low-profile trocars through a small umbilical incision. (b) Postoperative scars demonstrating positioning and proximity of trocars to the umbilicus.

(Figure 121.3) or using independently inserted, low-profile trocars [6, 10–12].

The suprapubic approach has more theoretical advantage in cases that require a sizable incision for specimen extraction, such as simple, radical, or donor nephrectomy or nephroureterectomy, in contrast to purely reconstructive surgery (e.g. LESS pyeloplasty) or surgery requiring extraction of small specimens (e.g. LESS cyst decortication or LESS partial nephrectomy). To allow for full access and ability to dissect circumferentially around the upper pole and posterolateral attachments of the kidney, it is useful to have bariatric and articulating laparoscopic instruments available.

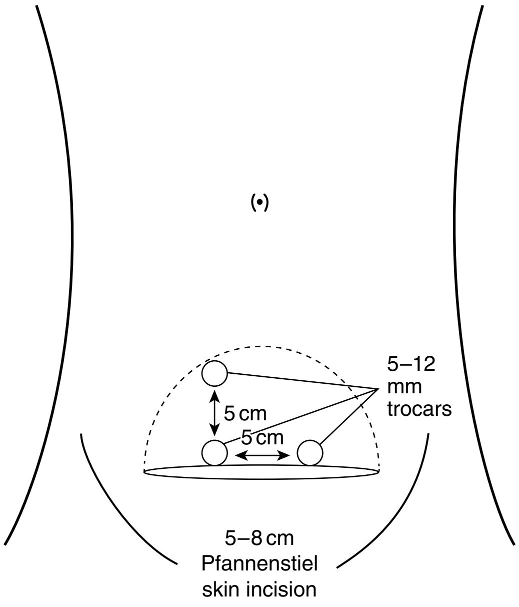

**Figure 121.3** Insertion of three 5-mm low-profile trocars through a Pfannenstiel incision.

Another approach gaining traction within recent years is single-incision triangulated umbilical surgery (SITUS). Retraction of the single umbilical incision allows the entry of several spaced working ports. Instrumentation is straight, standard laparosopic as spacing of the trocars allows triangulation of the target tissue.

## Use of accessory and needlescopic trocars

Although even complex reconstructive LESS procedures, such as pyeloplasty and partial nephrectomy, can be performed with no accessory points of entry [6], the use of accessory trocars or 1.9 mm needlescopic instruments has been reported extensively in the early experience of LESS. These added instruments act as an adjunct to the single-site approach and provide for instrument triangulation and added retraction, or can assist with intracorporeal suturing and knot tying. Accessory ports create a bridge between conventional laparoscopy and LESS, as surgeons learn LESS surgery. These ports play a critical role in challenging cases in which triangulation for adequate retraction and dissection is not adequately achieved with single-site access and available instrumentation.

With minimal to no morbidity, needlescopic instruments have been reported to enhance surgeon confidence and ensure patient safety during the diffusion of this new and challenging technique [4]. As experience with LESS increases and surgeons progress along the learning curve, the use of accessory trocars for assistance in triangulation and retraction will likely decrease. However, there will likely always remain an important role for accessory trocars or needlescopic instruments for more complex surgical cases. Moreover, additional access is always preferable to any compromise in safety or efficacy. Accessory trocars measuring from 5 to 12 mm in diameter have been reported. These are used by some urologists during LESS donor nephrectomy to allow for the expeditious and safe maneuvers necessary to limit the warm ischemia time of the renal allograft specimens. They also are adjuncts to LESS for complex reconstructive procedures or in patients with anatomic challenges requiring extensive adhesiolysis or body habitus limiting instrument flexibility. The site of accessory trocar placement can also be used as the location for drain placement at the culmination of the case.

## Extirpative surgery

### LESS nephrectomy

LESS nephrectomy can be performed for both “simple” nephrectomy and radical nephrectomy, for benign and malignant pathologies, respectively. Although done for differing indications, LESS nephrectomy has similar principles and maneuvers to conventional laparoscopic nephrectomy, with slight surgeon-specific modifications to overcome the novel challenges of the single-site approach of the operation [13].

The first laparoscopic extirpative surgery in urology was the laparoscopic nephrectomy reported in 1991, and this is now a relatively straightforward case often undertaken by new trainees prior to more complex renal surgeries [14]. Since the first LESS nephrectomy was reported in 2007 by Rane et al., the number has soared and remains the most common LESS urologic surgery performed [15]. A simple nephrectomy for non-oncologic indications allows for morcellation of the resection specimen. The most common location for trocar placement is at the umbilicus, and morcellation obviates the need to extend the umbilical trocar site incision, maximizing the cosmetic outcome [16]. However, extension of the incision is warranted in radical nephrectomies and nephroureterectomies to allow for passage of the entire kidney specimen intact for pathologic examination and appropriate staging without compromising the oncologic efficacy of the surgery.

Rane et al. described their initial experience with five LESS simple nephrectomies [16]. Their indications for simple nephrectomy included chronic reflux, recurrent infections, longstanding ureteropelvic junction obstruction, stone disease, and ureteral strictures, leading to poorly functioning symptomatic kidneys. In these cases of benign renal pathology, morcellation allows for an operative scar to be hidden within the anatomic folds of the umbilicus.

Since this report of LESS simple nephrectomies, other groups have reported LESS radical nephrectomy with adequate pathologic outcomes [5, 17, 18]. LESS radical nephrectomy has been reported through umbilical access as well as through a Pfannenstiel incision. In both circumstances, the incision is commonly 4–8 cm in length for purposes of specimen extraction, unless morcellation is employed. Despite requiring a larger extraction site, LESS radical nephrectomy still requires fewer incisions compared to conventional laparoscopy, and the incision is at least partially hidden within the umbilicus or within the skin creases of the suprapubic region, depending upon approach utilized.

In a series comparing LESS simple and radical nephrectomy to conventional laparoscopic nephrectomy, Raman et al. reported equivalent operative time, postoperative analgesic use, length of hospitalization, and rate of complications. Although the LESS cohort was found to have a lower recorded estimated blood loss, the change in hemoglobin concentration across the two patient groups was not statistically significant [17]. This was followed by a randomized controlled trial comparing LESS versus conventional multiport laparoscopic nephrectomy that demonstrated lower visual analog pain scores and decreased analgesic requirements for LESS surgery [19].

More recently, a similar study comparing patients with cT1–2 renal cell carcinoma showed superior postoperative Quality of Recovery-40 (QoR-40) questionnaire scores in the LESS group. Four out of five assessed dimensions were significantly improved in the LESS group; including emotional state, physical comfort, psychological support, and physical independence. Interestingly, pain was equivalent in the conventional laparoscopy and LESS groups [20]. Larger retrospective reviews have concluded LESS nephrectomy to have no significant differences in outcomes compared to the gold standard laparoscopic approach [21, 22]. A systematic review and meta-analysis of 25 retrospective studies showed that LESS nephrectomy is associated with longer operating time as well as a higher conversion to open rate compared with conventional laparoscopic nephrectomy. LESS was shown to offer advantages in terms of reduced postoperative pain, lower analgesic requirement, shorter length of stay, shorter recovery time, and better cosmetic satisfaction. Overall, there was no difference in terms of perioperative complication outcomes [23].

### LESS partial nephrectomy

Partial nephrectomy remains a challenging operation even when performed by multiport laparoscopy.

However, in selected patients, LESS partial nephrectomy has been demonstrated to be feasible and safe. LESS partial nephrectomy has been described without accessory trocars, technically replicating the conventional laparoscopic technique with careful hilar dissection for complete pedicle control, identification and excision of the tumor, and various hemostatic techniques coupled with the renorrhaphy (see Video 121.1) [5]. In efforts to minimize warm ischemia time and provide a hemostatic renorrhaphy, a 2 mm needlescopic accessory port is utilized by some experts for intracorporeal suturing [24]. As demonstrated by surgeons who have reported their experience with LESS partial nephrectomy, it is critical to convert to conventional laparoscopy in cases of limited exposure of the tumor resection site or when hemostasis is prohibitively challenging via a strict LESS approach.

Indications for conventional laparoscopic partial nephrectomy are expanding and now include resection of selected T1b tumors, central or hilar tumors, and multifocal tumors within the same kidney [25]. Currently, LESS surgery has been largely reserved for the strictest indications. In the renal LESS series reported to date, LESS partial nephrectomy was performed in a highly select patient population with ideal body habitus, limited prior abdominal surgery, and favorable tumor size and location.

A retrospective multi-institutional series analysis of a 190 cases was performed examining LESS partial nephrectomy and the resultant renal function as well as the short-term oncological outcomes. When hilar clamping was utilized, a significant increase in serum creatinine concentration and a significant decrease in estimated glomerular filtration rate (eGFR) were observed postoperatively and at six months. The degree of functional loss was correlated with the length of warm ischemia. The overall postoperative complication rate was 14.7%. Overall, survival rates were comparable to those following conventional laparoscopic partial nephrectomy. Furthermore, the authors found on univariate analysis that the robotic platform is a positive predictor for complication outcomes (predicts a complication is less likely to occur). On multivariate analysis, a low Padua Prediction Score was the only positive predictor for complications. It was concluded that the robotic platform can be a feasible and effective modality in terms of renal function and oncological control that may be likely to reduce postoperative complications [26].

When comparing robotic LESS to conventional robotic partial nephrectomy, one group found the robotic platform to have an increased warm ischemia time as well as total operative time but no significant differences in negative surgical margin rate, postoperative renal function, or complication rate. They also noted that the visual analog pain scale scores at discharge were significantly lower in the robotic cohort [27]. While these results are promising, these patient populations tend to be carefully selected, with the surgeries taking place at highly specialized facilities. One systematic review and meta-analysis comparing robotic LESS to conventional LESS partial nephrectomy highlights that these previous studies have shown promise in terms of complications, cosmesis, pain, as well as comparable postoperative renal function. Furthermore, robotic LESS partial nephrectomy has shown comparable oncological outcomes. However, they also show a trend for longer operative and warm ischemia times. They note the association between tumor size and positive outcomes, concluding that only highly selected patients should undergo robotic single-site approach. They see the benefits of the robotic approach, but emphasize the importance of technological innovations as well as an increase in high-quality data that appears to be lacking within the literature at this point [28].

## LESS nephroureterectomy

In addition to LESS radical and partial nephrectomy, LESS nephroureterectomy has been reported as an oncologic application of single-site surgery of the kidney. For the treatment of upper urinary tract transitional cell carcinoma, LESS nephroureterectomy has been reported by several centers [1, 5, 6]. As with conventional laparoscopy, both retroperitoneal and transperitoneal approaches have been described. Transperitoneal LESS nephroureterectomy has been reported via an umbilical as well as a Pfannenstiel single-site incision. Through a Pfannenstiel approach, after completion of laparoscopic mobilization and freeing of the kidney and ureter, a bladder cuff was performed in an open manner [6]. In reports of the retroperitoneal as well as umbilical approach to transperitoneal LESS nephroureterectomy, specimens were extracted through a separate Gibson incision measuring between 6 and 10 cm in length, through which a formal bladder cuff excision was also performed [5, 29]. This length of incision for management of the distal ureteral segment and intact specimen extraction was acknowledged in multiple published works as a contradiction to the goals of LESS to minimize total incisional length and associated pain and cosmetic concerns.

In addition, Lim et al. compared a traditional multiport robot-assisted approach to a robotic LESS platform. In this study, the robot-assisted LESS platform compared well in terms of oncological outcomes. However, the LESS approach had a significant increase of operative time, hospital stay, and blood loss. Furthermore, the LESS approach was more likely to need a blood transfusion [30].

## LESS donor nephrectomy

LESS donor nephrectomy has been pursued by advanced laparoscopists only after significant experience with LESS in other renal extirpative procedures. The technique described for LESS donor nephrectomy mimics the established methods of conventional laparoscopic living donor nephrectomy (LDN) first described in 1995 [31]. Important modifications unique to the LESS approach for LDN include the use of articulating or prebent instruments to overcome the challenges of single-port access and extra-long or bariatric instrumentation for adequate reach to the kidney, especially the upper pole and lateral aspects. Also, when selecting the mode of access for LESS donor nephrectomy, it is critical that the surgeon(s) preoperatively consider the approach to graft extraction, as minimization of ischemia time is imperative. With this in mind, the use of a multiport device that allows for extraction and rapid re-establishment of pneumoperitoneum may be preferable to clustered trocars.

Single-site donor series have been reported by several different transplant centers with advanced laparoscopists who were experienced at performing laparoscopic LDN [12, 32]. In this population of healthy volunteer donors, who are often related to the transplant recipients, safety is of the utmost concern. Therefore, the surgeon should maintain a low threshold to convert to multiport, hand-assisted, or open surgery in cases with a difficult anatomic approach or allograft procurement [1].

However, it is in this same population of young, healthy volunteers that the provision of a cosmetically superior result may be most valued by the patient. The initial publications on this less-invasive approach to renal allograft procurement describe efficacy and feasibility of LESS donor nephrectomy.

One study reporting a single-surgeon experience of six LESS cases matched to six conventional laparoscopic donor nephrectomies reported statistically comparable perioperative parameters, renal allograft characteristics, and postoperative pain [12]. Perioperative parameters evaluated and compared included operative time, warm ischemia time, estimated blood loss, and length of hospitalization. Postoperative pain was assessed by narcotic requirements and patient-reported scores on a visual analog pain scale. Notably, the median pain score reported at discharge in the cohort of LESS donor nephrectomy was zero on a 0–10 visual analog pain scale. None of the six LESS cases required conversion to conventional laparoscopy to complete the case safely, and all allograft specimens were adequate for successful transplantation and immediate function once implanted.

A matched-pair comparison of LESS donor nephrectomy to conventional donor nephrectomy revealed a quicker convalescence in the patient cohort undergoing LESS donor nephrectomy [33]. Parameters improved by the LESS approach included time on oral analgesics, time off work, and time to "100% recovery," as noted by patient questionnaires. In this study, warm ischemia time was statistically significantly higher in the LESS cohort; however, allograft function was noted to be immediate and comparable across the two groups.

Comparison analysis between Pfannenstiel LESS LDN compared to standard multiport LDN revealed significantly lower pain scores based on the visual analog pain scale, beginning on postoperative day one. All other perioperative parameters were equivalent between groups, including estimated blood loss, length of stay, and warm ischemia time [34].

A systematic review and meta-analysis of reports compared 461 LESS LDN cases to 1006 standard laparoscopic LDN. The review found laparoscopic LDN had a shorter operative time, without a significant difference in warm ischemia time. It also noted there was a greater likelihood of conversion to open for LESS LDN. The overall analgesic requirement was lower for LESS LDN. Moreover, there was no difference in the postoperative complication rate. The recipient renal function showed similar outcomes between groups. This review strengthens the argument that LESS LDN represents an emerging option for living kidney donation. This procedure offers comparable surgical and early functional outcomes to the conventional laparoscopic LDN, with a lower analgesic requirement. However, with a higher rate of conversion for LESS LDN, the technical challenge of LESS in LDN remains evident [35].

A recent Cochrane Review including three randomized control trials with a total of 179 patients was unable to determine if LESS LDN is an improvement upon laparoscopic LDN. Of all examined parameters, only pain scores at discharge differed significantly, favoring discharge. Interestingly, operative time and warm ischemia time were similar between the groups, suggesting that in experienced hands allograft function may not be affected with the LESS approach. However, the lack of consensus regarding the role of LESS in donor nephrectomy underscores the need for large, randomized control trials comparing LESS to conventional LDN [36].

## LESS adrenalectomy

The first conventional laparoscopic adrenalectomy was reported in 1992 [37]. Since then, laparoscopic adrenalectomy has been accepted as a feasible and safe minimally invasive option for the surgical treatment of various adrenal neoplasms [38]. For small to mid-size adrenal lesions, laparoscopic adrenalectomy has become standard practice not only for urologists but also general surgeons at some centers. Debate exists regarding the efficacy of laparoscopy for the treatment of known or suspected adrenal cortical carcinoma, particularly for larger masses.

One of the earliest reports of LESS adrenalectomy was of retroperitoneoscopic adrenalectomy via a 4.5 cm trocar without the use of insufflation [39]. In this report, 53 patients with adrenal tumors were treated successfully via this approach and one patient (1.9%) required conversion to open surgery secondary to excessive blood loss from an adrenal vein injury. Other approaches have been utilized in order to achieve consistent perioperative outcomes while maximizing cosmetic results. In a comparison of the transumbilical, transperitoneal subcostal, and retroperitoneal subcostal approaches, the transumbilical approach was rated as the most favorable cosmetically [40].

In a contemporary series, nine patients undergoing LESS adrenalectomy for benign adenoma were compared to 17 patients undergoing conventional laparoscopic adrenalectomy [41]. Patients were matched with regard to age, sex, surgical indications, and tumor size. Operative time, blood loss, and hospital stay were found to be equivalent. The LESS group demonstrated a shorter period of postoperative intravenous patient-controlled analgesia use.

A more recent meta-analysis compared LESS to conventional laparoscopic adrenalectomy including 704 total cases. It was determined that LESS patients benefited from shorter length of stay as well as improved pain scores. There were no significant differences in terms of the operation or oncological outcomes, concluding that LESS adrenalectomy could be the more preferred technique. This conclusion is strengthened by recent data showing that LESS has the fastest increase in yearly utilization with much of these increases being in Asia. In the United States, the trend is moving toward robot-assisted adrenalectomy [42].

## Reconstructive surgery

### LESS pyeloplasty

Pyeloplasty is the most common reconstructive upper tract urologic surgery performed. With the advent of laparoscopic pyeloplasty in 1993, there was a significant movement toward a minimally invasive approach rather than the large, muscle-traversing flank approach for open pyeloplasty, which was the former standard [43]. Since the development and diffusion of laparoscopic pyeloplasty by urologists, both dismembered and Y-V laparoscopic pyeloplasties have been performed in large series with reliable postoperative outcomes [44, 45].

As with LDN, patients undergoing pyeloplasty are often young and healthy, without malignant pathology, and cosmesis may be of greater concern to them. A cohort of LESS pyeloplasty patients demonstrated a younger mean and median age when compared to other LESS upper tract operations in a single institution experience of upper tract urologic LESS [5]. Heightened efforts to minimize the overall incision burden and subsequent appearance of cutaneous scars in this population seem appropriate. Ongoing research is aimed at further defining the quality of life and cosmetic advantages that LESS urologic surgery may provide.

LESS pyeloplasty can be performed with or without the use of accessory trocars [5]. All techniques and associated procedures can be performed via LESS, including dismembered pyeloplasty, Y-V pyeloplasty, pyeloscopy, and stone extraction. We advocate flexible cystoscopy and placement of a 7 Fr, 28 cm double-pigtail ureteral catheter prior to commencing with the LESS portion of the procedure. Other surgeons advocate a smaller 6 Fr stent to facilitate positioning of the scissor blade between the stent and ureteral wall, and thereby facilitating spatulation. Still other surgeons prefer an antegrade approach to stent placement during laparoscopy. Although we consider rigid straight laparoscopic instruments to be sufficient for nearly all LESS surgery, spatulation of the ureter may be facilitated by the use of articulating scissors in some cases.

Conventional laparoscopic salvage pyeloplasty has been reported with promising results [46, 47]. However, to date, LESS pyeloplasty is reserved for idealized patients undergoing primary pyeloplasty for congenital ureteropelvic junction obstruction. LESS pyeloplasty can be performed in the setting of a crossing vessel, as dismembered, transposed pyeloplasty can be performed effectively.

Short-term postoperative outcomes have been reported for LESS pyeloplasty and compared to historical controls undergoing conventional laparoscopic pyeloplasty. In a study reported by Raman et al., LESS pyeloplasty resulted in comparable perioperative and functional outcomes [48]. All perioperative parameters were equivalent, except for operative time and estimated blood loss, which were found to be significantly lower in the LESS cohort of patients.

A multi-institutional study by Schwartz et al. showed LESS pyeloplasty to be a safe option with success rates equivalent to conventional laparoscopic pyeloplasty [49]. In this series, the only clear benefit noted in the period of short follow-up was that of minimized incision size and postoperative scar formation, although postoperative pain and analgesic requirements were not assessed.

A more recent, longer term, multi-institutional study of 140 patients undergoing unilateral LESS pyeloplasty revealed a durable cure rate at mean follow-up of 14 months with a perioperative complication rate of 18.6%. Of these patients, 93.4% reported symptomatic resolution and 94.4% exhibited radiographic resolution of obstruction. Postoperative nuclear scans revealed improvement in 86.5% of patients. These findings were mirrored in a systematic review by Brandao et al. who concluded LESS pyeloplasty is comparable to conventional laparoscopic technique with regard to surgical and functional outcomes. Although LESS can be more technically challenging, it provides advantages in terms of decreased analgesic needs [50, 51].

LESS utilizing robotic assistance has also been explored. A pilot study recently reported the feasibility of a robot-assisted LESS pyeloplasty for ureteropelvic junction obstruction at two surgical centers. Of the 31 cases, two needed to be converted to either a standard laparoscopic or robotic procedure. No intraoperative complications were reported. The majority of postoperative complications were Clavien classification I or II. A success rate of 93%, defined as symptomatic and functional imaging improvement, at a median follow-up of 13 months was seen. Given this information, more prospective comparative studies versus standard robotic techniques are needed [52]. One systematic review highlights this sentiment, stating there is a need for more prospective studies [53]. Of the literature reviewed, they note that surgeons prefer the single-site approach because it makes dissection and suturing easier compared to the traditional robotic platform. However, a common complaint among surgeons was the issue with instruments clashing. They conclude the robotic LESS approach can become a viable option, but advances in technology appear to be the main roadblock in reaching the ultimate goal of providing a safe and easy surgical modality that can be widely disseminated among the general population.

## Ablative surgery

### LESS cryoablation

Cryoablation has been demonstrated as an oncologically effective means of providing focal ablation therapy for the treatment of small renal masses, maintaining a nephron-sparing result [54]. Both laparoscopic and percutaneous image-guided approaches have been well described for renal cryoablation. Benefits of the laparoscopic approach to renal cryoablation include direct visualization of probe placement, monitoring the ice-ball formation visually or with intraoperative ultrasonography, and the means to mobilize bowel or other adjacent structures safely away from the area of focal ablation [55]. Transperitoneal as well as retroperitoneoscopic entry have been reported, differentially used based primarily on the anatomic location of the renal mass being ablated.

The technique for LESS cryoablation, using both transperitoneal and retroperitoneal approaches, was first reported in a human series in 2008 [56]. Since this initial report, LESS cryoablation has been reported by a number of different institutions as part of larger urologic LESS series in the literature [1]. To date, the literature has demonstrated LESS cryoablation to be a successful approach with acceptable perioperative parameters when compared to conventional laparoscopy. Although only a small number of cases were observed in one study, there was no conversion to conventional laparoscopy showing overall promise for this modality [56]. However, LESS cryoablation is at a very early stage of the learning curve of LESS surgery with an obvious need for more studies.

Renal cryoablation provides an ideal opportunity for LESS because there is no specimen necessitating an extraction site. Also, intracorporeal manipulation is limited to mobilization of adjacent organs and intraoperative imaging with ultrasonography, while other LESS renal surgeries require advanced intracorporeal suturing techniques or vascular clamping and manipulation that are more easily achieved with the triangulation provided by conventional multiport laparoscopy.

### LESS cyst ablation/decortication

Laparoscopic and LESS management of renal cysts provides minimally invasive access to either aspirate and sclerose the cyst cavity, ablate the lining, or decorticate symptomatic renal cysts. Decortication by excision of the cyst wall with luminal fulgration using either an argon beam coagulator or electrocautery provides the most durable long-term outcome based upon rates of recurrence [57, 58].

Experience with LESS cyst decortication has often been presented in larger LESS series encompassing multiple operative procedures [1, 29, 59]. LESS cyst decortication has been reported through periumbilical access, providing a transperitoneal approach as well as a retroperitoneal approach through a multichannel access port placed in the flank. Operative techniques vary based upon the location of the renal cyst being targeted as well as the complexity of the dissection required to expose the cyst for decortication. A combination of standard laparoscopic and articulating laparoscopic instruments has been reported to aid in these LESS cases. Also, one report cited use of an operative laparoscope to further minimize the access ports required, allowing for successful retroperitoneal LESS cyst decortication [7]. An additional study described the use of a homemade glove port to facilitate LESS in symptomatic cyst decortication in 62 patients. No major operative complications were reported in this series [60].

Patients with large renal cysts, reported as large as 15 cm, have been safely and successfully managed with LESS surgery, with minimal intraoperative blood loss and discharge commonly on the first or second postoperative day [1, 7, 59]. The length of hospitalization is likely a result of the early learning curve of LESS surgery. As with laparoscopic renal cryoablation, conventional laparoscopic cyst decortication has been reported as an ambulatory operation in experienced centers [61]. Unfortunately, comparative studies with conventional laparoscopy are lacking. Future research should focus on comparative perioperative outcomes with conventional laparoscopy since conventional laparoscopy already provides such remarkable outcomes. However, if equivalent outcomes can be achieved, the improved cosmesis of LESS surgery alone makes it an attractive option.

## Robotic single-port surgery

Robotic surgery has become a mainstay in the treatment of a number of urologic conditions. Though its experience with LESS procedures is not as well described, there has been significant growth in this area within the last several years. The first urologic robotic LESS procedure was described in 2007 by Raman et al., who performed robotic LESS nephrectomy in porcine models [62]. Typically, a single-site incision is made at the umbilicus with multiple fascial incisions made for multiple port sites. A single port incision can also be made with a single fascial incision for the multichannel port.

To date, the robotic single-site emergence has led to more surgical centers attempting robotic LESS, resulting in comparison studies between the robotic LESS approach and the traditional robotic technique with initial positive results. However, this was not without immediate drawbacks and obstacles. Some of the early hurdles include: bulky components that would result in external clashing, limited access for the bedside assistant, difficulty maintaining triangulation toward the target anatomy, and inability to use the fourth arm. A number of studies have been performed reporting novel technologies or strategies seeking to improve efficacy and troubleshoot some of these challenges. Advances that have enhanced overall functionality and usability of the single-site robotic platform include: use of a multiport GelPort™ at a single incisional site previously described in this chapter, changes in the robotic platform to accommodate the single-site technique, and positional changes such as the “chopstick” technique, where the robotic arms cross each other at their point of entry [63].

The da Vinci SP1098 instrument arm is a new modification allowing the triangulation of target tissue during robotic single-port surgeries. The instrumentation is unique in that it is double-jointed, with elbow and wrist articulating joints, improving maneuverability and expanding the workspace. A recent cadaver trial focusing on retroperitoneal LESS radical and partial nephrectomy without comparison control group revealed no complications or conversions. Although large-scale data are lacking, this technology may be a solution to limitations caused by instruments entering from a single point and may expand the role of robotics in LESS surgeries. As practitioners and product developers continue to troubleshoot, the robotic single-site modality will continue to grow within urologic surgery [53].

## Future of LESS for upper tract urologic surgery

The dissemination of advances in surgical technique is dependent upon the realized value of these new developments. Furthermore, the technique must prove reproducible beyond selected centers of excellence. LESS has proven its versatility based upon the wide range of urologic operations for which it has been successfully employed as an extension of conventional laparoscopy. As experience with LESS expands in some centers, more novice surgeons, including residents and fellows enrolled in urology training programs, are being exposed to these new techniques within an apprenticeship model. Also, as skill centers are using inanimate box trainers and electronic simulators as an adjunct aide in laparoscopic training outside the operating room, new LESS training modules should be developed to augment the breadth of these simulator platforms.

A recent anonymous questionnaire was electronically mailed to members of the Endourological Society and the American Urological Association with regard to LESS. Although 44.7% of respondents had stated they had performed LESS, only 25% of those surgeons had done more than 10 cases. Only half of the respondents believe that LESS should be taught in residency, which may be a point of contention if LESS is considered strongly by accrediting bodies. The results also show that a majority of respondents (68.7%), no matter their experience in LESS, do believe in the cosmetic results. However, respondents also commonly felt that LESS does not produce a quicker recovery or improved postoperative pain, which contradicts much of the research presented throughout this chapter, increasing the need for more prospective comparative studies [64].

As LESS has gained traction to become more of a mainstream technique one would expect use to rise among minimally invasive urologists. Unfortunately, there is a relative lack of data regarding trends of utilization. A recent analysis of over 700 adrenalectomies performed worldwide at 14 institutions revealed 36% performed using LESS techniques versus 46% with conventional laparoscopy. While this speaks to the growth of LESS worldwide, larger studies on a variety of urologic procedures are necessary to adequate gauge patterns of use [42].

A number of research efforts are currently underway to develop improved instrumentation and access platforms to facilitate LESS. Motorized articulating instruments and robotic platforms will become available that will help overcome the inherent challenges of single-site surgery. Published reports have described the use of the da Vinci Surgical System as an adjunct to LESS urologic techniques [8, 65]. Currently, under investigation are magnetic anchors and intracorporeal robotic mechanisms with the goal of minimizing the number and length of incisions, as well as providing better triangulation in LESS cases [66]. These innovations are not only troubleshooting traditional LESS surgery, but also robotic LESS surgery, as described earlier. In the future, it is imperative that prospective studies focus on patient quality of life and postoperative satisfaction, keeping outcomes such as cosmesis in mind. These studies will continue to push the envelope in order to create a platform that can be distributed on a global basis without concerns for patient care and clinical outcomes.

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## 122

# Robotic Laparoendoscopic Single-site Lower Tract Surgery

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## Introduction

The use of robotic platforms in urologic surgery has become widely prevalent secondary to the benefits it provides over conventional laparoscopy, including enhanced three-dimensional optics, improved instrument control and dexterity, and superior ergonomics. These technological advancements have resulted in the adoption of robotics in laparoendoscopic single-site (LESS) surgery to surmount difficulties associated with intra-abdominal triangulation and intracorporeal suturing. The first robotic laparoendoscopic single-site surgery (RLESS) series was published in 2008 [1], and since that time, various studies have demonstrated its application in lower tract urologic procedures [2–8]. Although the benefits afforded by the application of the robotic platform are tremendous, major limitations inherent to single-site surgery still exist, including bulky external mechanics, instrument clashing, and limited space for the bedside assistant surgeon. Although many technical improvements have been described to tackle these challenges, pelvic RLESS is still evolving and has not been widely embraced [9, 10].

Several aspects of conventional robotics cross over to RLESS, including operating suite layout, instrumentation, and surgical draping. The main difference between the two approaches is port-site access and docking. RLESS typically utilizes ports that are more obliquely placed to one another in order to limit external clashing. The specific steps of each procedure are similar, though some creativity must be used when employing RLESS to address the aforementioned challenges. This chapter discusses the tools, techniques, published outcomes, and up-and-coming technology associated with specific urologic RLESS procedures of the lower urinary tract. In addition, a video has been included to demonstrate our technique for performing RLESS perineal radical prostatectomy utilizing a novel single-port robotic platform (see Video 122.1 ).

## Robotic docking for RLESS technique

In terms of docking, a few noteworthy differences exist between traditional multisite robotic surgery and RLESS. The authors typically prefer the da Vinci Si or Xi models versus the S model due to the improved optics and ergonomics. The Xi model offers a more compact, sleeker external profile of the patient cart, which may allow for decreased external clashing. In addition, only three robotic arms are using during pelvic RLESS surgery as there is limited space to accommodate the additional robotic instrument arm.

Other techniques which may limit external clashing include the "chopstick" technique popularized by Joseph et al., in which the robotic instruments are crossed at the fascial level in order to create more working space between the robotic arms outside of the surgical field [11]. This technique was previously utilized in the traditional LESS approach but proved to be very challenging due to the "reverse-handedness" associated with crossing of the instruments. A major benefit of applying the robotic platform to LESS is the ability to control each instrument electronically, permitting the interchange of instruments and master controllers, effectively removing the limitation of "reverse-handedness." The main limitation of the chopstick technique is the trade-off of external clashing for internal clashing. Crossing of the instruments at the fascial level results in the deflection of the instruments where their shafts

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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cross. The surgeon must always be aware of the position of each instrument to avoid any counter-springing associated with exaggerated movements.

## Pelvic surgery

### Radical retropubic prostatectomy

For radical retropubic prostatectomy we favor obtaining single-site access using a multichannel SILS port (Medtronic, Minneapolis, MN, USA). For this technique, all of the robotic ports occupy the same skin incision but enter the intra-abdominal space through separate fascial incisions. The robotic camera port, bedside assistant port, and insufflation tubing are placed through the SILS port at the lower aspect of the umbilicus. Arrangement of the operative suite, patient positioning and docking are the same as conventional robotic radical prostatectomy, with the patient positioned in dorsal lithotomy and steep Trendelenburg with the robotic cart docked between the patient's legs. The multichannel port is inserted at the inferior aspect of the umbilicus through the linea alba of the rectus fascia. The 8 mm lateral robotic ports are placed at the lateral-most inferior edge of the skin incision and are skived through the subcutaneous fat as far laterally as possible to approximate the positioning used for the traditional approach. The fourth instrument arm is not used for the RLESS technique. Using this port arrangement, the "chopsticks" method is not needed.

The major steps of performing RLESS retropubic radical prostatectomy are the same as those used for the conventional robotic approach. Initially the bladder is mobilized to develop the space of Retzius using an 8 mm curved monopolar scissor in the right arm and an 8 mm ProGrasp forceps or a 5 mm Schertel grasper in the left arm. Use of a 30° up scope initially may be beneficial for controlling and ligating the urachus. The bladder is dropped from the anterior abdominal wall, and the anterior surface of the prostate is defatted to expose the endopelvic fascia and dorsal venous complex (DVC). The endopelvic fascia is opened, and the DVC is identified and controlled with 2-0 braided polyglactin suture using an 8 mm robotic needle driver in the right arm. The junction between the bladder and prostate is then identified, and the bladder neck is opened in order to expose the urethral catheter. Identification and dissection of the bladder neck is facilitated by having the catheter balloon deflated and the catheter advanced all the way into the bladder. Once the bladder neck is open, the catheter is pulled up into the field. A "marionette" suture is used to secure the catheter to the anterior abdominal wall, as was explained in our initial RLESS series [1]. This allows for anterior retraction of the prostate during posterior dissection. Once the prostate is completely freed from the bladder neck, the anterior Denonvilliers' fascial layer is identified and opened to reveal bilateral vas deferens and seminal vesicles. When nerve sparing is not performed, energy may be used during this dissection. If nerve sparing is planned, energy should be avoided. The posterior dissection is performed from the base of the prostate to the apex, carefully releasing the rectum. Once the posterior plane is complete, bilateral nerve sparing is performed (when appropriate), along with bilateral control of the prostatic vascular pedicles. Once this is done, attention is turned to the prostatic apex. We typically perform a meticulous apical dissection to ensure the longest urethral length possible while avoiding positive margins. The urethra is sharply transected. Once the prostate is removed from the pelvis, bilateral pelvic lymph node dissection is performed. Once the lymph nodes are removed, the vescicourethral anastomosis is performed using two 8 mm robotic needle drivers in the left and right arms. We typically perform our anastomosis in a running fashion with two 2-0 poliglecaprone 25 sutures on RB-1 needles. At the end of the procedure, the anastomosis is tested by instilling 200 ml of sterile saline into the bladder, and a 10 mm Jackson–Pratt drain is routinely left. A separate facial stab incision is made for placement of the drain, but the drain is externalized via the same skin incision used for the multichannel port, thereby limiting the number of skin incisions.

### Robotic single-port transvesicle enucleation of the prostate

In 2010, our institution described robot-assisted single-port transvesicle enucleation of the prostate (R-STEP) [6]. This technique involves the use of the GelPort (Applied Medical, Rancho Santa Margarita, CA, USA) through a suprapubic incision that allows port placement directly into the bladder for transvesicle enucleation. Patients are placed in low lithotomy position, and cystoscopy is performed prior to port placement in order to define the apical limits of the prostate using a Collins knife. The bladder is filled with irrigation, and the skin incision is marked from the level of the dome of the bladder downward toward the pubis. Identification of the cranial-most extent of the incision is facilitated with the use of a spinal needle placed under cystoscopic vision directly into the bladder. Once this limit is defined, a 3 cm skin incision is made through the fascia, and the perivesicle fat is dissected away to expose the underlying detrusor. Two stay sutures are placed along both sides of the detrusor opening. The bladder is opened transversely between the stay sutures. A 16 Fr catheter is placed into the bladder, and the balloon is inflated with 5 ml of sterile water. The GelPort is then placed through the wound in order to allow access into the bladder. We use a 12 mm port at the 6 o'clock position for the robotic camera and insufflation, two 5 mm ports on the right and an 8 mm robotic instrument port on the left. The GelPort gel pad comes with a premade hole in the center to assist with trocar placement, which is closed prior to placement of the gel pad over the wound retractor since it is not used in this technique. Once all the ports are placed, the bladder is insufflated to 20 mmHg. An upward-facing 30° scope is used during this procedure to improve visualization and to limit instrument clashing. The 5 mm harmonic scalpel is used in the right arm and a 5 mm deflecting Schertel grasper is placed in the left. A circular incision is made around the prostatic adenoma between the prostate and bladder neck. Care is taken to identify and avoid the bilateral ureteral orifices during this initial dissection. The avascular plane is developed between the prostatic adenoma and prostate capsule, and enucleation is carried out from the prostatic base to the apex. The incision made at the apical prostate at the beginning of the case assists with identification of the apex during this dissection. Once this is complete and bleeding is controlled, a 24 Fr three-way hematuria catheter is placed into the bladder with 30 ml of sterile water in the balloon. The specimen is removed from the bladder via the GelPort site, and the bladder is closed in a running fashion with 2-0 absorbable suture. The rest of the wound is closed in the standard fashion, using 0-0 PDS for the fascial closure.

## Perineal robot-assisted laparoscopic prostatectomy

Our institution has recently begun performing robot-assisted radical prostatectomy via a perineal approach in select patients [7]. Perineal robot-assisted laparoscopic prostatectomy (P-RALP) is beneficial in cases with prior history of extensive abdominal surgery, radiation, or gastrointestinal or urinary diversions. In addition, removal of the prostate from a perineal approach offers similar benefits to a posterior, space-of-Retzius-sparing technique by preserving the endopelvic fascia and pelvic floor diaphragm [12–15]. The steps of this procedure are outlined in Video 122.1 that accompanies this chapter.

To begin, a 3–4 cm semilunar perineal incision is made between the ischial tuberosities, similar to open perineal radical prostatectomy, and the central tendon is divided. A GelPOINT multichannel port (Applied Medical) is placed after the space is created by transection of the rectourethralis muscle (Figure 122.1). We utilize a 12 mm camera port, two 8 mm robotic ports, and a second inferior 12 mm port for assistant access (Figure 122.2).

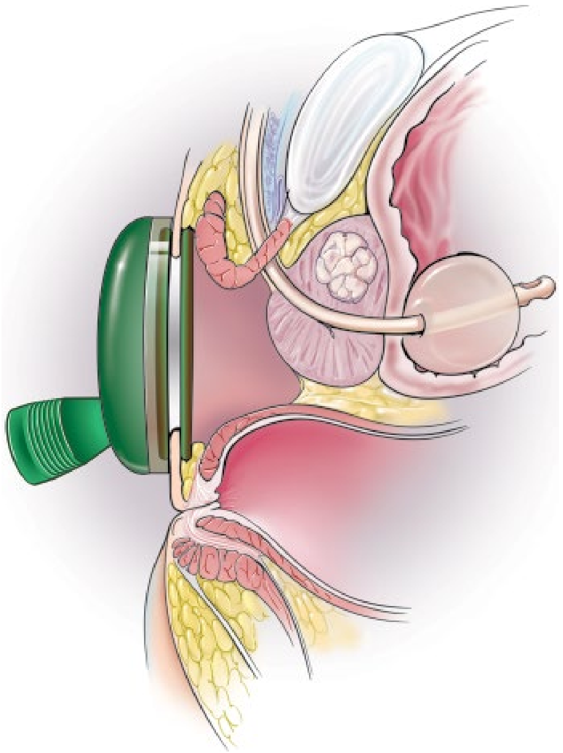

**Figure 122.1** GelPort access for perineal RLESS radical prostatectomy. *Source:* Cleveland Clinic, Ohio, USA. Reproduced with permission of Cleveland Clinic Center for Medical Art and Photography © 2015–2017.

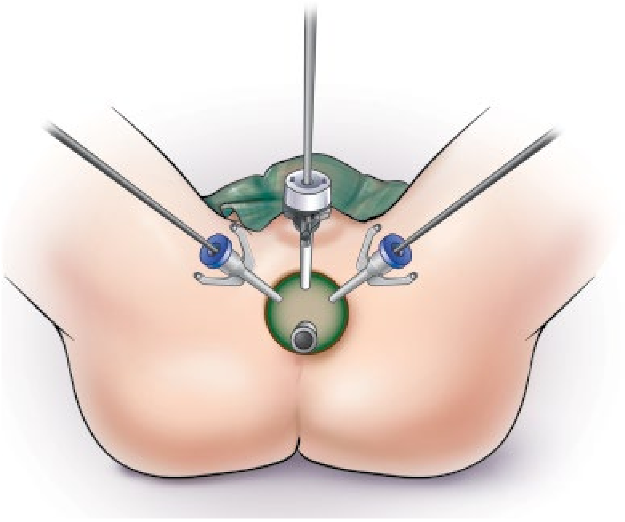

**Figure 122.2** Port placement with the 12 mm camera port placed anteriorly, the 12 mm assistant port placed posteriorly, and two 8 mm robotic ports placed laterally on either side. *Source:* Cleveland Clinic, Ohio, USA. Reproduced with permission of Cleveland Clinic Center for Medical Art and Photography © 2015–2017.

Once the robot is docked, the posterior prostatic space is developed to expose the levator ani muscles on either side. The levator fibers are split along the lateral aspects of the prostate, and Denonvillier's fascia is opened. This is done in a fashion to preserve the neurovascular bundles bilaterally. The posterior plane of the prostate is followed to find the insertion of the seminal vesicles and vas deferens bilaterally. The bilateral vascular pedicles to the prostate are identified and ligated (Figure 122.3). The prostatic apex is dissected, and the urethra is cut sharply (Figure 122.4). The catheter is clipped prior to transection in order to maintain fluid in the catheter balloon so that the catheter can be used for traction on the prostate. The junction between the bladder neck and prostate is identified, and the bladder neck is opened (Figure 122.5). The catheter is removed, and the remaining prostatic attachments are completely released. The vesicourethral anastomosis is performed in a running fashion over a new catheter beginning anteriorly (Figure 122.6). The anastomosis is tested with 200 ml of sterile saline. At this point, the robot may be undocked and the prostate removed via the perineal incision.

Currently, we have published on our P-RALP results in two patients with promising outcomes [8], and since our

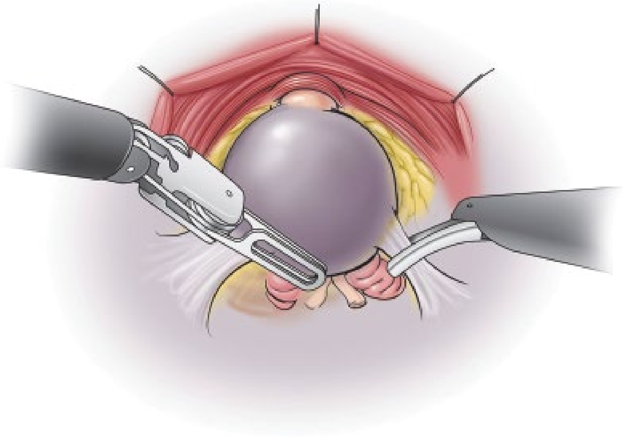

**Figure 122.3** Division of the prostatic pedicles. *Source:* Cleveland Clinic, Ohio, USA. Reproduced with permission of Cleveland Clinic Center for Medical Art and Photography © 2015–2017.

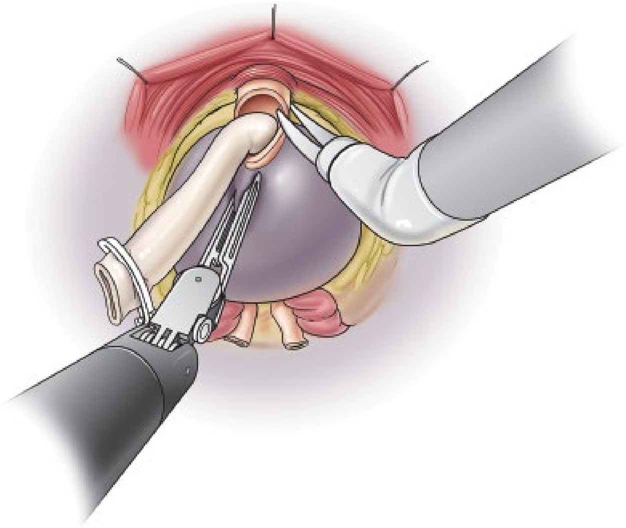

**Figure 122.4** Apical dissection and urethral transection with preservation of the dorsal venous complex. *Source:* Cleveland Clinic, Ohio, USA. Reproduced with permission of Cleveland Clinic Center for Medical Art and Photography © 2015–2017.

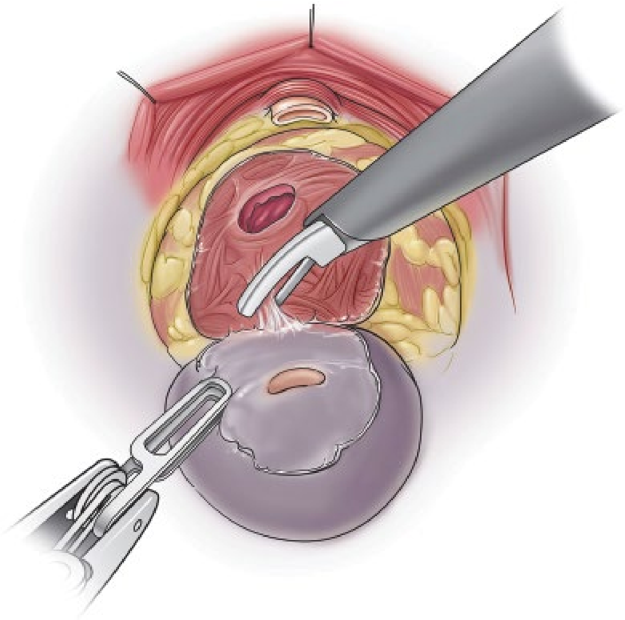

**Figure 122.5** Bladder neck dissection. *Source:* Cleveland Clinic, Ohio, USA. Reproduced with permission of Cleveland Clinic Center for Medical Art and Photography © 2015–2017.

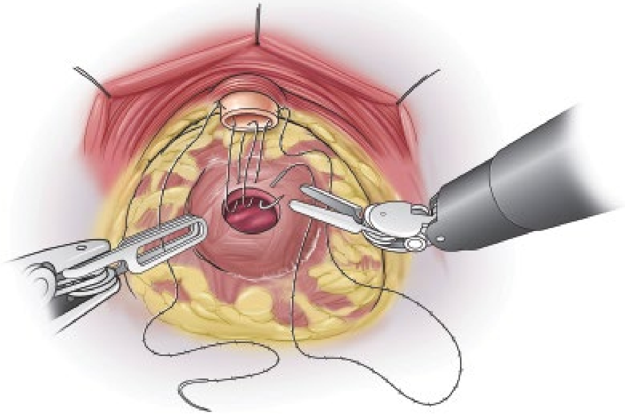

**Figure 122.6** Vesicourethral anastomosis. *Source:* Cleveland Clinic, Ohio, USA. Reproduced with permission of Cleveland Clinic Center for Medical Art and Photography © 2015–2017.

initial publication, our experience has grown to include five additional patients with good oncologic control and functional outcomes. This approach is feasible and thus far has not required conversion to standard open, robotic or laparoscopic techniques. We also have demonstrated the feasibility of this approach in a cadaveric model using a novel single-port robotic platform. This platform will be discussed later in this chapter. The P-RALP technique is still in its infancy, and our future experience with this approach is forthcoming.

### Radical cystectomy

The initial LESS radical cystectomy series, which included three patients with muscle-invasive bladder cancer, was published in 2010 by Kaouk et al. [16]. Mean estimated blood loss was 217 ml, mean operative time was 315 minutes, and mean length of stay was 6 days. All diversions were performed via the umbilical port site with minimal extension of the incision. Median node yield was 16. All surgical margins were negative, and there were no recurrences at 2-year follow-up. In 2012, White et al. published a series of RLESS cases, which included three radical cystectomies with extended pelvic lymph node dissections [4]. Rectal injury occurred in one case. This was recognized intraoperatively and repaired during the surgery with no sequelae. Data regarding outcomes after single-site radical cystectomy are limited in the literature. The aggressive nature and possible lethality associated with muscle-invasive bladder cancer has greatly limited RLESS as a widespread treatment option, as oncologic outcomes of conventional open and robotic approaches greatly outweigh the cosmetic benefits associated with single-site surgery. Therefore, more studies are required before RLESS techniques are deemed viable options for muscle-invasive bladder cancer.

## New single-port technology

Combining LESS with the robotic platform has greatly enhanced our surgical capability by offering increased articulation and stability for precise suturing and dissection. While the da Vinci robotic system has substantially improved our ability to perform single-site surgery, it was not originally designed for this purpose. For this reason, an innovative purpose-built, RLESS system has been developed. In contrast to the original robotic design for single-site surgery that required the use of multiple separate ports, the da Vinci single-port (SP) system only uses a single port to introduce the instruments and camera. This system uses the same base of the patient sidecart as the da Vinci Xi robotic system and is adapted onto a single arm.

Kaouk et al. described the first clinical application of the new single-port robotic system in 19 patients, 11 of whom underwent single-site robotic prostatectomy [17]. There were no conversions to open, contemporary robotic, or laparoscopic techniques, and high-grade complications only occurred in two patients. Functional outcomes over a 3-year follow-up were comparable to standard techniques. This new single-port robotic technology represents a step forward in minimally invasive surgery. It is unique as it allows for intracorporeal triangulation, while eliminating instrument clashing seen with other methods of single-site surgery. The SP999 platform was used by our group in a cadaveric model to perform three perineal radical prostatectomies, including two perineal pelvic lymph node dissections. The outcomes from this feasibility study are not yet published. Mean operating time was 210 minutes, and no conversions to alternative techniques were required. No intraoperative complications were seen.

More recently, a next-generation single-port robotic system (SP1098) has been evaluated for performing extraperitoneal urologic procedures in a cadaveric model [18]. Three perineal radical prostatectomies and two perineal pelvic lymph node dissections were successfully performed using this novel SP platform. Its application was found to be to be feasible in extraperitoneal abdominal and pelvic surgery. Most recently, the SP1098 was used to perform perineal radical cystectomy and extended pelvic lymphadenectomy to the level of the inferior mesenteric artery in two male cadavers without complications or conversions, though this series has not yet been published. Further clinical trials will be needed in order to better define the role of the SP1098 role in minimally invasive single-site surgery.

## Conclusions

The adaptation of the robotic platform to LESS has greatly improved the ability to perform single-incision pelvic surgery, mainly by instituting improved optics and articulating wrist technology as offered by robotic instrumentation. Although this approach has improved over time, there has not been widespread adoption of RLESS secondary to innate challenges that still exist, including instrument clashing and limited bedside access for the surgical assistant. A novel device specifically designed for single-port robotic surgery will be introduced in the near future and will improve our ability to perform these procedures. The field of minimally invasive surgery continues to expand its horizons with each new technique and device that comes to market. There is no doubt that these new approaches will continue to push the limits of minimally invasive urology, especially as it relates to lower urinary tract surgery.

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# SECTION 7

# Image-guided Diagnostics and Therapeutics

## Part 1 Upper Tract

## 123

# Diagnosis of Renal Masses: Radiological

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## Introduction

Over the last 35 years, the evaluation of renal masses has been revolutionized by technical advances in ultrasound, multidetector computed tomography (MDCT), magnetic resonance imaging (MRI), positron emission tomography–computed tomography (PET-CT), and positron emission tomography–magnetic resonance imaging (PET-MRI) [1–4].

It is estimated that 50% of people over the age of 50 years have at least one renal mass that can be detected on cross-sectional imaging [5–7]. Most of these lesions are benign simple cysts that can be diagnosed with confidence and require no further evaluation or treatment [8]. However, most renal neoplasms are now found incidentally while evaluating the patient for other suspected pathology [1]. The role of the radiologist is not only to detect these renal lesions, but also to distinguish between benign and malignant masses, and to help direct the management of these lesions.

Over the past 20 years, the treatment of renal masses has become increasingly individualized, with therapeutic options ranging from radical nephrectomy, laparoscopic nephron-sparing surgery, to laparoscopic or imaging-guided cryotherapy and radiofrequency ablation [9–14]. Novel molecular targeted chemotherapy has also been instrumental in prolonging patient survival in patients with advanced renal neoplasms.

This chapter reviews the role of CT, MRI, ultrasound, PET-CT, and PET-MRI in guiding the increasingly sophisticated process of characterizing and managing renal masses. Guidelines concerning the most efficacious use of the various imaging modalities with a view toward optimizing patient management are presented.

## Imaging techniques

### Multidetector CT

Recent improvements in MDCT technology allow thinner collimation and faster scanning that provides multiphasic, high-resolution images of the kidneys. These hardware developments, coupled with advances in three-dimensional imaging software and the availability of cheaper data-storage capacity, have provided new opportunities for imaging renal and urinary tract pathology. Isotropic imaging of the kidneys, ureters, and bladder is now possible, providing two-dimensional multiplanar reformations (MPR), CT urography (CTU), and three-dimensional imaging formats, with minimal artifacts, all derived from a single data acquisition [15, 16]. The kidneys can be scanned in less than 5 seconds, allowing for acquisition of thin-section images during the corticomedullary, nephrographic, and excretory phases. This multiphasic evaluation permits high-resolution imaging of not only the renal parenchyma but also the renal vasculature and collecting system.

Evaluation of a renal mass by CT requires a dedicated multiphasic CT protocol which may include: a precontrast scan; arterial phase (15–25 seconds delay) scan; corticomedullary phase (35–80 seconds delay) scan; nephrographic phase (85–180 seconds delay) scan; and excretory phase (>3 minutes delay) scan. The radiation dose in the CT urography protocol is approximately 10–12 mSv. In order to reduce the patient radiation dose, the precontrast, nephrographic phase, and excretory phase scans are the ones most commonly obtained [15–17].

Noncontrast scans of the kidneys are performed initially to evaluate for the presence of fat or calcification in the

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Companion website: www.wiley.com/go/smith/textbookofendourology

mass and to detect nephrolithiasis. This scan also provides a baseline from which to quantitate lesion enhancement on postcontrast scans. The scans performed during the arterial or corticomedullary phase, while limited for mass visualization, nicely display the renal vasculature, which is critical for surgical planning, particularly when partial nephrectomy is being considered. Arterial phase scans best show small hypervascular neoplasms and the renal arteries. The nephrographic phase optimizes mass visualization. The delayed phase scans are helpful in assessing the relationship of the renal mass to the renal collecting system and also visualizing the remainder of the urinary tract. The data from these various series can then be reconstructed at thinner intervals and transferred to a workstation where multiplanar reformatted images, maximum intensity projection (MIP) images, and 3D volume rendered images can all be created [15–17].

Contrast enhancement and subsequent de-enhancement are characteristic features of renal malignancies. A renal lesion is considered to be enhanced when its density increases more than 20 Hounsfield units (HU). If the density of the lesions increases between 10 and 20 HU, it is considered indeterminate for enhancement and requires further testing. While these criteria seem straightforward, the accuracy of determining enhancement varies based on the type of CT scanner used as well as technical factors including the kilovoltage and amperage of the X-ray beam, pixel size, image noise, slice thickness, beam-hardening artifacts, and artifacts related to large body habitus. The size of the lesion is also important because volume averaging commonly occurring in lesions smaller than 10 mm in size.

Pseudoenhancement occurs when a cyst, usually <2 cm, appears to artifactually enhance because it is surrounded by strongly enhancing parenchyma. This typically occurs during peak renal enhancement and should be suspected when a lesion is homogeneous and measures less than 10 HU on an unenhanced CT scan [18–21].

Dual-energy CT (DECT) is a recent development that involves the simultaneous acquisition of CT data at two different peak tube voltages and has the potential to reduce radiation dose. By exploiting the differences in energy-related attenuation of tissues within the body, DECT potentially can characterize tissue composition to a greater extent than that possible with single-energy techniques. When this technique is applied to remove the iodine contribution for a postcontrast image, a virtual noncontrast image can be produced. This technique exploits the fact that soft tissue and iodine demonstrate unique attenuation differences at different tube voltages, allowing for material decomposition. This technique also makes it possible to measure iodine concentration (instead of attenuation values) within the lesion. Enhancing renal masses demonstrate the presence of iodine, whereas benign, nonenhancing lesions have an absence of intralesional iodine.

## Magnetic resonance imaging

Significant advances in MR imaging hardware and software with routine use of phased-array coils and parallel imaging permit fast and high spatial resolution imaging of the kidneys. Short breath hold scans can produce superb multiphase renal images without significant peristaltic or respiratory motion artifacts [22–25]. The following imaging sequences should be obtained when evaluating a renal mass with MR: coronal T2-weighted single-shot turbo spin-echo sequence to serve as a localizing scan; axial T2-weighted gradient and spin-echo sequence with fat suppression to search for renal mass invasion of the adjacent fat; a dual-echo axial T1-weighted gradient-echo sequence with in-phase and opposed-phase images to search for fat within the tumor; and an axial T1-weighted fat-suppressed gradient-echo sequence for dynamic imaging using 20 ml of intravenous gadolinium with precontrast and postcontrast images obtained during the arterial, corticomedullary, and nephrographic phases to assess tumor vascularity. The physiologic principles behind the various dynamic postcontrast phases described in the MDCT section also hold true for dynamic MR imaging [26].

MR-derived functional imaging in the form of diffusion-weighted imaging (DWI) is now part of the routine MR evaluation of the kidneys and has been found to be very useful in assessing the likely malignant potential of renal parenchymal masses and transitional cell neoplasms. The apparent diffusion coefficient (ADC) values of these neoplasms is significantly higher than those of normal renal parenchyma and normal urothelial mucosa. The ability of DWI to identify changes in the molecular level has dramatically changed the diagnostic approach of radiologists, which was solely heretofore based on morphological criteria. It can improve the diagnostic accuracy of conventional MRI, assist the assessment of tumor response to treatment regimens and detect tumor recurrence with better spatial resolution, negative radiation, and diagnostic accuracy compared to PET-CT. The ability to quantify the diffusion has also led to potential prediction of tumor aggressiveness and grade which directly correlate with patient prognosis and management.

MRI is generally employed as a secondary imaging test when better characterization of a mass found on MDCT or ultrasound is needed. MRI is used as a primary imaging test in patients who have a severe allergy to iodinated contrast material or who are pregnant. Because of the risk of nephrogenic systemic fibrosis, MRI with gadolinium-based agents should be performed with caution in patients with poor renal function. Gadolinium-based contrast agents have been classified, based on the chemical structure of the ligand, as linear versus macrocyclic. The rates of dissociation of gadolinium from macrocyclic ligand agents are slower than dissociation from linear ligands and are thus considered to be more "stable." Accordingly, these macrocyclic agents (e.g. gadoterate meglumine, gadobutrol, and gadoteridol) are preferable to linear agents when assessing urinary tract pathology in these patients.

MRI may become more commonly employed for following renal lesions given the increased concerns regarding cumulative radiation dose. This is particularly applicable in young patients.

The chemical-specific tissue characterization capabilities of MRI are particularly helpful in characterizing certain types of renal lesion. Confident characterization of hemorrhagic cysts can be problematic on CT because the lack of enhancement of a small, dense renal mass may be difficult to confirm. Hemorrhagic cysts usually have high signal on T1-weighted images on MRI. The signal intensity of hemorrhagic or proteinaceous cysts on T2-weighted images is variable, ranging from low to mildly increased signal compared with renal parenchyma, but usually lower signal than seen in adjacent cerebrospinal fluid or other simple cysts. The combination of high signal on T1-weighted images and the lack of enhancement on MR imaging are diagnostic of a hemorrhagic renal cyst [22–26].

MR imaging is also useful in characterizing complex renal cysts. Septations within complex renal cysts that are vague on CT are readily depicted with MRI. Because fluid signal on T1-weighted images is usually darker than the low attenuation seen by CT, contrast enhancement within the septations is usually more apparent on MR than on CT, especially with subtraction images [22–26].

MR is more sensitive than CT in the detection of macroscopic fat within lesions such as angiomyolipomas (AMLs). Although most AMLs can be characterized with CT, it may be difficult to obtain accurate CT density measurements on small lesions. MR can confidently characterize AMLs in two ways. First, frequency-selective chemical fat suppression will result in subjective signal loss within fat-containing regions of the lesion. Second, chemical shift artifact will show a sharp dark interface between the AML and normal renal parenchyma [22–26].

## Ultrasound

Although CT is the premier imaging test in patients with suspected renal pathology, ultrasound is often the first imaging test ordered for renal evaluation. Despite its technical limitations, a large number of renal tumors can be correctly characterized sonographically. Recent advances in gray-scale and color flow Doppler techniques, as well as tissue harmonics, have enhanced the ability of ultrasound to distinguish solid from cystic lesions, and to make the diagnosis of a simple renal cyst [27–30]. Sonography is employed on a daily basis for evaluating lesions detected incidentally on CT which are not clearly simple cysts.

Lesions that are felt to represent hyperdense cysts either contain hemorrhage or proteinacious fluid. Those containing proteinacious fluid are typically simple on ultrasound, whereas those containing blood can appear heterogeneous and partly solid.

Ultrasound is useful in evaluating complex cystic lesions and detecting septations or minimal mural nodularity. This technique, however, is operator dependent and can be extremely limited in obese patients or when there is a large amount of adjacent bowel gas. Sonography can be quite useful for assessing the presence of renal vein thrombus with 75% sensitivity and 96% specificity, and 100% accuracy for detecting thrombus in the inferior vena cava [29, 30]. Intraoperative ultrasound has become a useful tool in guiding the surgeon during nephron-sparing surgery of small renal cell neoplasms.

## Positron emission tomography–computed tomography

Most malignancies exhibit increased metabolic activity, leading to increased utilization of glucose. PET imaging exploits the fact that the glucose analog $^{18}$F-2-fluoro-2-deoxy-glucose (FDG) shows increased intracellular accumulation in malignant tissue. PET-CT is a fixed combination of PET and CT scanners in a combined imaging system. The nearly simultaneous data acquisitions lead to minimization of spatial and temporal mismatches between modalities by eliminating the need to move the patient during the exam. The result is a fused image that provides biological and anatomic information. Imaging metabolic information of tumor tissue provides often more sensitive and specific information concerning the extent of malignancy than anatomic information alone [31–34].

Although FDG-PET is a well accepted method for the detection and staging of a number of malignancies, including lung, breast, colorectal, and esophageal cancer, it currently has a limited role in evaluating renal cell carcinoma (RCC). Several studies have shown that FDG-PET has a high specificity, but its sensitivity is inferior to that of CT and MR imaging in the evaluation of suspicious primary or metastatic RCC. FDG-PET surpasses the 90% sensitivity mark only for lesions at least 2 cm in diameter [31, 32]. Although there are studies that report sensitivity of FDG-PET to be as high as 94%, it is generally accepted that malignancy cannot be ruled out with a negative study. RCCs have inconsistent FDG uptake, which may be due to hypo- or isometabolism relative to background tissues, lack of accessibility of FDG, or heterogeneity of glucose transporter expression [33, 34].

### Positron emission tomography–magnetic resonance imaging

PET-MRI combines the unique tissue characterization of MRI – achieved through an array of conventional and emerging pulse sequences – with the quantifiable functional and molecular information provided by PET, thereby providing distinct potential clinical advantages over other imaging modalities. PET-MRI has many potential advantages over PET-CT. The improved lesion detection within the kidneys of MRI compared with that of CT is expected to achieve an overall diagnostic advantage for PET-MRI over PET-CT. In addition, lesion margins may be better defined by MRI than by CT in certain locations. Preliminary data also suggest that lesion registration is improved through hybrid PET-MRI, an advantage that will potentially improve tissue segmentation, attenuation correction, and ultimately PET quantification.

PET-MRI offers practical advantages for patients requiring both PET and MRI examinations for oncologic assessment by providing both modalities within a single appointment and imaging session. Radiation exposure is also reduced because CT is not used in the imaging protocol.

Finally, PET-MRI allows accurate, temporally and spatially aligned multiparametric imaging that combines high-contrast anatomic MR images with the quantitative power of molecular imaging of both PET and MRI, including DWI, perfusion MRI, and MR spectroscopy. This potential creates numerous opportunities for characterizing tumor biology across all of the dimensions of imaging offered by PET and MRI.

## Cystic renal masses

Incidentally discovered renal cysts are commonly found on cross-sectional imaging studies. Strict imaging criteria have been developed by Bosniak to categorize renal cysts as benign, malignant, or indeterminate, and to guide in the management of these lesions. The Bosniak Classification (Table 123.1) of renal cystic was first described in 1986 [35] but has undergone several modifications [36–39]. Although initially described for lesions found on CT, the criteria can be applied to MRI with overall similar accuracy [40]. In some cases MRI may depict additional septa, thickening of the wall, or enhancement which may lead to an upgraded Bosniak Classification.

**Table 123.1** Bosniak classification of cystic renal masses.

| Category | Features |
|---|---|
| I | A simple water-attenuation cyst with a hairline-thin wall, without septa, calcification, or solid components; no contrast enhancement |
| II | Bosniak type I with a few thin septa or fine calcification in the wall or septa |
| | Sharply marginated, nonenhancing, uniformly high-attenuation lesions of <3 cm |
| IIF | Bosniak type II cystic lesion with minimal enhancement of a hairline-thin septum or wall or minimal thickening of the septum or wall; the cyst might contain calcification that might be nodular and thick but there is no contrast enhancement |
| | Uniformly high-attenuation lesions of >3 cm |
| III | Bosniak type IIF cystic lesion with thickened irregular walls or septa, and contrast enhancement |
| IV | Enhancing soft tissue components or mural nodules |

### Category I

These lesions are benign simple cysts requiring no further diagnostic imaging or follow-up (Figure 123.1). On CT, these lesions must have a paper-thin wall, have entirely fluid attenuation measuring between 0 and 20 HU, and they must demonstrate no enhancement following the intravenous administration of contrast medium. These lesions do not contain septations or calcifications.

### Category II

These lesions are also benign, but are minimally complicated (Figures 123.2–123.4). They may contain a few paper-thin septations. They may also contain fine curvilinear mural or septal calcification. This category also includes hyperattenuating cysts which measure less than 3 cm, are round and sharply marginated with at least one-quarter of the lesions extending outside the renal parenchyma. Most importantly, they must demonstrate uniform high attenuation and no enhancement with intravenous contrast. Cysts that measure between 20 and 40 HU are usually proteinacious cysts and have a density of greater than 40–50 HU are likely to be hemorrhagic. The latter will appear complex on ultrasound. They may appear solid or semisolid due to clot retraction and could be miscategorized by ultrasound.

Dual-energy CT is most helpful in depicting hemorrhagic renal cysts (see Figure 123.3).

Kang et al. attempted to differentiate high-attenuation renal cysts from RCCs on unenhanced CT scans [16]. They retrospectively evaluated the attenuation values and degree of uniformity/heterogeneity in 56 hyperdense

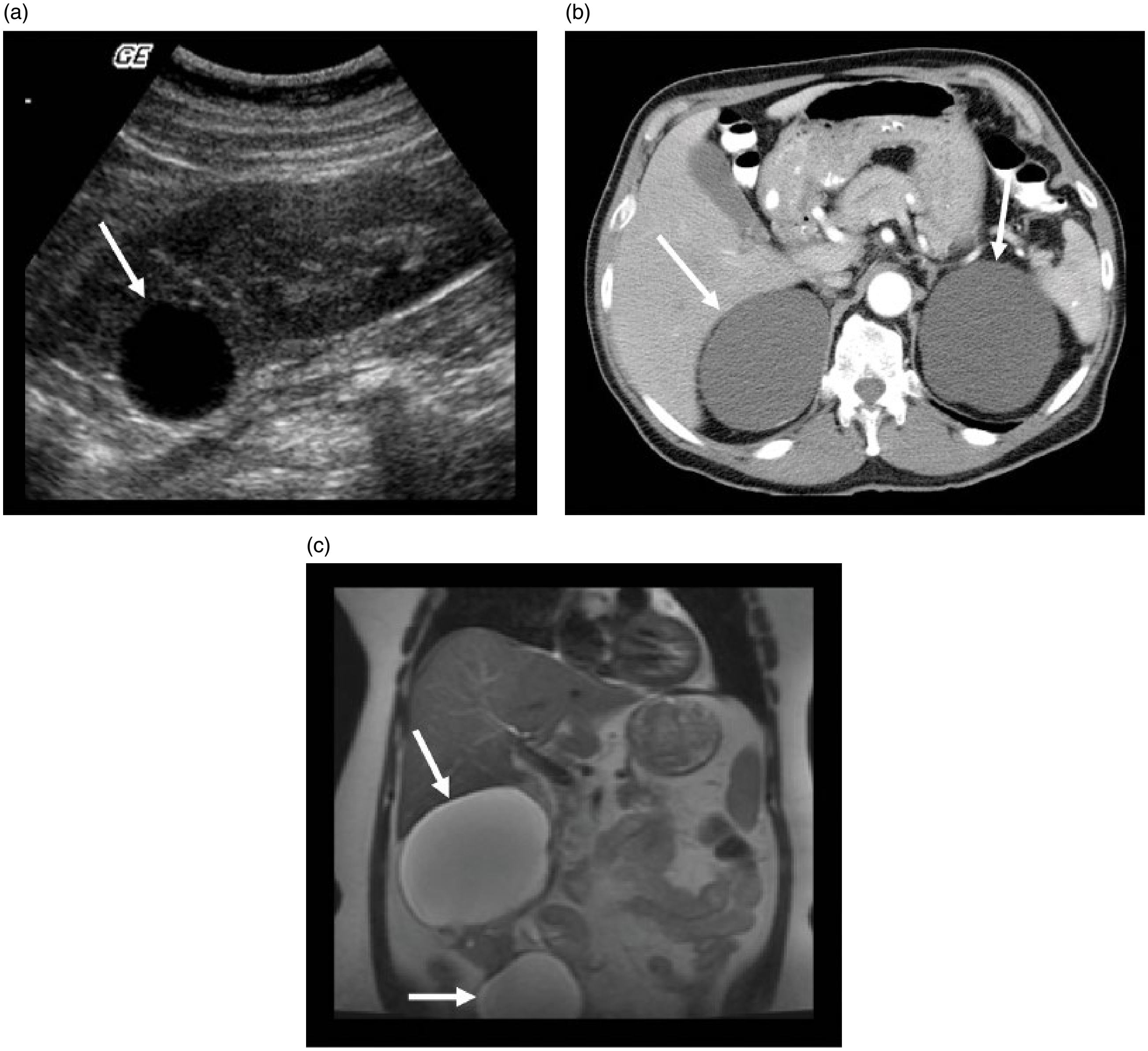


**Figure 123.1** Bosniak type I renal cyst. (a) Longitudinal sonogram shows a well marginated, anechoic cyst (arrow) along the posterior aspect of the upper pole of the right kidney. (b) Axial contrast-enhanced CT scan shows large, bilateral, nonenhancing water density renal cysts (arrows). (c) Coronal T2-weighted MR image shows well-marginated, hyperintense cysts (arrows) with paper-thin walls in the upper and lower poles of the right kidney. Note the absence of mural thickening or nodularity.

renal cysts and 54 RCCs. The mean attenuation for hyperdense cysts was 53 HU and for RCCs was 38 HU, but there was significant overlap when evaluating attenuation values alone. However, when evaluating uniformity versus heterogeneity of the lesion, the authors concluded that a homogeneous, hyperattenuating renal masses with an attenuation of 70 HU or greater, had a 99.9% likelihood of being a benign, high-attenuation renal cyst. Most RCCs in their study had attenuation values lower than those of renal parenchyma (20–30 HU) and were often heterogeneous in attenuation. High-attenuation renal cysts can in many cases be differentiated from RCC on unenhanced CT [16, 41, 42].

### Category IIF

These lesions are likely benign but require a period of observation or follow-up (the F stands for follow-up) to prove their benignity. These lesions may contain an increased number of septa or have minimal septal or

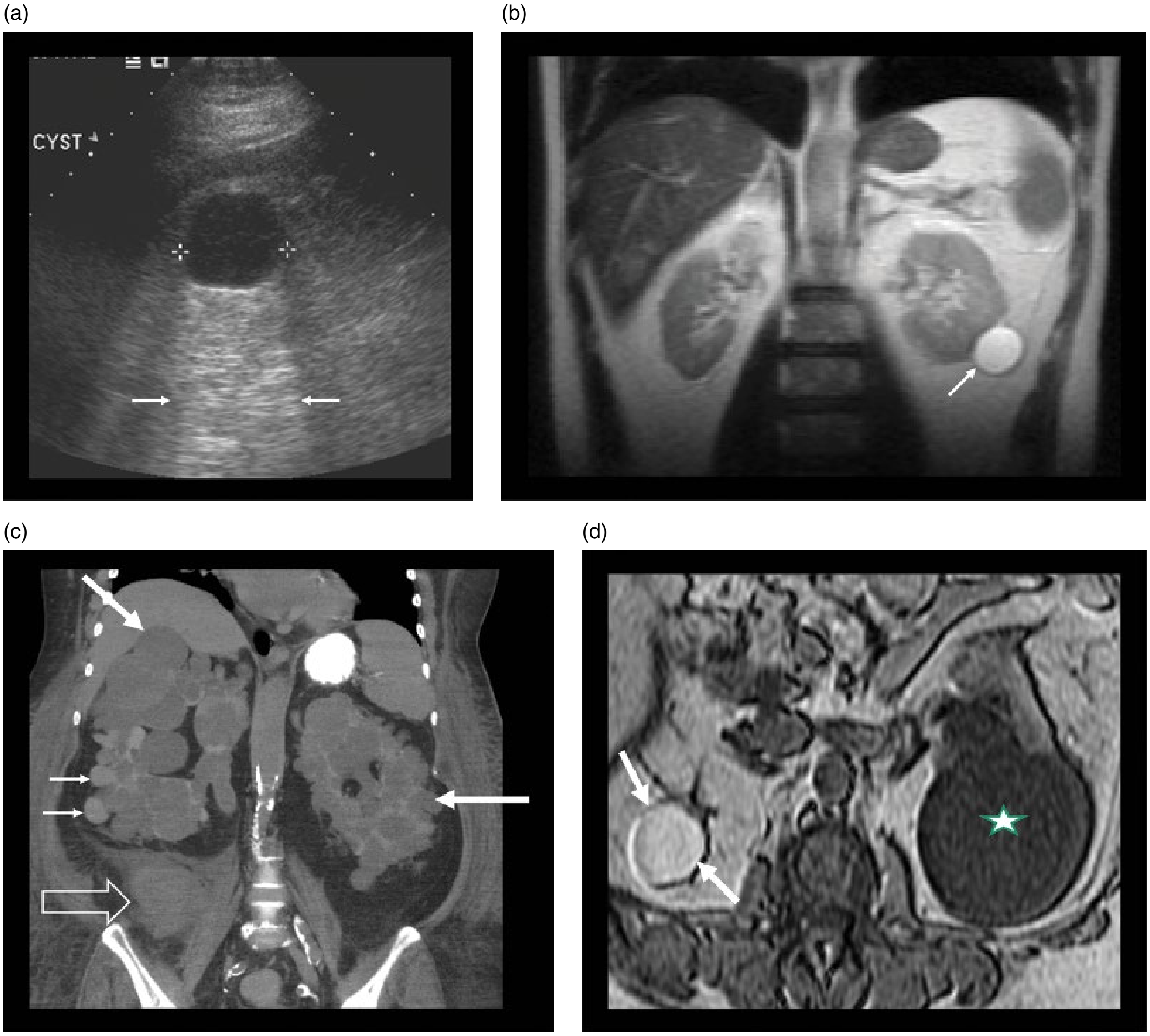


**Figure 123.2** Bosniak type II renal cyst. (a) Transverse sonogram shows a well-marginated cystic structure (cursors) with fine, low-level internal echoes. Note the acoustic enhancement (small arrows) posterior to the cyst. (b) Coronal T1-weighted MR image shows a hyperintense cyst (arrow) indicating the presence of hemorrhage and/or mucin. (c) Coronal unenhanced CT scan in a patient with adult polycystic kidney disease demonstrates multiple simple (type I) (large solid arrows) and hyperdense (type II) (small solid arrows) renal cysts. The high attenuation within the cysts is due to hemorrhage. There is a renal transplant (open arrow) in the right iliac fossa with surrounding hemorrhage. (d) Axial T1-weighted images reveal a hyperintense hemorrhagic (type II) right renal cyst (solid arrows) and a hypointense left simple (type I) renal cyst (star).

mural thickening. Category IIF lesions may contain thick, irregular, or nodular calicifications. When a high-attenuation lesion is completely intrarenal, the smoothness of its wall cannot be assessed. Accordingly, completely intrarenal high-attenuation lesions as well as lesions greater than 3 cm in diameter are included in this category. These lesions may also have a slightly indistinct interface with the adjacent renal parenchyma [33–37].

These lesions should be reimaged with CT or MRI in six months and then annually or every other year for 5 years. Stability over time suggests these lesions are benign, recognizing that some malignant lesions can grow slowly and that cysts can enlarge. Therefore on follow-up imaging their morphologic characteristics must be evaluated in addition to their size. If there is any increase in the thickness or in the irregularity of the wall or septa, surgical

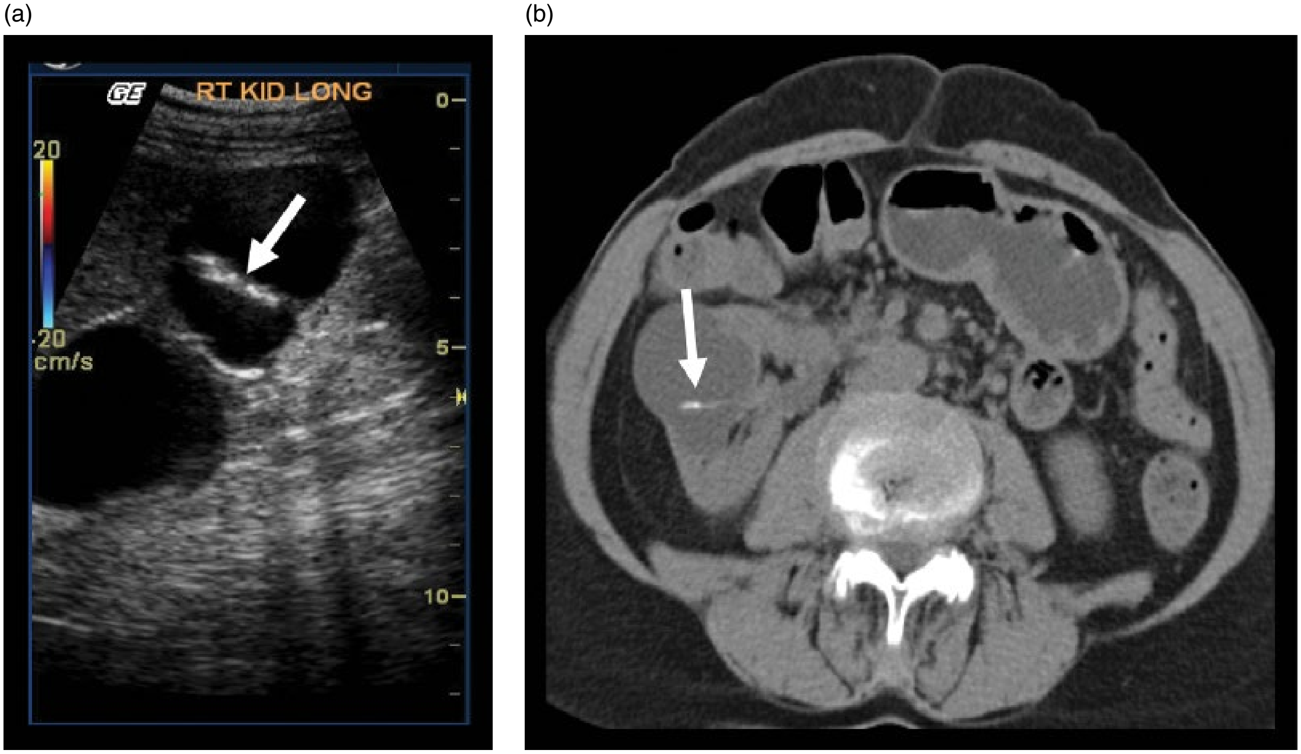


**Figure 123.3** Bosniak type II renal cyst. (a) Longitudinal sonogram shows minimal thickening and calcification of a septation (arrow) in a patient with right renal cysts. (b) This calcification (arrow) is better appreciated on this transverse unenhanced CT scan. This lesion otherwise fulfills the imaging criteria for a simple cyst.

exploration is indicated. MRI can be particularly useful in evaluating hemorrhagic cystic renal masses and evaluating for the presence of septal or mural enhancement. The introduction of the IIF category in 1993 has prevented unnecessary surgery in large numbers of patients [33–37].

### Category III

These are truly indeterminate lesions which cannot be diagnosed accurately as benign or malignant based on their imaging appearance (Figure 123.5). They contain thick walls or thick septa which demonstrate measurable enhancement. They may contain more extensive, thickened, and irregular calcifications. At pathology, these lesions are multilocular cysts, infected or hemorrhagic cysts, multilocular cystic nephromas, or cystic RCCs. The risk of malignancy in this group has been reported to range up to 59%. Since a significant number of patients with Bosniak type III lesions undergo surgery for ultimately benign disease, some have advocated biopsy in this patient cohort [1, 4, 20].

### Category IV

These lesions are clearly malignant and require surgical removal (Figure 123.6). They may have findings similar to category III lesions but also have enhancing soft tissue components adjacent to the wall or septa. These lesions are usually cystic clear cell carcinomas (accounting for 4–15% of all RCCs), multilocular cystic RCCs, cystic nephromas, and mixed epithelial and stromal tumors [35–38].

## Multilocular cystic nephromas

Multilocular cystic nephroma is a benign renal neoplasm that has biphasic age and sex distribution. Two-thirds of multilocular cystic renal tumors occur in a predominately male pediatric population between three months and 2 years old. Approximately one-third occur in a mostly female population, with a peak incidence in the fifth and sixth decades of life. Presenting symptoms depend on the age of the patient. Children typically present with a painless, progressively enlarging, palpable abdominal or flank mass that has a variable growth rate and may be discovered incidentally. Adults may have a variety of nonspecific signs and symptoms, including abdominal and flank pain, urinary tract infection, and hypertension. Microscopic or gross hematuria can occur in either group cysts. Variable degrees of obstruction of the renal collecting system can occur due to herniation of the tumor, which can lead to urinary tract infection.

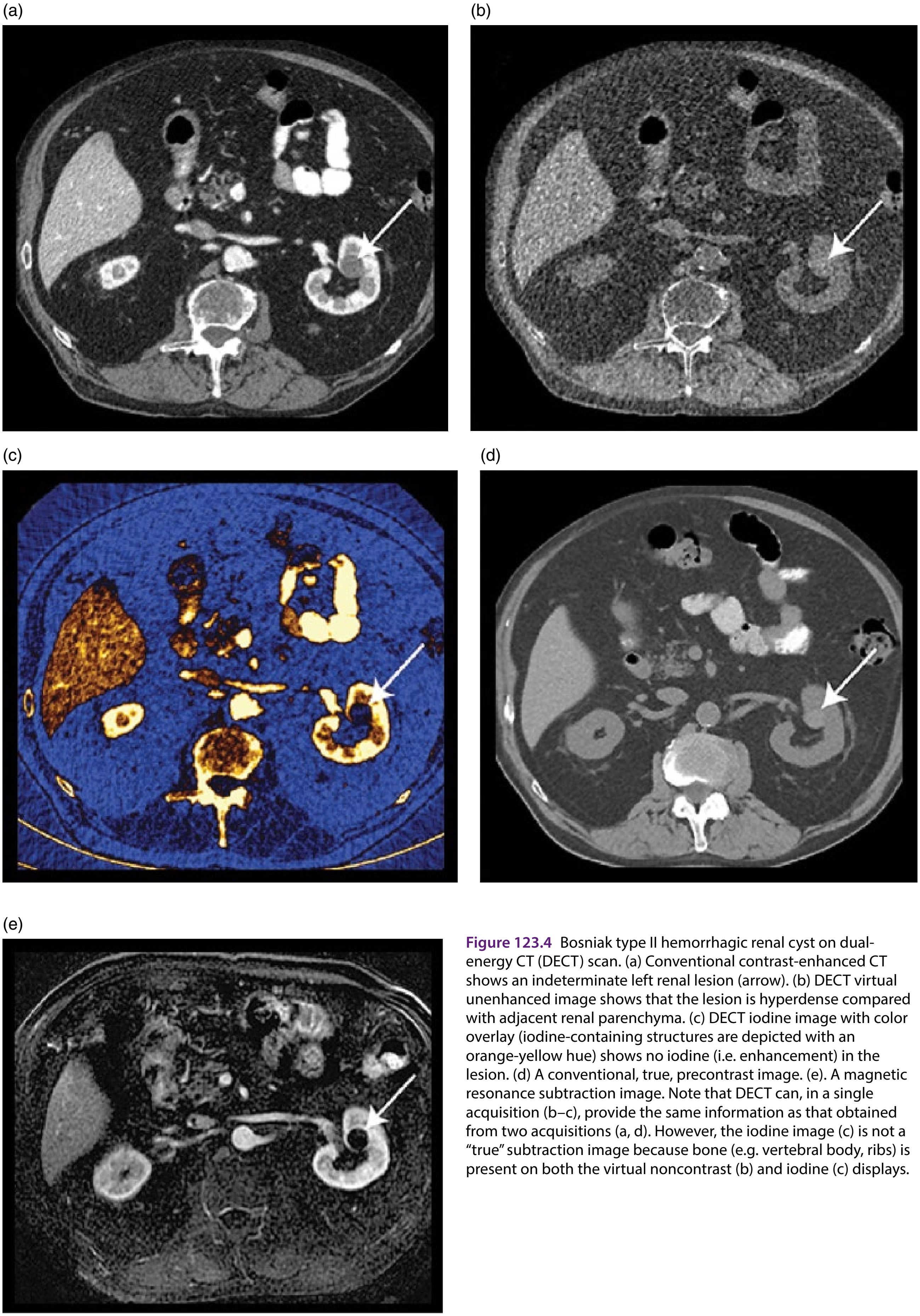


**Figure 123.4** Bosniak type II hemorrhagic renal cyst on dual-energy CT (DECT) scan. (a) Conventional contrast-enhanced CT shows an indeterminate left renal lesion (arrow). (b) DECT virtual unenhanced image shows that the lesion is hyperdense compared with adjacent renal parenchyma. (c) DECT iodine image with color overlay (iodine-containing structures are depicted with an orange-yellow hue) shows no iodine (i.e. enhancement) in the lesion. (d) A conventional, true, precontrast image. (e). A magnetic resonance subtraction image. Note that DECT can, in a single acquisition (b–c), provide the same information as that obtained from two acquisitions (a, d). However, the iodine image (c) is not a "true" subtraction image because bone (e.g. vertebral body, ribs) is present on both the virtual noncontrast (b) and iodine (c) displays.

Most adult patients are asymptomatic and these lesions are discovered incidentally. A complicated cystic lesion is typically identified on cross-sectional imaging (Figure 123.7) [35–38].

## Benign solid renal masses

Most solid renal masses can be accurately characterized with cross-sectional imaging so that biopsy is not necessary [43, 44]. This is particularly true for angiomyolipomas (AMLs) (Figures 123.8–123.10) and RCCs, the two most common solid renal lesions in adults. There are several pseudotumors that can mimic solid renal lesions which must be excluded in order to avoid further evaluation or unnecessary surgery. Occasionally a prominent column of Bertin, a dromedary hump, or persistent fetal renal lobulation can simulate a renal mass on ultrasound, but these can usually be correctly diagnosed with CT or MRI. These pseudolesions have a similar contrast enhancement profile to normal renal parenchyma. In the case of persistent renal fetal lobulation, a normal renal pyramid is present within the center of the bulging portion of renal parenchyma.

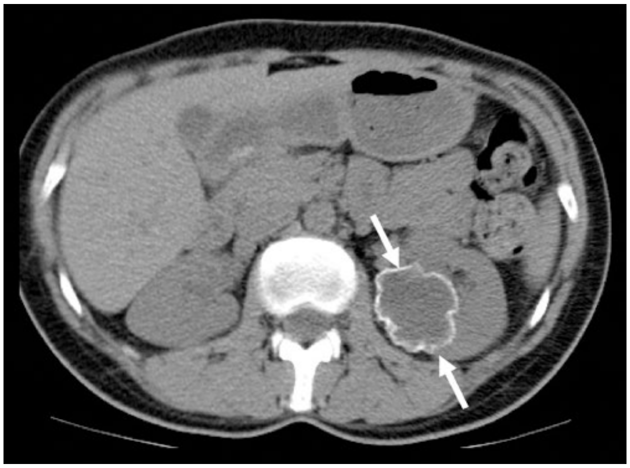


**Figure 123.5** Bosniak type III cystic renal lesion. Axial unenhanced CT scan shows thick, irregular calcification (arrows) associated with a low-density renal mass. This lesion proved to be a renal cell carcinoma.

Benign lesions that can simulate a renal neoplasm include focal acute pyelonephritis [45], renal abscess (Figure 123.11) [46], renal hematoma (Figure 123.12) [47, 48], focal xanthogranulomatous pyelonephritis (XPG) [49, 50], arteriovenous malformations (AVMs) (Figure 123.13) [51–53], and acute focal infarction (Figure 123.14). Extremely rare entities such as extramedullary renal hematopoiesis, tuberculoma related to therapy for bladder cancer, and splenorenal fusion can also mimic a renal mass.

Often the clinical history or additional findings on CT can be useful in making the correct diagnosis. For example, stranding in the adjacent perinephric fat should raise suspicion for acute pyelonephritis, although there are rare infiltrative renal tumors such as medullary RCC that can demonstrate this finding. In the case of focal pyelonephritis, there is a wedge-shaped area of heterogeneous hypoattenuation with no well-defined wall and no bulge

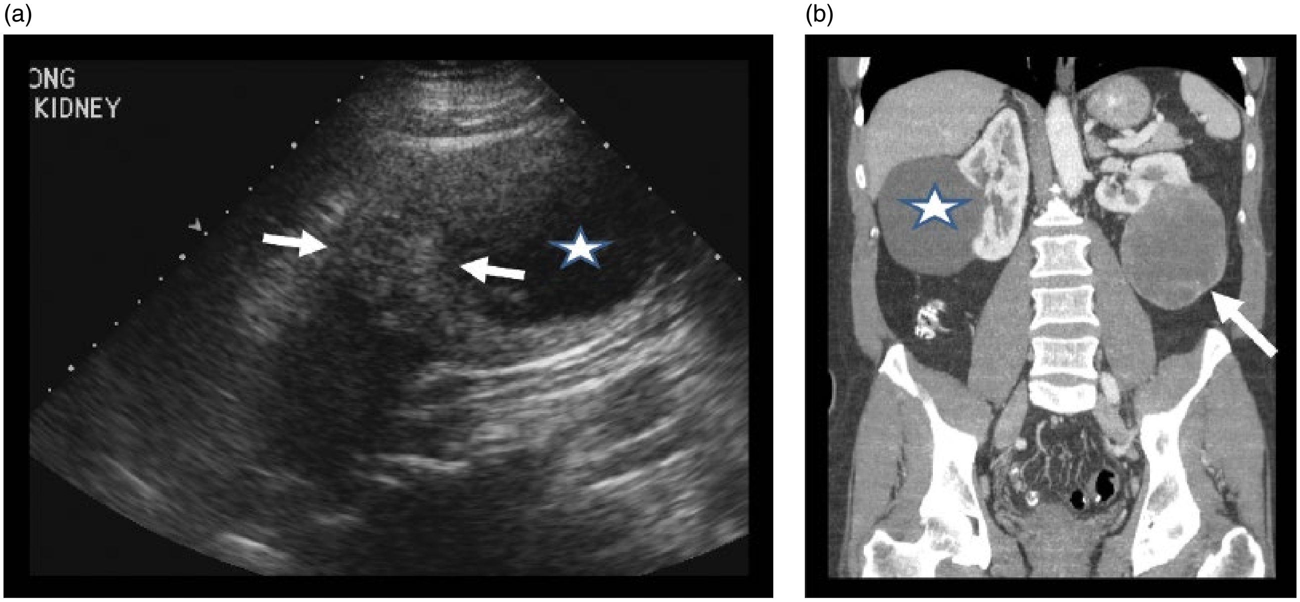


**Figure 123.6** Bosniak type IV cystic renal lesion. (a) Longitudinal ultrasound of the left kidney shows a lower pole mass that has mural thickening superiorly (arrows) and a more cystic component inferiorly (star). (b) Coronal reformatted contrast-enhanced CT image shows mural and septal enhancement (arrow) of this mass. Note the Bosniak type I cyst at the lower pole of the right kidney (star).

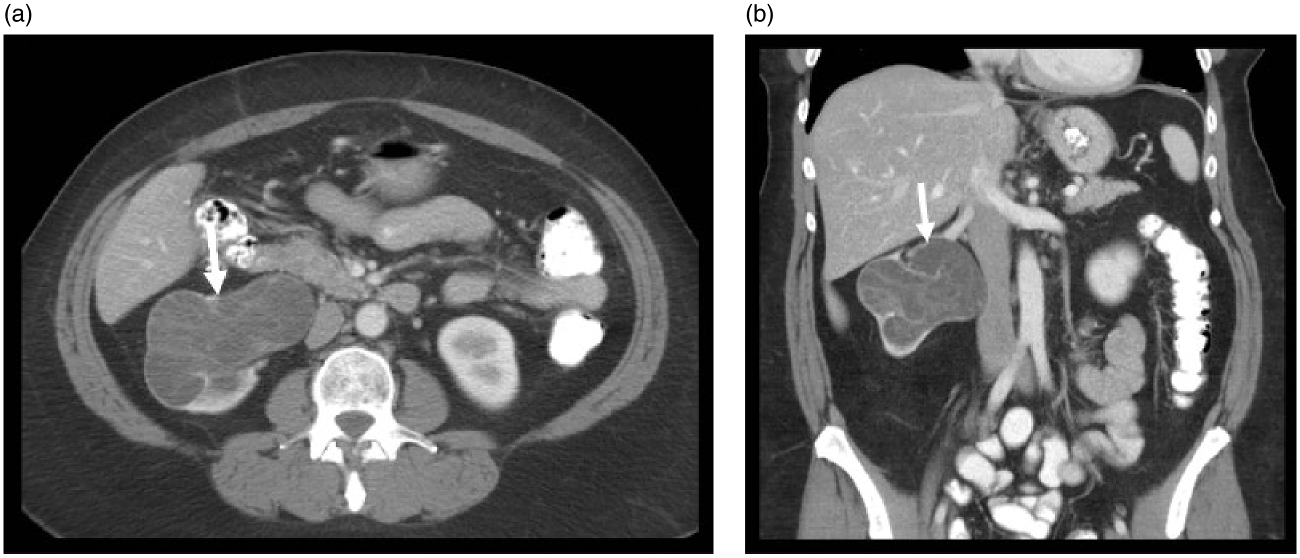


**Figure 123.7** Multilocular cystic nephroma: CT features. Axial (a) and coronal reformatted (b) images disclose a multiseptated central cystic mass (arrows) involving the left renal pelvis.

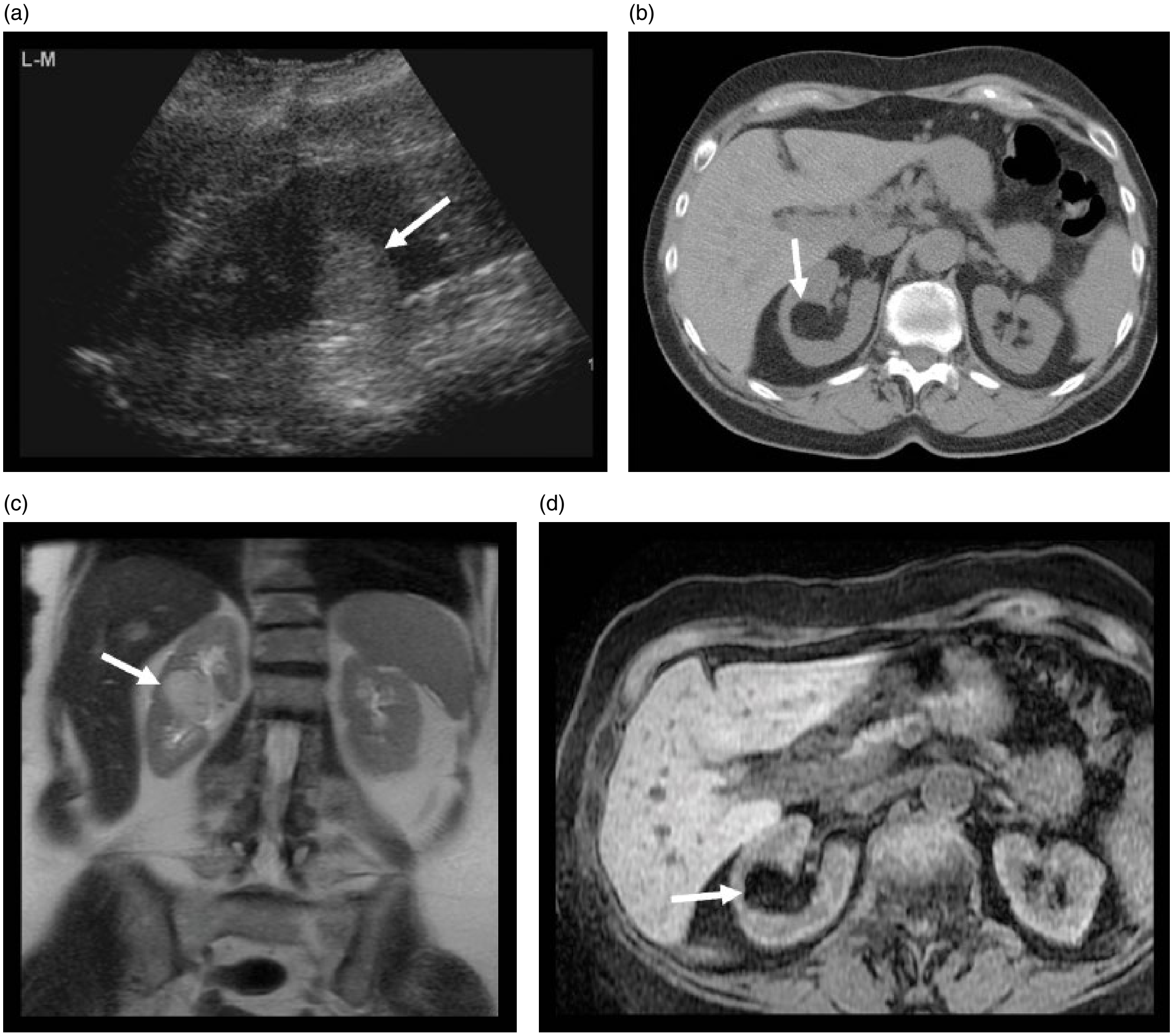


**Figure 123.8** Renal angiomyolipoma: imaging features. (a) Longitudinal sonogram demonstrates a well-marginated uniformly hyperechoic renal mass (arrows). (b) Axial unenhanced CT scan shows a well-circumscribed, fat-containing right renal mass (arrow), with a density of −85 HU. (c) This mass is hyperintense on this T1-weighted coronal MR image. (d) This lesion (arrow) shows signal dropout on this axial, fat-suppressed MR image.

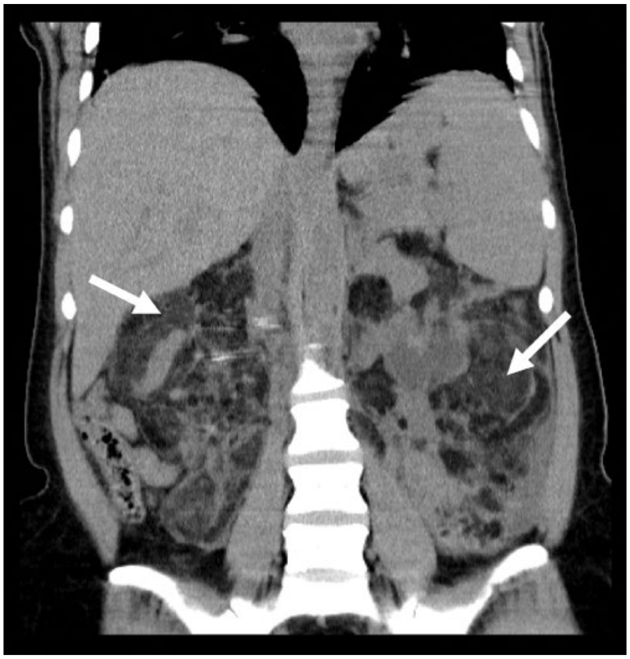


**Figure 123.9** Multiple renal angiomyolipomas replace the kidneys in this patient with tuberous sclerosis. Coronal reformatted CT scan shows multiple fat-dense renal lesions (arrows).

on the renal surface, features which help distinguish it from RCC. If there is still a question about the nature of the mass a follow-up scan showing healing and resolution can be helpful [45, 46].

AVMs can be intraparenchymal (see Figure 123.13) or in the renal sinus, but observing that the mass enhances to the same degree as the renal artery should be the clue to the correct diagnosis on CT and MRI. The feeding renal artery to the AVM is often enlarged as well. On gray-scale ultrasound an AVM appears as an anechoic structure that fills with color on color Doppler sonography. On noncontrast MRI scans, AVMs manifest as intralesional flow voids that show early enhancement, abnormal tortuous vessels, and an early draining vein following the intravenous administration of contrast medium [51–53].

Focal XGP can be difficult to distinguish from an RCC, but the presence of a staghorn calculus, which occurs in 70% of cases, is a helpful clue. There may be low attenuation within the associated collecting system mass due to presence of lipid-laden macrophages. This disorder typically occurs in diabetic patients [49, 50].

When renal hematomas (see Figure 123.12) occur in the setting of trauma, the diagnosis is usually straightforward. However, renal hematomas can also occur spontaneously in patients who are anticoagulated, have a coagulopathy, or vasculitis. Typically, radiologists are not privy to this information to assist in the diagnosis. On noncontrast CT images, the hematoma may be hyperdense, and there should be no contrast enhancement. Occasionally, active extravasation of contrast material may be visualized. Hematomas are more easily diagnosed with MRI because of the typical signal characteristics of blood.

Subepithelial renal pelvic hematomas (Antopol–Goldman lesions) are a rare cause of a heterogeneously dense or hyperdense masses in the renal pelvis. They do not show contrast enhancement and may cause worrisome extrinsic compression on the renal collecting system. These lesions are often confused with renal pelvic malignacies, and in most cases, patients underwent nephrectomy for what was thought to be malignant disease [1].

## Angiomyolipomas

AMLs are the most common benign mesenchymal renal neoplasms and are composed of fat, smooth muscle, and vascular tissue [54–57]. They typically occur sporadically in middle-aged patients, and are four times more common in females than males. Tuberous sclerosis, an autosomal dominant disease, accounts for 10–20% of all individuals with AML. The lesions in tuberous sclerosis are seen in younger patients and with equal frequency in males and females. The lesions in the sporadic form are usually less than 5 cm in diameter, however AMLs seen in tuberous sclerosis can be much larger and are often multiple and bilateral [58]. Although benign, AMLs often increase in size over time and larger tumors have a propensity to bleed (see Figure 123.8). AMLs have a greater tendency to grow when they are multiple.

The imaging appearance varies according to the proportion of fat, muscle, and blood vessels. Since 95% of AMLs contain macroscopic fat (see Figures 123.7–123.10), the diagnosis can usually made with confidence on unenhanced CT when there are one or more regions of fat in a noncalcified renal lesion. They typically are well marginated, cortical in location, and predominantly fatty lesions with heterogeneous regions of soft tissue attenuation interspersed throughout the mass. Although the soft tissue components of the mass may enhance with intravenous contrast, this is not a dominant feature of most AMLs [54–58].

Sonographically, small angiomyolipomas appear as uniformly hyperechoic lesions (see Figure 123.8). Unfortunately this sonographic appearance is also seen in 32% of small (<3 cm) RCCs. Echogenic carcinomas are more likely to have a hypoechoic rim and cystic areas, while AMLs are more likely to demonstrate acoustic shadowing and no hypoechoic rim. These findings are not sufficiently sensitive or specific to confidently make the diagnosis so that CT or MRI is required for further evaluation. Larger AMLs are more complex on ultrasound and difficult to diagnose. On MRI (see Figure 123.8), most AMLs can be readily

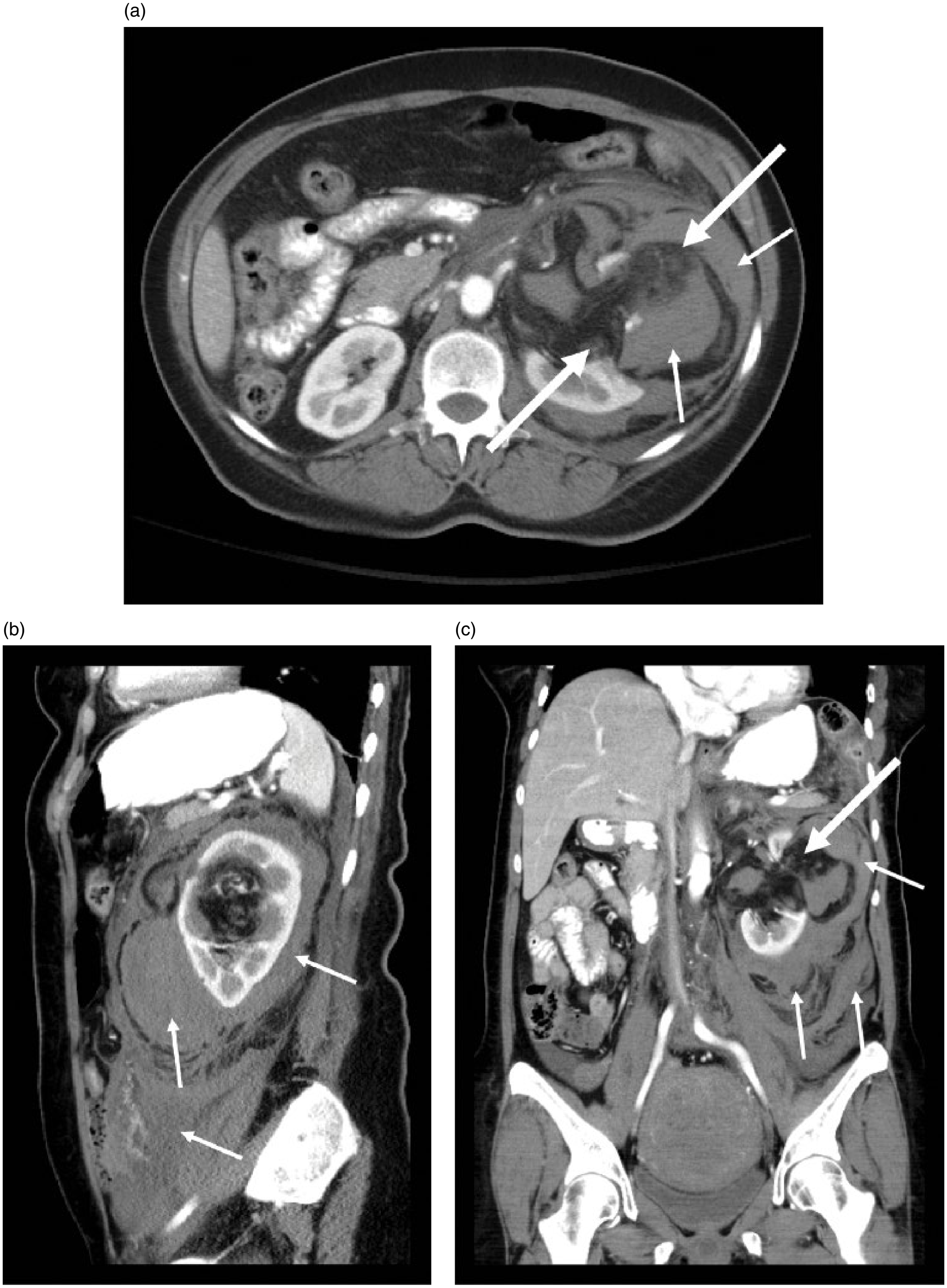


**Figure 123.10** Hemorrhagic angiomyolipoma: CT features. Axial (a), sagittal (b), and coronal (c) CT images show a large fat-containing angiomyolipoma (large arrows) associated with a large renal and perirenal hematoma (small arrows).

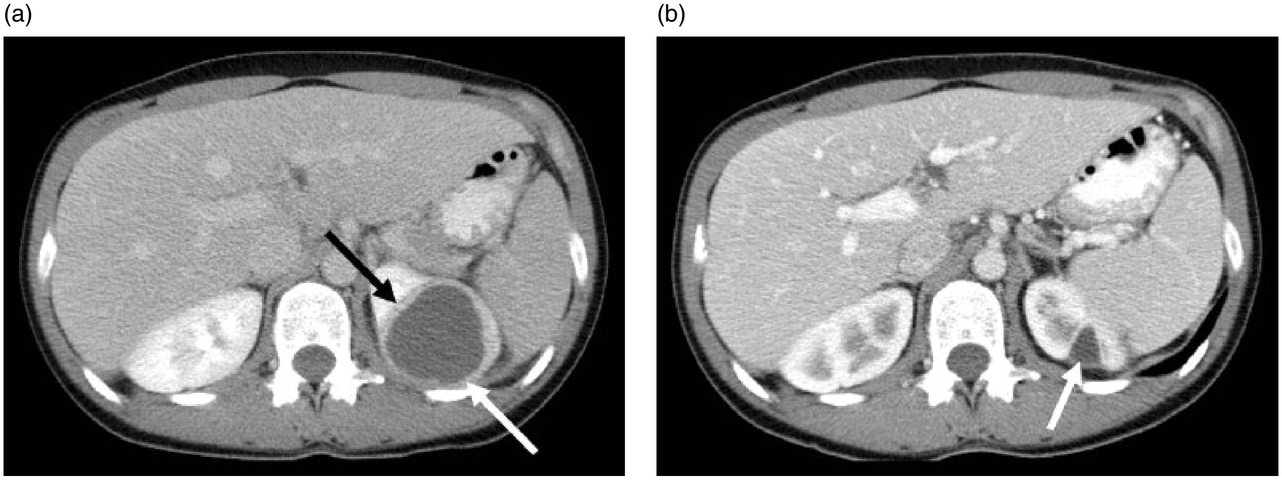
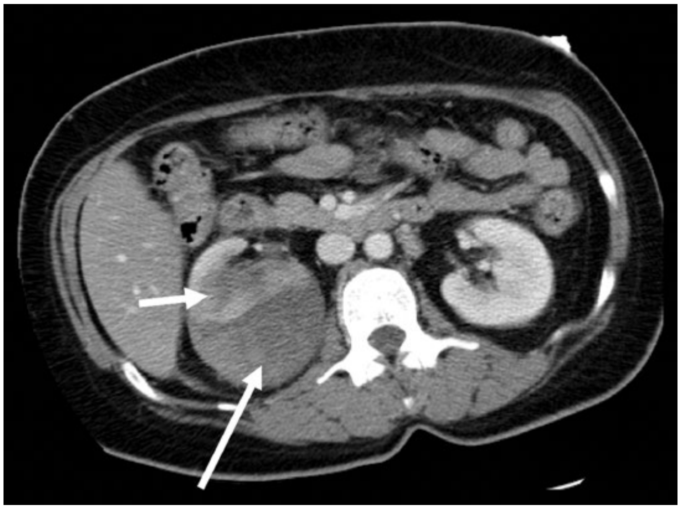


**Figure 123.11** Renal abscess causing a low-density renal mass. (a) Transverse contrast-enhanced CT scan shows a thick-walled low-density mass (arrows) at the upper pole of the left kidney. (b) Scan obtained three months after the completion of antibiotic therapy shows a much smaller residual renal mass (arrow).

**Figure 123.12** Perinephric hematoma causing a Page kidney. Axial contrast-enhanced CT scan shows a large perinephric hematoma (long arrow) causing compression of the right kidney. Notice the diminished nephrogram of the compressed right kidney (short arrow).



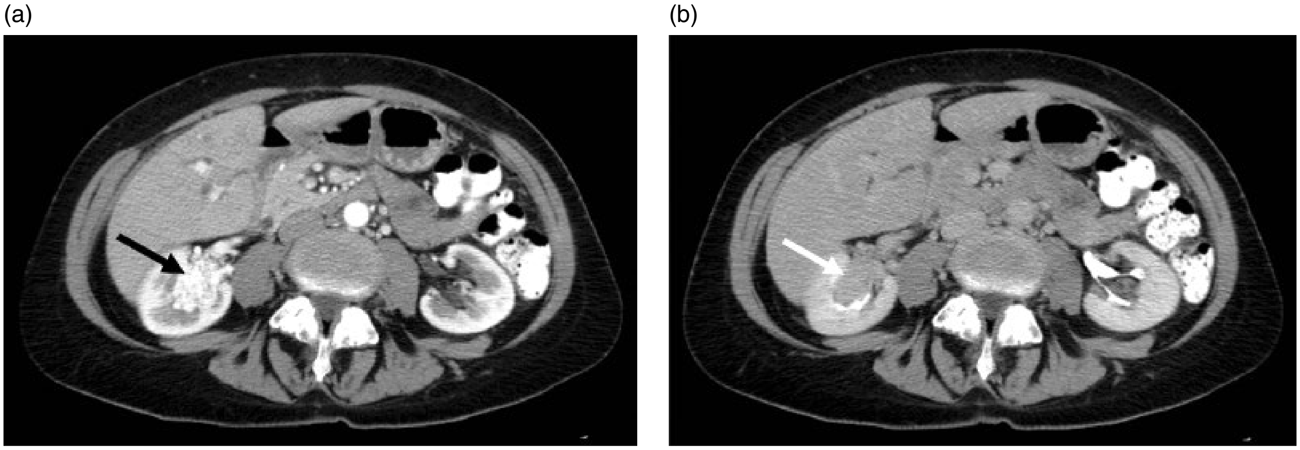


**Figure 123.13** Arteriovenous malformation simulating a renal pelvic mass. (a) Axial CT scan obtained during the corticomedullary phase of enhancement shows multiple tubular enhancing structures (arrow) in the right renal pelvis. (b) On the excretory phase images, they simulate a right renal pelvic tumor (arrow). Parapelvic cysts are present in the left kidney.

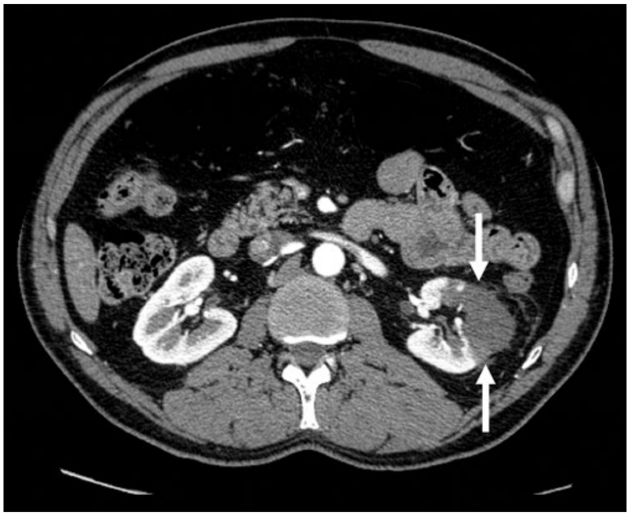


**Figure 123.14** Renal infarct simulating a hypovascular renal mass. Axial CT image depicts a wedge-shaped region of markedly decreased enhancement (arrows) along the lateral aspect of the interpolar region of the left kidney.

characterized with fat-suppression techniques including combined T1-weighted regular (in-phase) and fat-suppressed images or combined T1-weighted in-phase and out-of-phase spoiled gradient-echo sequences [54–58].

The absence of a complete elastin layer in the blood vessels of AMLs predisposes these lesions to aneurysm formation and hemorrhage. The aneurysms commonly seen on angiography may not be appreciated on cross-sectional imaging studies. Hemorrhage is not uncommon. When the lesions bleed, they can present a diagnostic dilemma as the fat may be masked by the hemorrhage. Lesions larger than 3.5–4.0 cm in diameter are believed to have an increased risk of hemorrhage, and are often electively resected with nephron-sparing surgery. In patients with high surgical risk and those with tuberous sclerosis who may have limited renal reserve, selective arterial embolization can be performed [54–58].

There have been reported cases of macroscopic fat in clear cell RCCs. In these cases, extensive calcification is also present in the mass. Since calcification in AMLs is extremely rare, and since fat without calcifications in RCC is extremely rare, a fatty noncalcified renal mass is considered diagnostic of AML. Other fat-containing renal lesions which are extremely rare and are not usually included in the differential diagnosis are lipoma, liposarcoma and, oncocytomas [54–58].

Lipid-poor AMLs (approximately 5%) pose a diagnostic problem in that they appear as solid enhancing masses which have been considered indistinguishable from RCCs based on imaging findings. However, recent studies have suggested that a small (<3 cm) hyperattenuating lesion on noncontrast CT which demonstrates homogeneous enhancement has a strong likelihood of being a benign lesion. This lesion can be further evaluated with MRI to assess for microscopic fat. Percutaneous biopsy can also be performed on these lesions [54–58].

## Oncocytoma

Oncocytomas are benign renal cell neoplasms that account for approximately 5% adult renal epithelial neoplasms in surgical series. They are more common in men than women, and their peak incidence is in the seventh decade. There are some imaging features that suggest the diagnosis of oncocytoma including homogeneous enhancement and a central stellate fibrotic nonenhancing scar in approximately a third of cases. The scar can appear high signal on T2-weighted sequences. Classic CT (Figure 123.15), MRI, and angiographic findings for oncocytoma include a spoke-wheel pattern, a homogeneous tumor blush, and a sharp, smooth rim. Oncocytomas typically do not have perinephric stranding.

Unfortunately, the imaging features of oncocytomas demonstrate considerable overlap with those of RCCs, particularly the chromophobe type, and therefore cannot be reliably used for diagnosis. A central scar and segmental enhancement inversion (in which early contrast-enhanced images show relatively more enhanced and less enhanced intralesional components with inversion of their relative enhancement on later images) are present in at least 10% of cases of both renal oncocytomas and of chromophobe RCCs with no significant difference between the two entities [59–62].

Indeed, oncocytomas often manifest as a complex hypervascular mass that is sometimes associated with adjacent neovascularity and perinephric stranding, findings worrisome for a clear cell carcinoma. Advances in immunocytochemical analysis and cytogenetics may be helpful in distinguishing oncocytoma from RCC in the future, but at the time of this publication, oncocytomas cannot be reliably diagnosed with percutaneous biopsy, and they typically are surgically resected [59–62].

## Other benign solid renal masses

There are other benign solid renal lesions that cannot be reliably distinguished from RCCs, though some have imaging features that may suggest the diagnosis. Papillary adenomas and renomedullary interstitial cell tumors are less than 5 mm in diameter and are common at autopsy [4].

Metanephric adenomas are usually solid and hyperattenuating on noncontrast CT and contain calcification in 20%. Hemangiomas and lymphangiomas typically arise in the renal pyramids or pelvis. Leiomyomas commonly

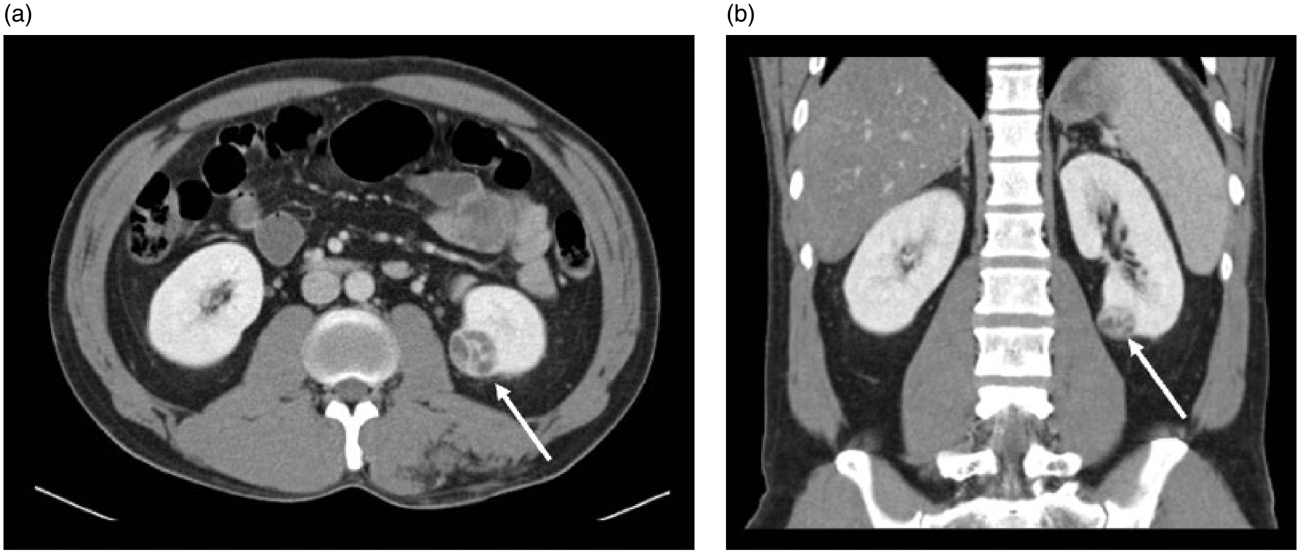


**Figure 123.15** Renal oncocytoma: CT features. An enhancing mass with a "spoke-wheel" appearance (arrows) masses is identified at the lower pole of the left kidney on these axial (a) and coronal (b) contrast-enhanced CT scans.

appear as well-circumscribed homogeneous exophytic solid masses that demonstrate uniform enhancement with intravenous contrast. Juxtaglomerular cell neoplasm (reninoma) is an endocrine tumor, which typically occurs in the second or third decades of life, and is twice as common in females than males. Patients present with hypertension and hypokalemia. These lesions typically appear as well-circumscribed cortical tumors less than 3 cm in diameter. Despite the fact that they are such vascular lesions pathologically, they appear hypovascular on contrast CT, possibly due to renin-induced vasoconstriction [4].

Mixed epithelial and stromal tumors consist of solid and cystic areas that may herniate into the renal pelvis. The observation of some of these features may be sufficient to raise the possibility of a benign lesion and in some cases biopsy should be considered rather than immediate surgery [4].

## Renal cell carcinoma

RCC is the eighth most common malignancy and accounts for 2–3% of new cancers in the United States. RCC typically presents in the fifth to seventh decades of life, and is two to three times more common in men and slightly more common in black people than white. The tumors are usually solitary, but can be multifocal in 6–25%. In patients with certain genetic conditions, such as von Hippel–Lindau disease (Figure 123.16), hereditary papillary renal cancer (Figure 123.17), and possibly tuberous sclerosis, multifocality is common. Indeed, multifocal tumors are seen in 87% of patients with von Hippel–Lindau disease [63–65]. RCC is also more common in patients with acquired cystic renal disease, with a three to six times increased risk in patients on long-term dialysis [63, 64]. Because RCCs may be multifocal or bilateral, both kidneys must be scrutinized when staging the lesion prior to surgical or percutaneous intervention.

In recent years, the incidence of RCC has increased due to several factors. In large part this is secondary to the increased incidental detection on imaging studies. Now nearly two-thirds of renal neoplasms are found incidentally compared to approximately 10% in the early 1970s. There has also been an increased rate of survival in patients with RCC, primarily because these lesions are found when small in asymptomatic individuals. There is some evidence suggesting that asymptomatic tumors are smaller and of lower grade and earlier stage than symptomatic lesions. The overall 5-year survival rate is approximately 85% for incidentally detected tumors compared to 53% in symptomatic individuals [63, 64]. Therefore, radiologists have played and continue to play a significant role in finding early cancers and improving patient survival.

According to the 1997 Heidelberg Classification, the most common RCC histologic subtypes are: clear cell adenocarcinoma (65–75%); papillary adenocarcinoma (15%); chromophobe (5%), collecting duct (1%); and unclassified carcinomas (4%). Clear cell RCC, also known as conventional RCC, has a much greater malignant potential than papillary and chromophobe RCCs. Since the prognosis varies among the subtypes of RCC (Box 123.1), being able to distinguish these with imaging can have important clinical implications in the management of certain groups of patients [66–72].

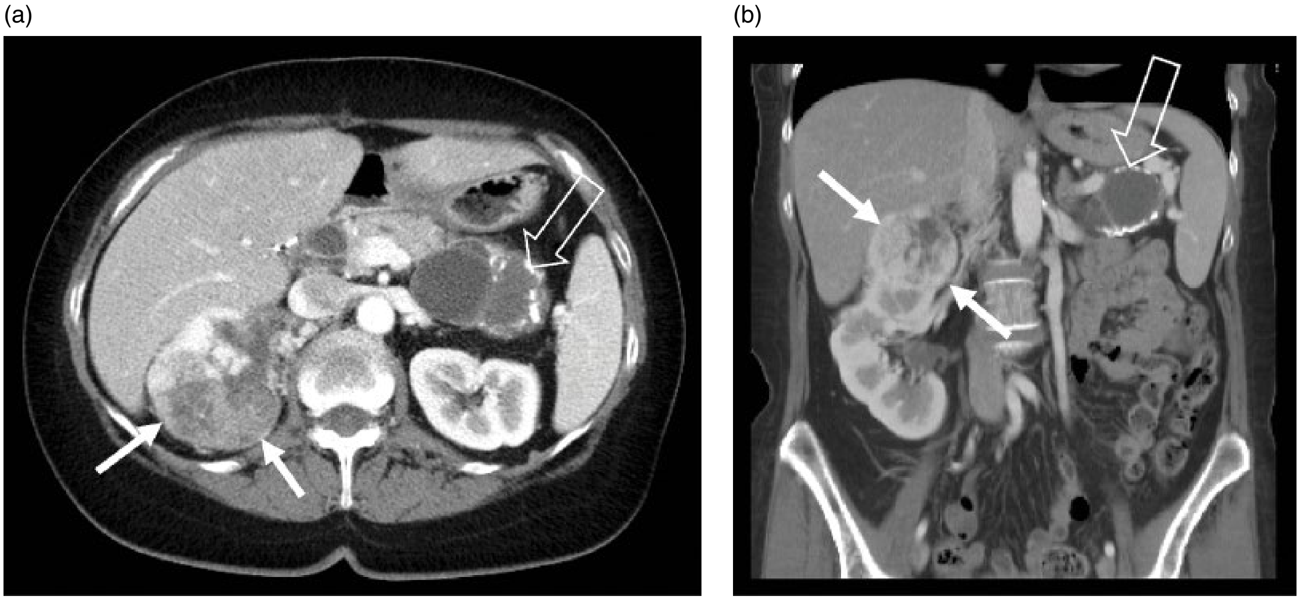


**Figure 123.16** Synchronous renal cell carcinoma and mucinous adenocarcinoma of the pancreas in a patient with von Hippel–Lindau syndrome. Axial (a) and coronal reformatted (b) CT images show a clear cell renal cell carcinoma in the upper pole of the right kidney (solid arrows) and calcified and noncalcified cystic lesions (open arrow) in the pancreatic body and tail. The calcified cystic lesion was a mucinous cystadenocarcinoma.

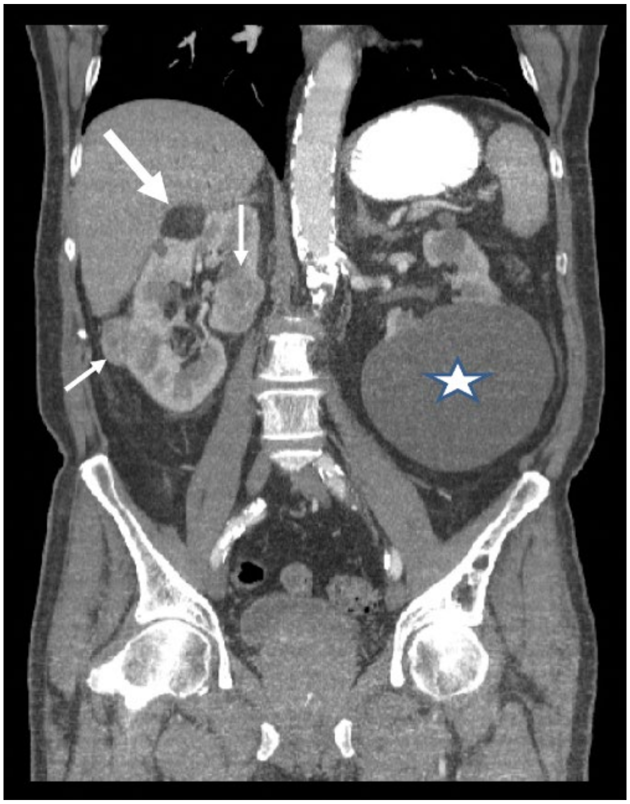


**Figure 123.17** Hereditary papillary renal cancer. Coronal reformatted contrast-enhanced CT image shows synchronous hypervascular neoplasms in the right kidney (small arrows). Note the angiomyolipoma (large arrow) and the large left benign renal cyst (star)

**Box 123.1 Histologic subtypes of renal cell carcinoma.**

- Clear cell renal cell carcinoma
- Multilocular clear cell carcinoma
- Papillary renal cell carcinoma
- Chromophobe renal cell carcinoma
- Collecting duct carcinoma
- Translocation carcinoma
- Renal cell carcinoma associated with neuroblastoma
- Mucinous tubular and spindle cell carcinoma
- Renal cell carcinoma unclassified

Clear cell RCC is the most vascular type of all malignant renal cortical tumors, as shown by its greater degree of enhancement after administration of intravenous contrast material. It most commonly presents with a mixed enhancement pattern of both hypervascular soft tissue components and low attenuation areas that correspond to necrotic or cystic changes. Kim et al. [73] showed that an increase in attenuation of 84 HU in the corticomedullary phase differentiates clear cell from non-clear cell tumors with a sensitivity of 74% and a specificity of 100% [73].

Papillary RCC, on the other hand, demonstrates a low degree of enhancement relative to renal cortical enhancement in either a homogeneous pattern or with low-level peripheral enhancement. A low tumor-to-aorta enhancement ratio or tumor-to-normal renal parenchyma enhancement ratio is highly indicative of papillary RCC [74, 75].

Chromophobe RCCs are more variable in their degrees and patterns of enhancement. Renal medullary carcinoma is a recently described malignant renal neoplasm occurring in patients with sickle cell anemia. It is centered in the medulla and microscopically exhibits reticular, yolk-sac, or adenoid cystic appearance. This neoplasm exhibits aggressive behavior [66–72].

In general, the presence of calcifications in a solid renal mass (Figure 123.18) suggests malignancy. Rarely, a malignant renal tumor may be diffusely calcified [76].

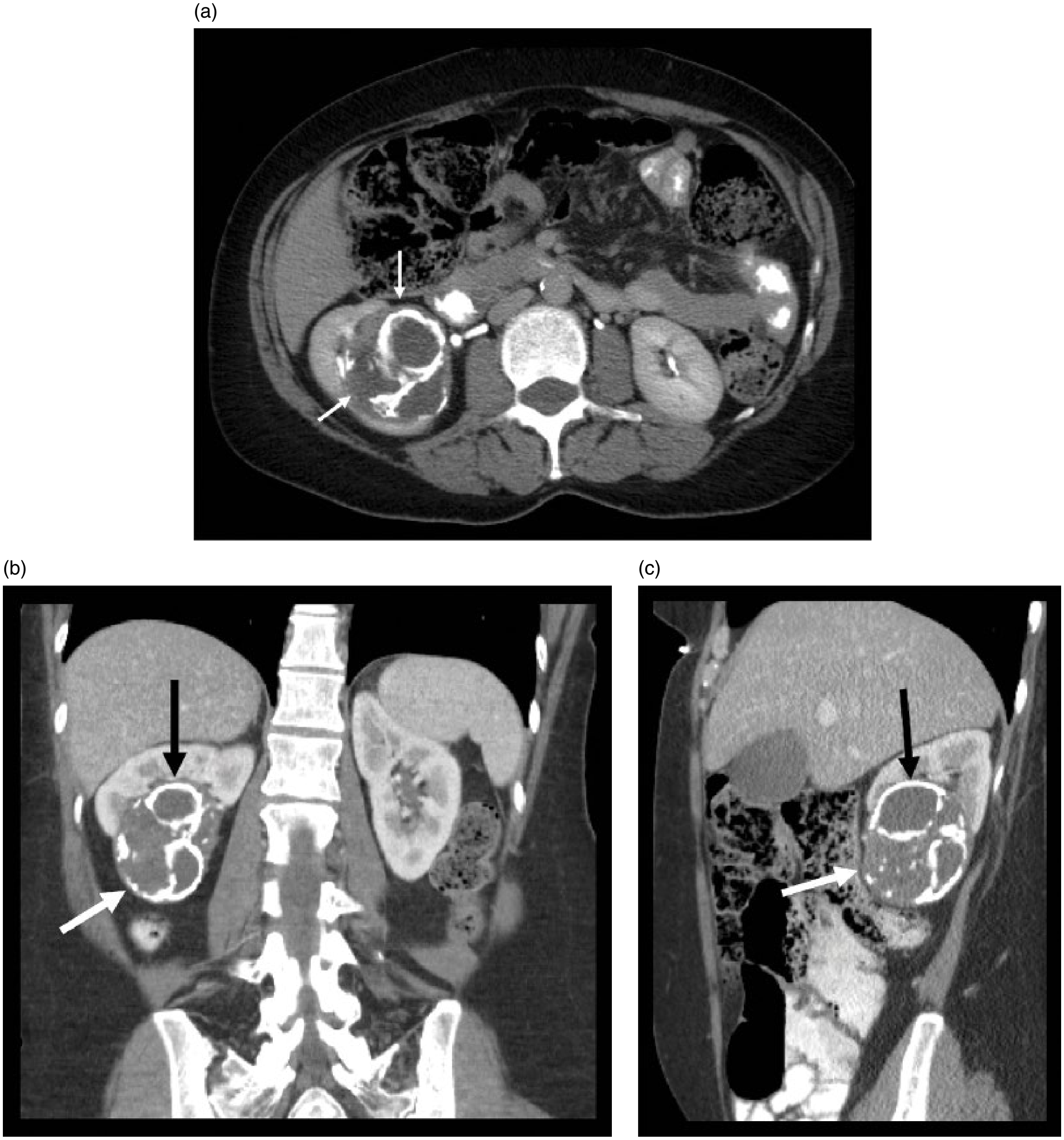


**Figure 123.18** Calcified renal cell carcinoma. Calcified renal cell carcinoma (arrows) is seen at the lower pole of the right kidney on these axial (a), coronal reformatted (b), and sagittal reformatted (c) contrast-enhanced CT images.

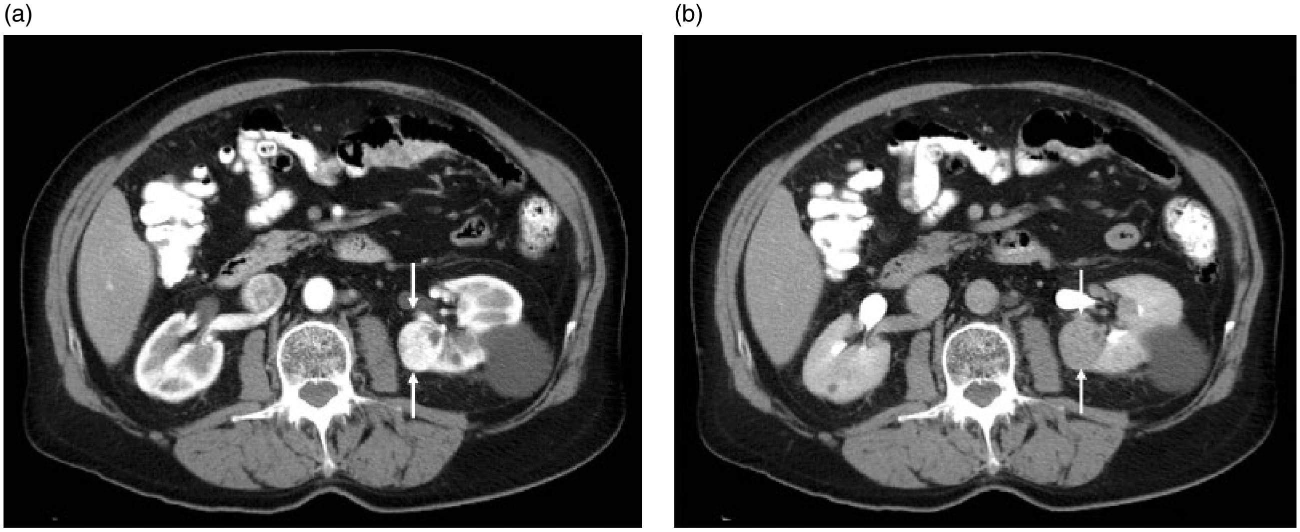


**Figure 123.19** De-enhancement of renal cell carcinoma: CT findings. (a) Scan obtained during the cortical medullary phase shows an enhancing mass along the medial aspect of the left kidney (solid arrows). A simple renal cyst is also present. (b) Three-minute delayed images show that the contrast material has rapidly washed out of the tumor (arrow) and it is now hypodense relative to normal kidney. Bilateral simple renal cysts are present.

RCCs typically show de-enhancement of contrast of >15 HU when the corticomedullary and excretory phases are compared (Figure 123.19).

## Staging renal cell carcinomas

RCCs spread via a number of pathways. They may invade locally, initially through the renal capsule into the adjacent perinephric fat. Upper pole tumors may invade the ipsilateral adrenal gland. More advanced tumors can involve the adjacent musculature or extend beyond Gerota's fascia to involve the liver, spleen, pancreas, duodenum, and colon. RCCs may invade the renal vein and propogate into the inferior vena cava and right atrium. Hematogenous metastases most commonly go to the lungs and bone. RCCs can also spread by lymphatic routes, beginning with renal hilar lymph nodes and then regional para-aortic lymph nodes [77–83],

Accurate preoperative staging of patients with RCC is of paramount importance in selecting the most suitable therapy, guiding surgical intervention, and assessing patient prognosis. The 40-year-old Robson classification of RCC was replaced with the TNM staging system developed in 2002 by the American Joint Committee on Cancer and the International Union Against Cancer (Tables 123.2 and 123.3), because the latter adapts more easily to changing patterns of diagnosis and therapy for RCC. Indeed, it appears that TNM staging is evolving with the advancement of surgical techniques, and is now being challenged by the advent of new, minimally invasive treatment methods such as cryoablation and radiofrequency ablation. MDCT and MRI are superb in T-staging of local tumor extent and M-staging of distant metastasis. However, both imaging tests perform less well with N-staging. Since FDG-PET appears to be unreliable in the detection of RCC and its metastases, research efforts should be directed at finding malignant adenopathy of RCC [77–83].

### T-staging

TNM classes T1 and T2 include all primary RCCs that are confined to the renal capsule (Figures 123.20–123.24). The current TNM classification of 2002 distinguishes between T1a, which defines an RCC with a maximum diameter of 4 cm or less, and T1b, which defines an RCC whose maximum diameter is larger than 4 cm but smaller than 7 cm. Aside from potential differences in prognosis, the most likely reason for the migration of definitions for TNM classes T1 (now T1a and T1b) and T2 lies in the development of new surgical techniques of renal tumor resection [77–83].

It may be difficult to detect subtle invasion of RCC beyond the renal capsule on cross-sectional imaging. Anatomically, the true renal capsule represents the fibrotic outer surface layer surrounding the renal parenchyma. This layer, however, is ill-defined or missing in the renal hilum. Pathologically, RCC induces reactions within the kidney and within the perirenal fat that may make it difficult to distinguish between the true renal capsule and pseudocapsular structures [78, 79].

In terms of T3b and T3c lesions, both MR and MDCT are comparable in assessing tumor invasion of the renal vein and extension into the inferior vena cava either below or above the diaphragm. Extension of RCC tumor

**Table 123.2** American Joint Committee on Cancer (AJCC) TNM Staging System for Kidney Cancer.

| Classification | Description |
|---|---|
| T | Primary tumor |
| Tx | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| T1 | Tumor ≤7 cm in greatest dimension, limited to kidney |
| T1a | Tumor ≤4 cm in greatest dimension, limited to kidney |
| T1b | Tumor >4 cm but ≤7 cm in greatest dimension, limited to kidney |
| T2 | Tumor >7 cm in greatest dimension, limited to kidney |
| T2a | Tumor >7 cm but ≤10 cm in greatest dimension, limited to kidney |
| T3 | Tumor extends into major veins or perinephric tissues, but not into the ipsilateral adrenal gland and not beyond Gerota's fascia |
| T3a | Tumor extends into the renal vein or its subsegmental branches, or invades the pervicalyceal system, or invades perirenal and/or renal sinus fat but not beyond Gerota's fascia |
| T3b | Tumor extends into the inferior vena cava below diaphragm |
| T3c | Tumor extends into the inferior vena cava above the diaphragm or invades the wall of the inferior vena cava |
| T4 | Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland) |
| **N-classification** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Metastasis in regional lymph node(s) |
| **M-classification** | |
| M0 | No distant metastasis |
| M1 | Distant metastasis |
| Mx | Distant metastasis cannot be evaluated |

*Source: AJCC Cancer Staging Manual*, eighth edition, 2017 published by Springer International Publishing. Used with permission.

thrombus above the diaphragm defines TNM class T3c (Figure 123.24 and 123.25) [78, 79].

T4 lesions are characterized by tumor extension of through Gerota's fascia. This assessment may be difficult on cross-section imaging when the fascia is only minimally transgressed.

**Table 123.3** AJCC prognostic groups.

| | |
|---|---|
| Stage I | T1 N0 M0 |
| Stage II | T2 N0 M0 |
| Stage III | T1–T2 N1 M0 or T3 N0–N1 M0 |
| Stage IV | T4 Any N M0 or Any T Any N M4 |

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### N-staging

Involvement of regional lymph nodes has several different classifications in the TNM system (Tables 123.2 and 123.3). The most important lymph nodes to evaluate

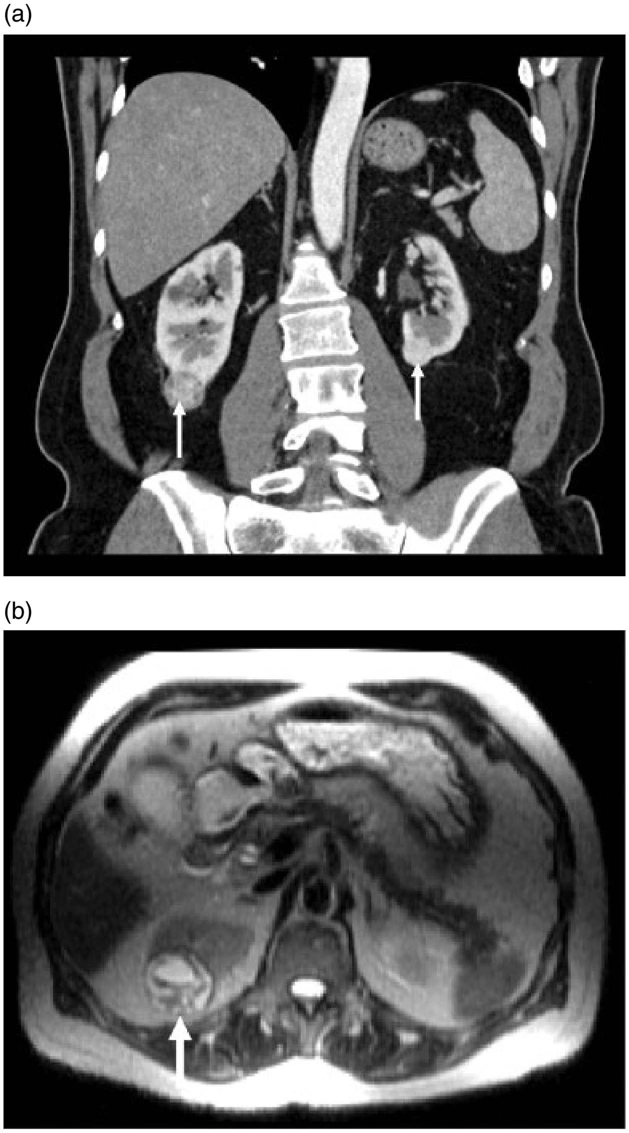

**Figure 123.20** T1a renal cell carcinoma. (a) Coronal reformatted CT image shows bilateral small lower pole renal tumors (arrows) which are limited by the renal fascia. (b) Axial T2-weighted MR images show a complex renal neoplasm (arrows) confined by the renal fascia.

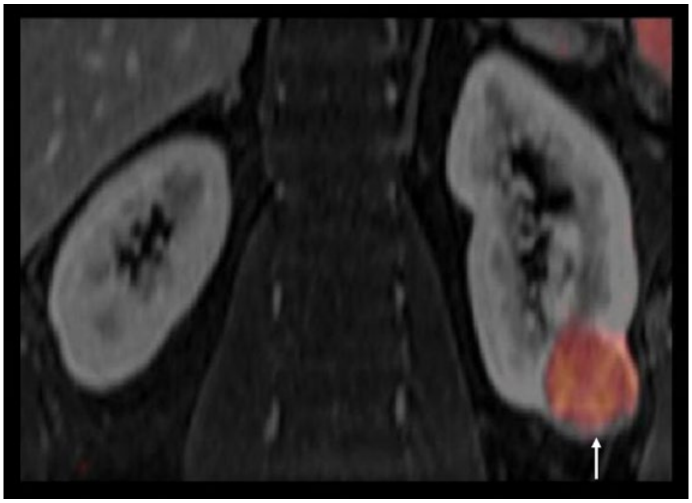

**Figure 123.21** T1a renal cell carcinoma. Coronal PET-MRI image shows a 3 cm mass in the lower pole of the left kidney that is FDG avid (arrow).

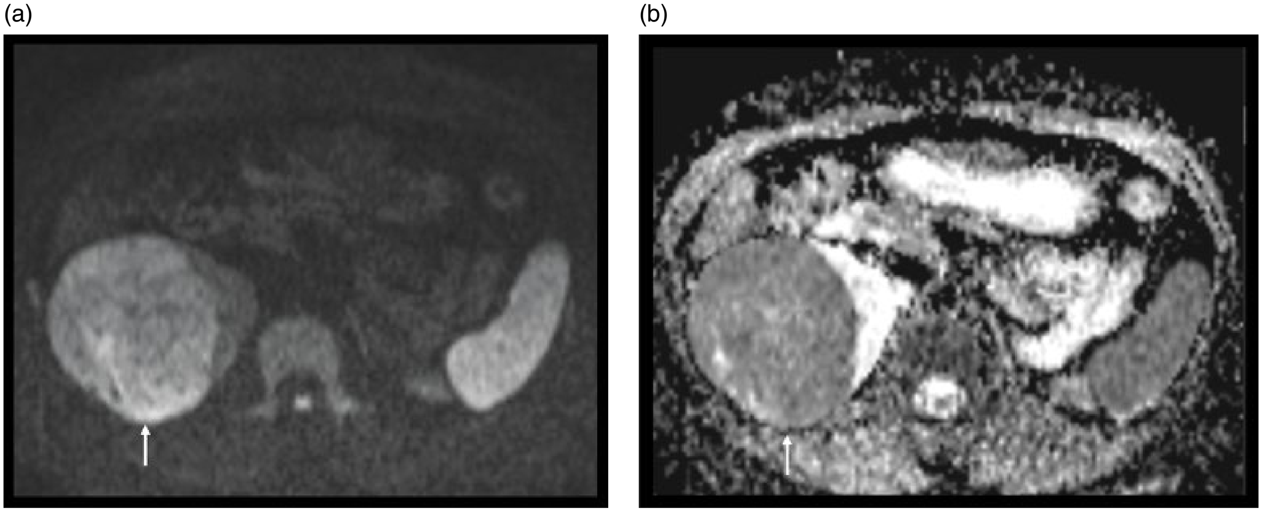

**Figure 123.22** T1b renal cell carcinoma. Functional, diffusion-weighted imaging. Axial diffusion-weighted sequence ($b = 800$) (a) and ADC map (b) reveal restricted diffusion of this neoplasm (arrow) with a low ADC value.

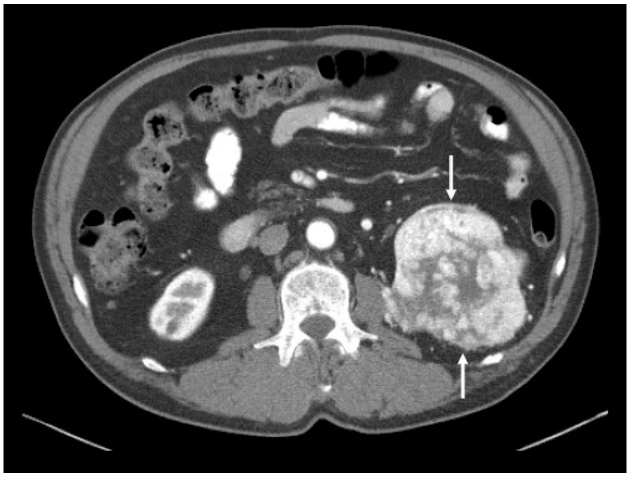

**Figure 123.23** T2 renal cell carcinoma. Axial CT image shows a 7.5 cm enhancing mass (arrows) at the lower pole of the left kidney. It abuts but does not invade the psoas muscle and was confined by Gerota's fascia.

when staging patients with RCC include: nodes along the renal arteries and paracaval lymph nodes for right-sided tumors; para-aortic lymph nodes for left-sided tumors (see Figure 123.24b); and nodes located at the levels of the renal hilum or renal artery. Metastasis in regional lymph nodes without synchronous distant metastasis is found in 10–15% of patients with RCC [83, 84].

As with most neoplasms, the detection of lymph node metastases remain problematic in patients with RCC. Current MDCT and MRI criteria for suggesting adenopathy are lymph nodes that have a short-axis diameter of 1 cm or more and the presence of a prominent node that is more spherical rather than kidney-shaped and has lost its hilar fat. In addition, asymmetric grouping of three or more smaller lymph nodes may also be a sign of lymphatic tumor spread to the renal hilum. Further confounding the accuracy of cross-sectional imaging in detecting

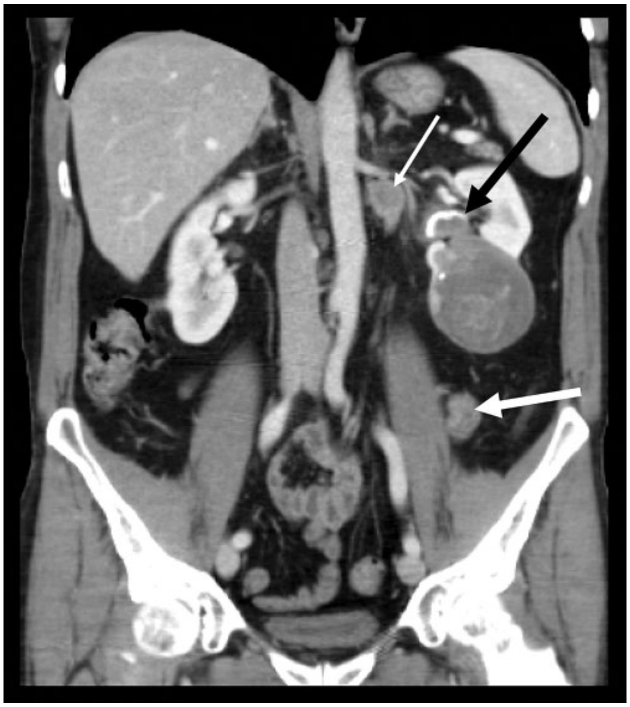

**Figure 123.24** T3a, N2 renal cell carcinoma. Coronal reformatted CT image obtained during the excretory phase shows tumor invasion of the renal pelvis (black arrow). There is left renal hilar adenopathy (small white arrow) and a left paraspinous metastasis (large white arrow).

adenopathy is the fact that more than 50% of enlarged regional lymph nodes exhibit only hyperplastic or inflammatory change pathologically [83, 84].

### M-staging

Distant metastases from RCC, M1 disease, includes all metastases that are either extranodal or involve nonregional lymph nodes. Metastases are most frequently found in the lung (31%) (Figure 123.26), bone (15%) (Figure 123.27), brain (8%), and liver (5%). However, any other organ can be involved [28]. While metastatic RCC requires systemic therapy, surgical excision of the primary lesion appears to be an integral part of systemic therapy for metastatic RCC [85].

MDCT is the preferred means of M-staging patients with RCC because it is superior to MRI in detecting pulmonary metastases. As stated before, FDG-PET at the present time appears too unreliable to recommend its routine use in the staging of RCC [86, 87].

## Transitional cell carcinoma

Urothelial tumors of the renal calices and pelvis account for approximately 7% of primary renal tumors and 5% of all urinary tract neoplasms. Transitional cell carcinomas (TCCs) comprise 90% of pelvicalyceal tumors, with squamous cell carcinoma (which is radiologically indistinguishable from TCC) and adenocarcinomas accounting for 10% of these neoplasms. Patients with previous or current urothelial neoplasm of the bladder are at increased risk of developing TCC of the kidney. Indeed upper tract urothelial tumors have similar risk factors, epidemiologic distribution, and pathologic features. Other risk factors include certain chemical exposures, nonsteroidal anti-inflammatory drug (NSAID) abuse and tobacco use. Because of the multicentric nature of TCC, the urotheluium of the kidneys, ureters, and bladder must be assessed in its entirety prior to treatment to exclude synchronous lesions. During follow-up studies metachronous tumors must be excluded as well [88–98].

The intravenous pyelogram (IVP) has traditionally been the initial screening examination for the detection of upper urinary tract neoplasms for patients with hematuria. The IVP, however, has been shown to miss 40% of upper tract cancers. This technique has been replaced by CTU using MDCT [88–98].

There are three general appearances of TCC on MDCT:

- TCCs may appear as small, hypodense lesions in the renal collecting system (Figure 123.28) demonstrating soft tissue attenuation (<40 HU). On noncontrast images, these tumors have a density of approximately 30 HU, which can be differentiated from urine (0–20 HU), blood clot (50–75 HU), and calculi (>100 HU). There is moderate enhancement with washout on delayed images following intravenous contrast administration, but the degree of enhancement is usually less than that seen in patients with RCC. Some 85% of these lesions are early-stage, superficial papillary neoplasms, that on the excretory phase of CTU appear as a sessile filling defect within the high-density contrast excreted into the renal collecting system. In more advanced cases, the tumor expands the collecting system with compression of the renal sinus fat.
- TCCs may manifest as mural thickening (Figure 123.29), usually symmetric, of the renal collecting system, resulting in circumferential narrowing of the lumen. This may lead to focal caliceal obstruction. The thickened wall may demonstrate enhancement, but a thick enhancing wall can also be seen with infection or with inflammation related to calculi, hemorrhage, recent stent placement or removal, or other surgical manipulation. In some cases biopsy may be necessary to distinguish benign from malignant etiologies.
- TCCs may appear as an infiltrating hypoenhancing renal mass with poorly defined margins. Because TCCs arise from the urothelium, they are more centrally

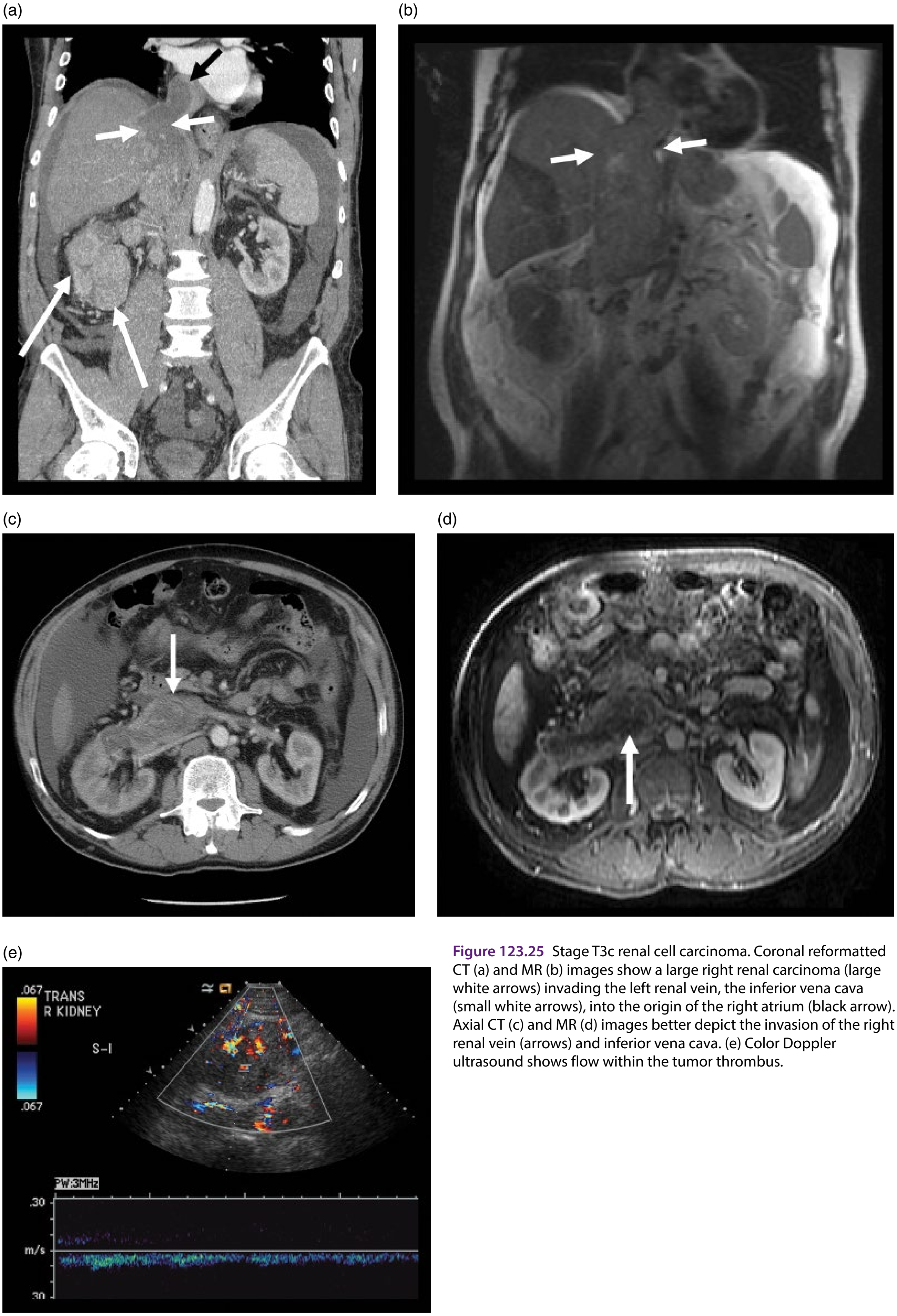

**Figure 123.25** Stage T3c renal cell carcinoma. Coronal reformatted CT (a) and MR (b) images show a large right renal carcinoma (large white arrows) invading the left renal vein, the inferior vena cava (small white arrows), into the origin of the right atrium (black arrow). Axial CT (c) and MR (d) images better depict the invasion of the right renal vein (arrows) and inferior vena cava. (e) Color Doppler ultrasound shows flow within the tumor thrombus.

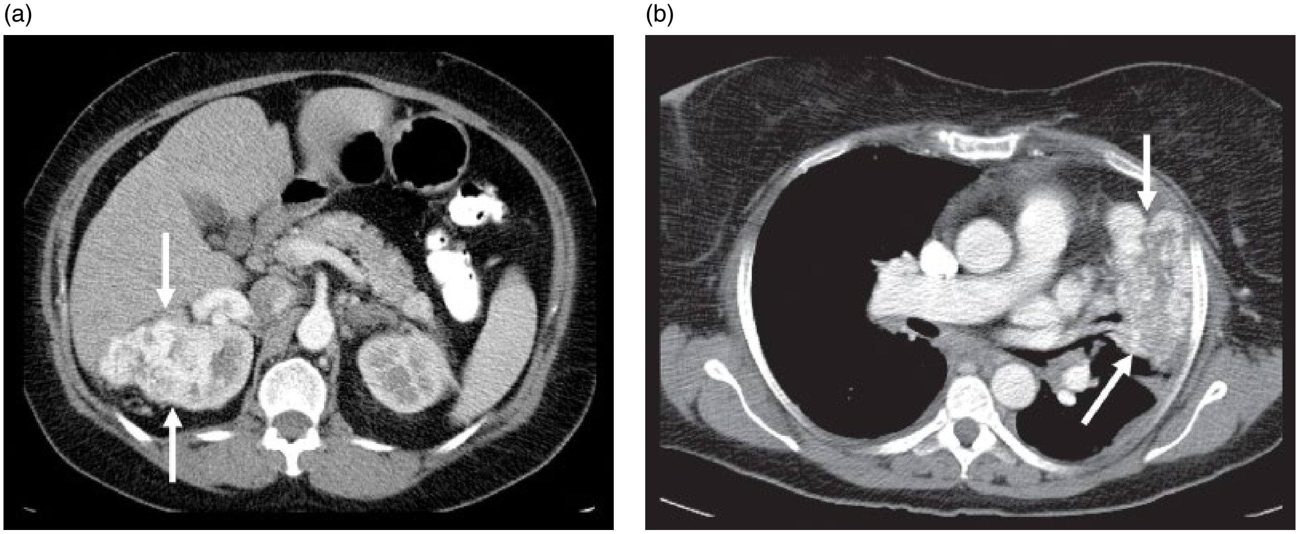

**Figure 123.26** M1 renal cell carcinoma. (a) Axial, contrast-enhanced CT scan shows a hypervascular right renal mass (arrows). (b) Hypervascular metastasis (arrows) is present in the left chest which also invades the pleura.

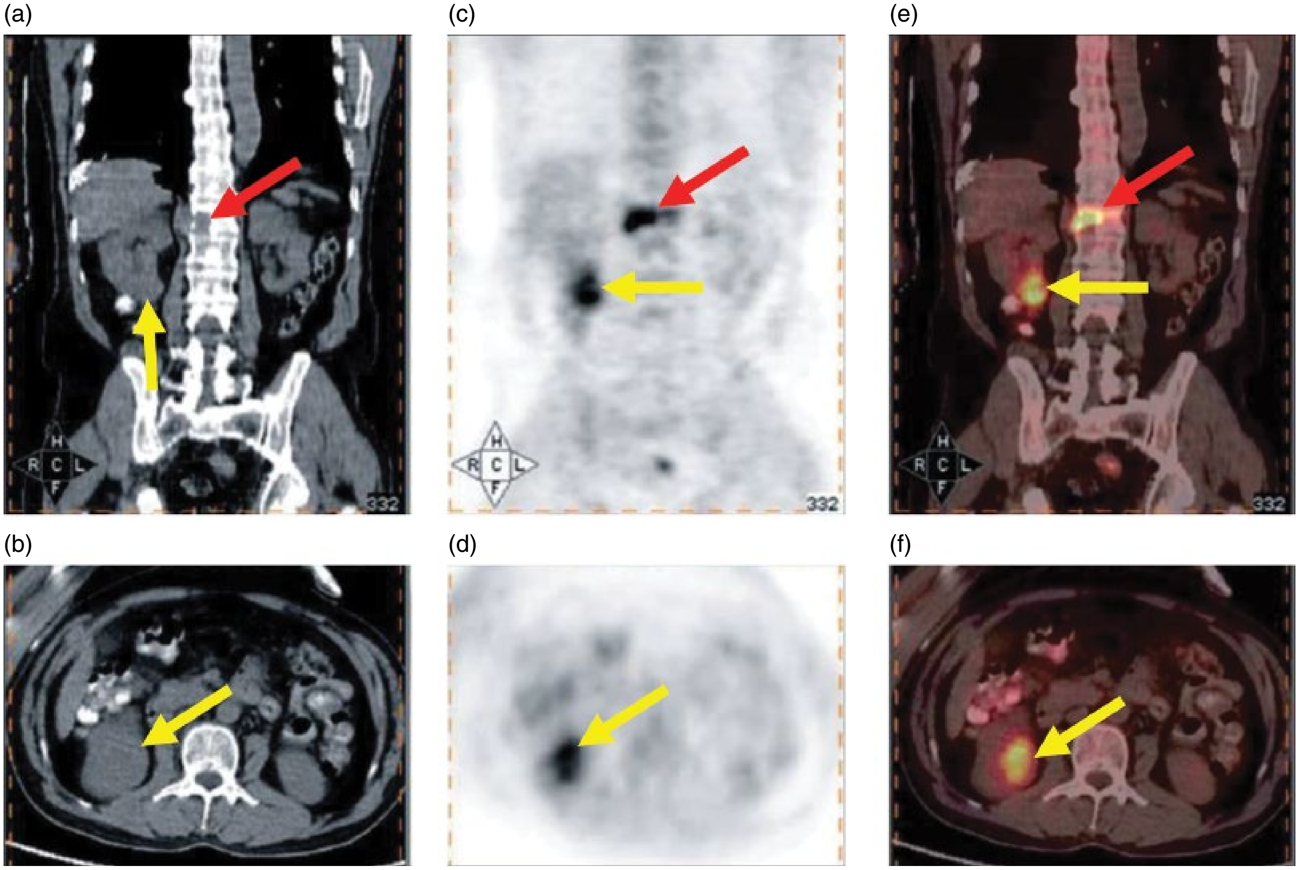

**Figure 123.27** M1 renal cell carcinoma: PET-CT. (a) Coronal CT image. (b) Axial CT image. (c) Coronal PET image. (d) Axial PET image. (e) Fused coronal PET-CT image. (f) Fused axial PET-CT image. Yellow arrows = primary renal cell carcinoma. Red arrows = metastases to the L1 vertebral body.

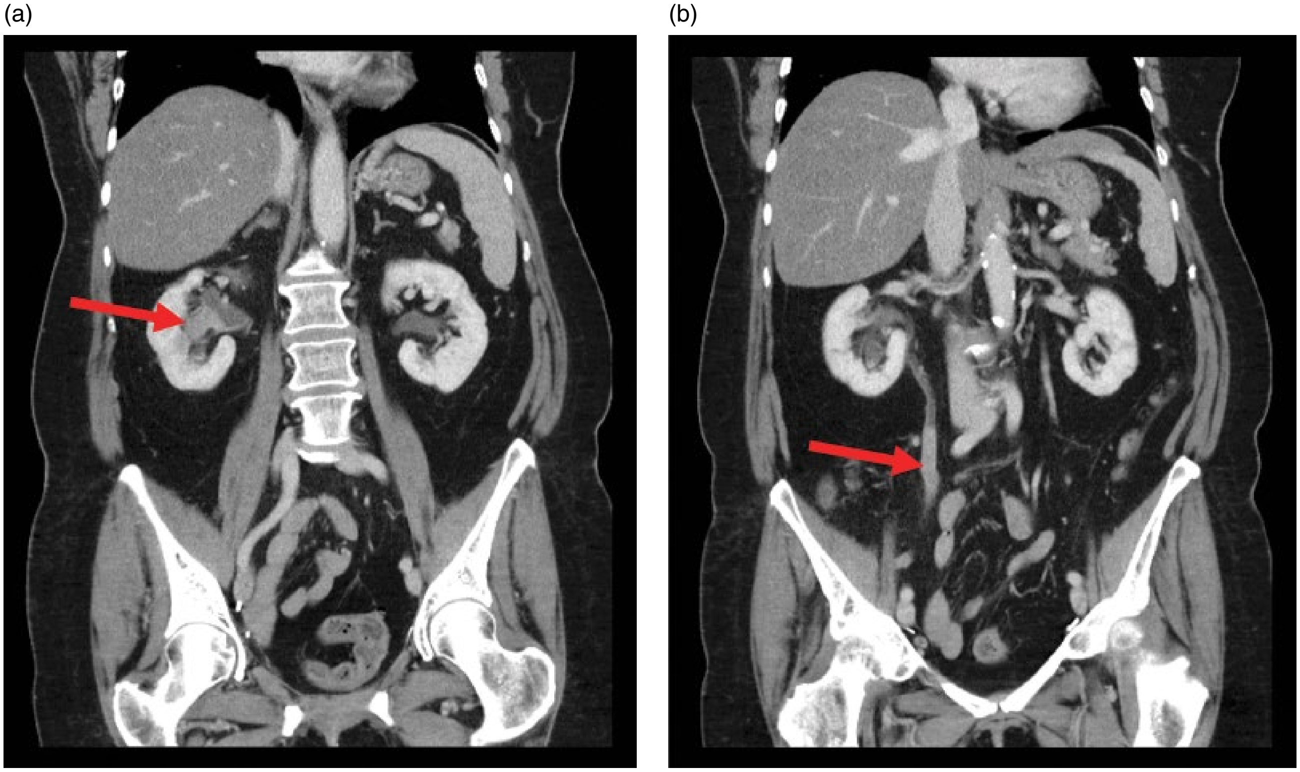

**Figure 123.28** Transitional cell carcinoma: coronal reformatted CT images. (a) There is a soft tissue mass occupying the inferior aspect of the right renal pelvis (arrow). (b) At a slightly more anterior level, a synchronous mass (arrow) is identified in the right mid ureter.

located than most RCCs. TCCs may contain stippled calcification and may be large and necrotic. They may distort the normal renal architecture. When RCC expands the kidney, the renal contour is usually preserved, in contradistinction to RCC. There may be obliteration of the renal sinus fat by tumor [88–98].

## Renal lymphoma

The kidney is one of the most common sites of extrarenal lymphoma. Nearly one-third of patients with non-Hodgkin's lymphoma will have renal involvement at autopsy. Indeed, lymphoma is the third most common metastasis to the kidney following carcinoma of the lung and breast. The antemortem diagnosis is only made in 0.5–8.3%. The cells in lymphoma infiltrate between and do not destroy normal renal cells and do not exhibit fibrosis so the effect on renal function is typically minimal [99–102].

Since the kidneys normally do not contain lymphoid tissue, most cases of renal lymphoma are due to direct extension or hematogenous metastases. Retroperitoneal lymphoma can invade the renal capsule directly or infiltrate the renal sinus fat encasing the ureter, renal pelvis, and renal vessels. Lymphoma can then extend into the renal parenchyma via the medullary pyramids. When lymphoma involves the renal parenchyma by direct extension or hematogenous spread, it initially involves the renal interstitium, using vessels, collecting ducts, and nephrons as scaffolding [99–102].

There are five major patterns of presentation of renal lymphoma radiologically:

- Multiple renal masses that are often hyperdense compared to normal renal tissue on noncontrast CT scans due to the hypercellularity of the tumor. On contrast-enhanced scans, these lesion present as multiple, bilateral, hypodense (Figure 123.30) intraparenchymal masses leading to a differential diagnosis of metastases, renal infarction, and renal infection.
- Diffuse renal infiltration causes nephromegaly but the renal arteries and veins remain patent despite encasement by tumor. On the early postcontrast images, the renal parenchyma appears remains relatively hypodense. On the nephrographic phase, relatively diminished enhancement is identified and there may be slight delay in excretion during the excretory

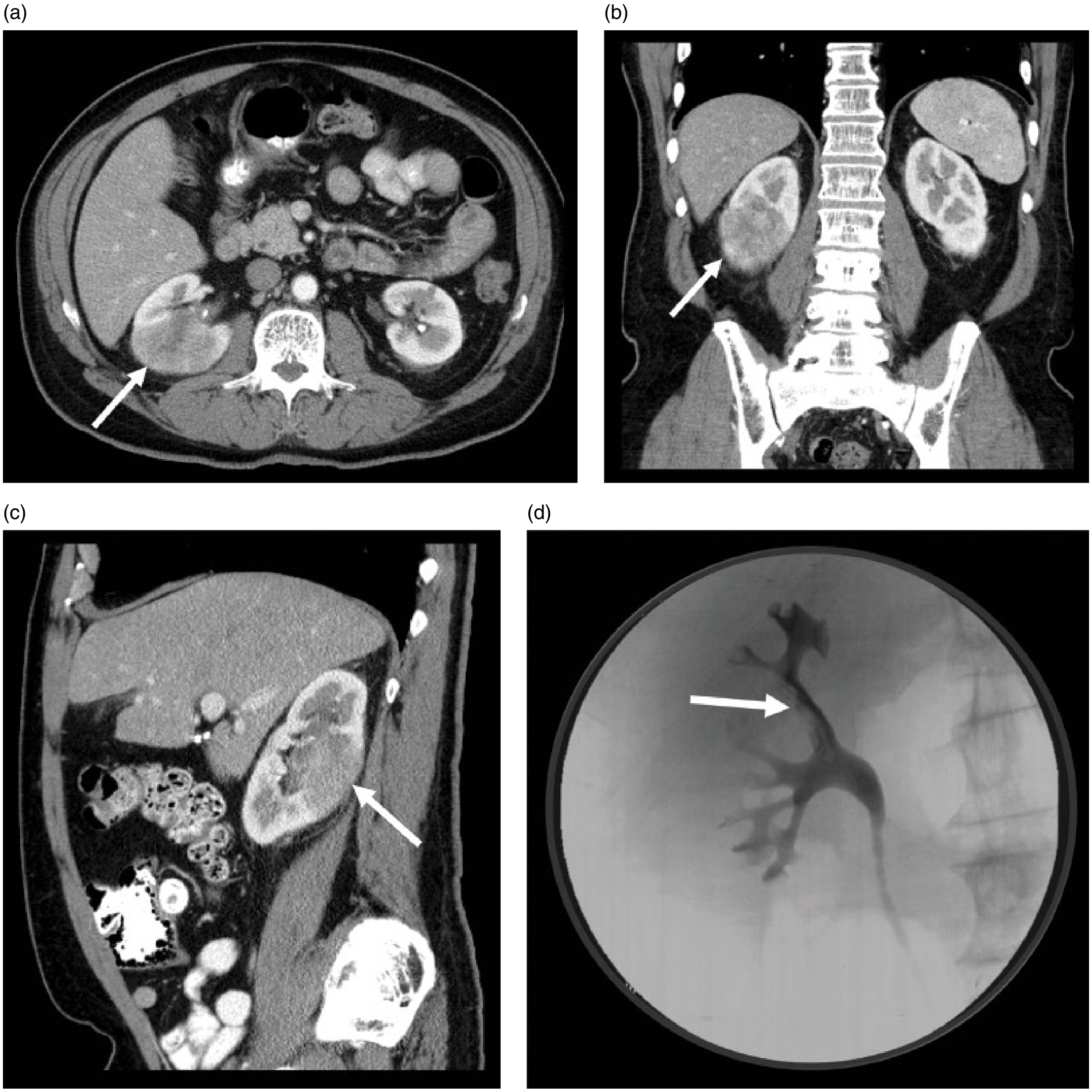

**Figure 123.29** Transitional cell carcinoma of the right kidney: imaging findings. Axial (a), coronal (b), and sagittal (c) CT images show a large hypodense mass (arrows) extending from the renal pelvis into the renal cortex. (d) Retrograde pyelogram image shows the mass (arrow) deforming the renal pelvis.

phase. The differential diagnosis of this presentation of renal lymphoma includes RCC, TCC, and diffuse renal infection.

- The renal capsule or renal sinus may also be directly invaded by contiguous involvement from retroperitoneal lymphoma. Retroperionteal adenopathy is present and this may cause hydronephrosis.
- More rarely, renal lymphoma presents as a solitary, hypoattenuating, intraparenchymal mass simulating a cortical tumor.
- Capsular (Figure 123.31) or perirenal involvement by lymphoma may occur with diffuse retroperitoneal adenopathy. The differential diagnosis in these cases includes perirenal hematoma and metastases [99–102].

## Renal metastases

Renal metastases are quite common in patients with extrarenal neoplasms, found in 7–13% of large autopsy series [17, 20]. The primary neoplasms that most commonly metastasize to the kidneys are: lung (Figure 123.32), breast, and gastrointestinal cancers [85]. These metastases usually have an indolent clinical behavior so were seldom discovered antemortem prior to the advent of cross-sectional imaging. By the time renal metastases are present, the patient usually has advanced disease. On rare occasions, a solitary renal metastasis may arise many years after the diagnosis of the primary neoplasm [1, 2].

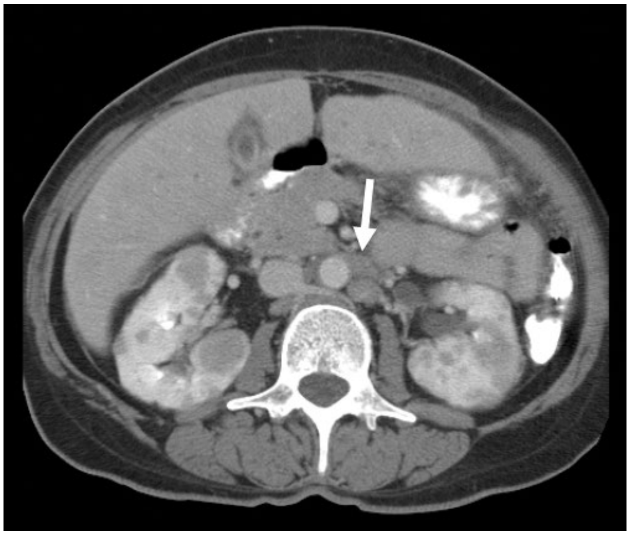

Figure 123.30 Renal lymphoma: CT findings. Multiple hypodense renal masses are present on this contrast-enhanced CT scan. Note the retroperitoneal adenopathy (arrow) as well.

Renal metastases, like lymphoma, can display an expansile or less commonly an infiltrative growth pattern. Most commonly, multiple bilateral masses are present. Solitary exophytic metastases are more common in patients with colon cancer, and perinephric tumor extension is identified in patients with melanoma [1, 2].

Patients who present with a solitary renal lesion and a known extrarenal primary tumor are a diagnostic challenge since the lesion may either be a metastasis or a synchronous renal neoplasm. The imaging findings in patients with renal metastases reflect the pathologic pattern of involvement and the nature of the primary tumor. A well-marginated hypovascular mass may be indistinguishable from a papillary RCC or lymphoma. Since infiltrative growth is atypically of renal cortical tumors, a solitary infiltrative renal mass in a patient with an extrarenal neoplasm most likely represents metastasis. Percutaneous biopsy will be needed for confirmation in these patients [25].

## Imaging and nephron-sparing surgery

Cross-sectional imaging plays a vital role in the selection and preoperative evaluation of patients for nephron-sparing surgery (Figure 123.33) and ablation [10–14]. MDCT nicely depicts the position of the kidney, anatomic variants, the depth of renal parenchymal invasion, the relationship of the tumor to the pelvicalyceal system,

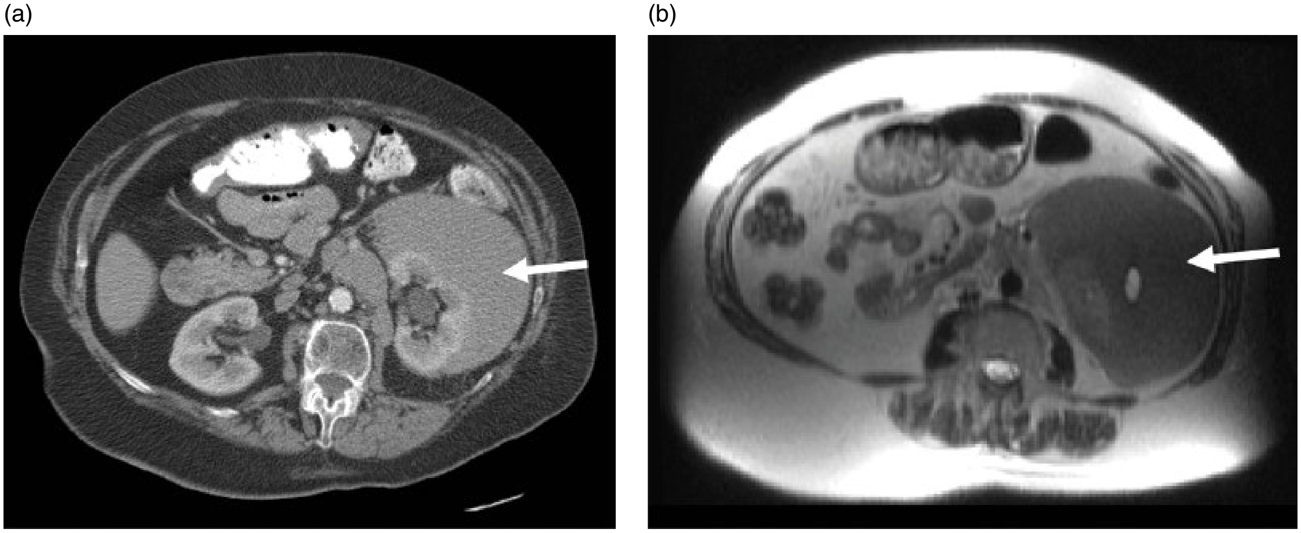

Figure 123.31 Perirenal lymphoma: imaging findings. Axial CT (a) and MR (b) images show a homogenous soft tissue mass (arrows) encasing the lateral aspect of the left kidney.

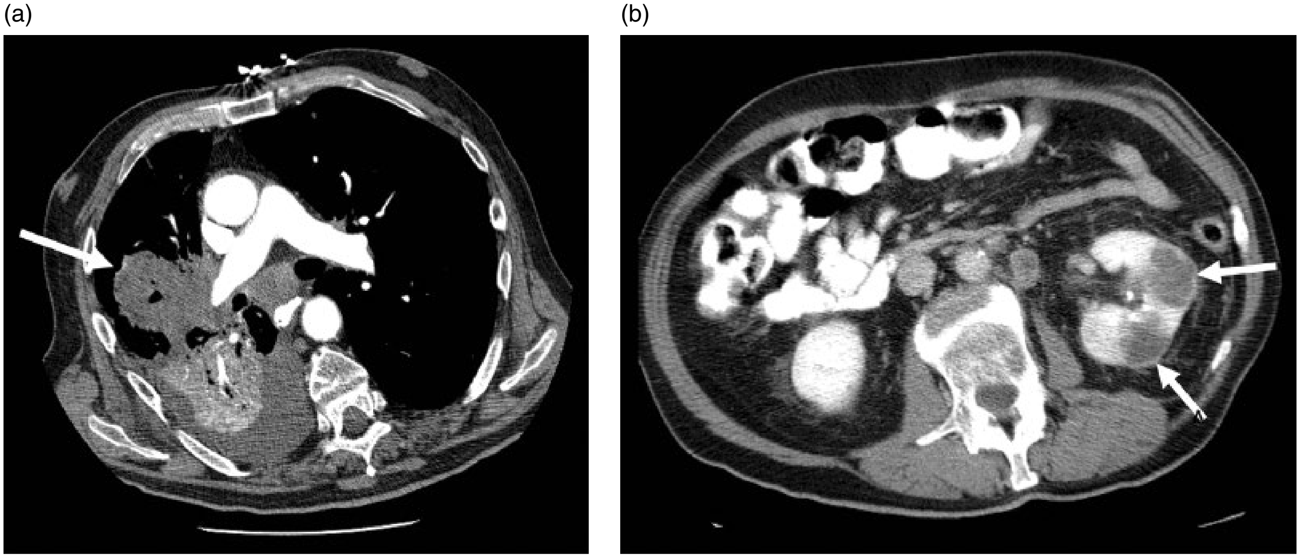

**Figure 123.32** Metastatic lung cancer to the kidneys. (a) Contrast-enhanced CT scan of the chest shows a large cancer of the right upper lobe (arrow) invading the right hilum with mediastinal adenopathy. (b) Scan at the level of the kidneys show two hypodense metastases (arrows).

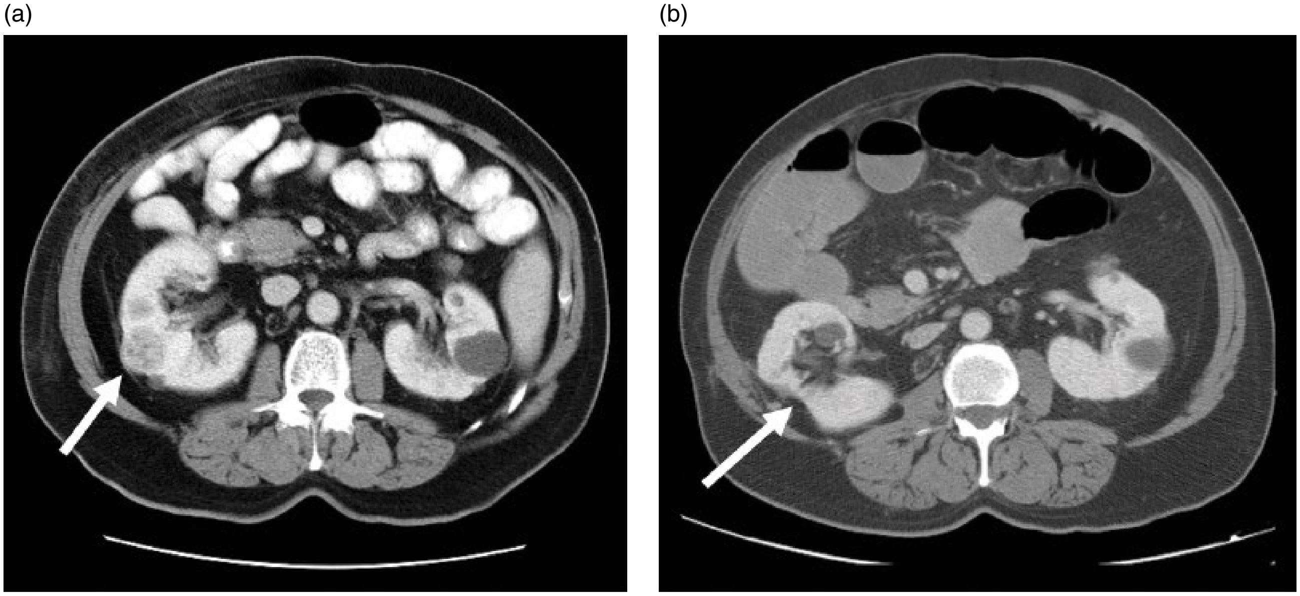

**Figure 123.33** Nephron-sparing surgery: CT features. (a) Small hypervascular cortical right renal cell carcinoma (arrow) prior to surgery. (b) Deformity of the lateral aspect of the right kidney (arrow) is evident postoperatively.

and detailed anatomic information concerning the renal arteries and veins.

Radiofrequency ablation (Figure 123.34) and cryoablation are now a commonly used alternative in the management of renal tumors. Tumors less than 4 cm in size are the best candidates for ablation. Renal tumors can be classified into three areas from an interventional standpoint: exophytic, parenchymal, or central. Exophytic lesions are the safest to treat. Central tumors are more challenging because of the proximity of the renal vessels, collecting system, and ureter. Tumor proximity to the vessels may lead to direct vascular injury or inadequate tumor margin treatment due to the heat sink effect. The ureter can also be injured, resulting in laceration or stricture [10–14]. Intraoperative ultrasound can show small tumors not detected at the time of surgery by conventional means.

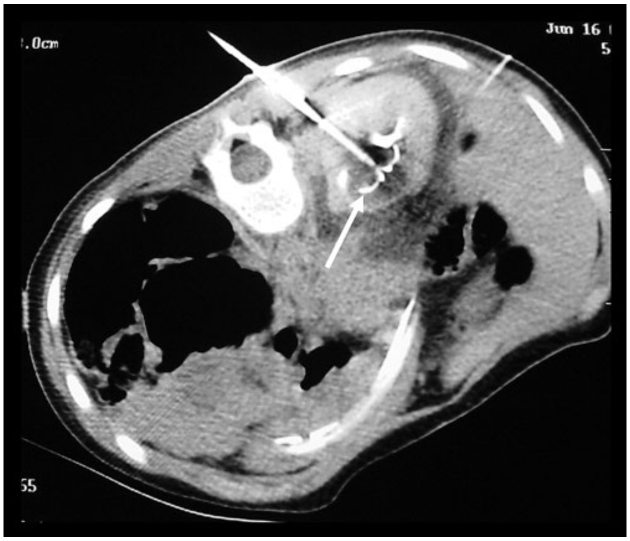

**Figure 123.34** Radiofrequency ablation probe (arrow) deployed in a renal neoplasm. Note the patient is in the prone oblique position.

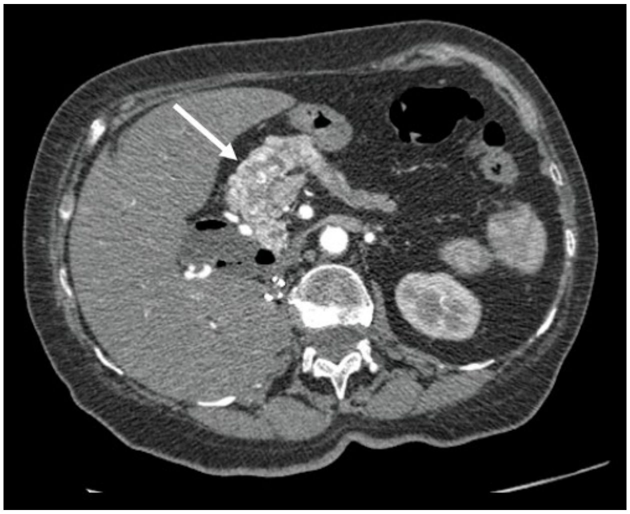

**Figure 123.35** Hypervascular metastasis from renal cell carcinoma to the pancreatic head. Contrast-enhanced CT shows a large, nonobstructing mass in the pancreatic head which developed 7 years following resection of a right-sided renal cell carcinoma.

## Recurrent cancer

Some 20–30% of patients with RCC that appears localized at the time of surgery relapse following radical nephrectomy. In the majority of cases, recurrence manifests as distant metastases rather than local disease, which occurs in less than 5% of cases. The stage of tumor at the time of presentation is the most important determinant of recurrent tumors. Other factors that increase the likelihood of recurrence include the presence of lymph node infiltration, high Furhman grade on histology, and the presence of sarcomatoid (spindle cell) architecture [103–105].

The median time from nephrectomy to relapse is 15–18 months and 85% occur within 3 years. Tumors that involve lymph nodes tend to recur early, whereas very late relapse can be seen with isolated metastasis to the lung, bone, pancreas, or skeletal muscle. Lung metastases account for 50–60% of distant relapses. These metastases may produce parenchymal consolidation or manifest as a hemorrhagic or lymph node-related mass [103, 104].

Recurrent metastases in the pancreas typically appear hypervascular on CT (Figure 123.35) and MRI, unlike the typically hypovascular masses seen in primary pancreatic adenocarcinoma. These metastases often develop quite late following resection of the primary neoplasm [103, 104].

Local recurrence is unusual and produces an enhancing mass at the site of nephrectomy. These tumors may infiltrate the adjacent quadratus lumborum and psoas muscles. The colon and small bowel can be directly invaded and when advanced can produce mesenteric nodal disease or peritoneal carinomatosis [103, 104].

MDCT is the imaging test of choice for the detection of local recurrent disease and distant metastases. If the patient has a contrast allergy, gadolinium-enhanced MRI of the abdomen and pelvis can be performed along with a noncontrast CT scan of the chest. Although not recommended in the initial evaluation of patients with renal malignancies, FDG-PET may have a role in the detection of recurrent distal metastases, especially if conventional studies are equivocal and in diffentiating recurrent tumor from postoperative fibrosis.

## Conclusions

State-of-the-art MDCT, ultrasound, MRI, PET-CT, and PET-MRI are leading to the earlier detection, better characterization, and improved staging of renal masses. As our increasing understanding of the diversity of renal neoplasia has been accompanied by innovative surgical and ablative techniques, cross-sectional imaging remains the linchpin in individualizing the treatment and follow-up of patients with renal masses. Biomedical imaging plays an increasingly important role in all phases of cancer management, including screening, diagnosis, biopsy guidance, staging, prognostic assessment, selection of a treatment plan, prediction and monitoring of treatment response, and assessment for recurrent disease.

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# 124

# Renal Mass Biopsy

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## Introduction

Biopsy of renal tumors (BRT) was not accepted by urologists as a standard diagnostic method until recently [1–3]. Classically, indications for BRT extended to cases where a reasonable doubt existed on the presence of a renal cell carcinoma (RCC) and a differential diagnosis needed to be ruled out (e.g. metastases of other primary cancers, lymphoma, retroperitoneal masses of unknown diagnostic, suspicion of infectious process) and more recently to determine RCC subtype in metastatic cases with the aim of driving the choice of systemic therapy.

Surveys among urologists showed that the majority did not perform BRT, even in the presence of indeterminate lesions [4, 5], Major reason for abstention were the presence of false negative results or low predictive value and the uncertain value of biopsy in directing or changing management. Although the post-test probability of a diagnosis of RCC in cases with a negative renal mass biopsy was estimated at 18%, recent literature shows that a second biopsy in case of a nondiagnostic initial biopsy shows cancer in 75–80% of cases [6–8].

However, in a rapidly changing scenario where presentation of RCC is shifting to the early stages, the incidence of radiological small renal mass (SRM) has increased [9], the knowledge that up to 25% of those SRMs are benign, and the broadening therapeutic options or observation options (e.g. ablation and active surveillance), preoperative histological filiation of a renal mass is increasingly recommended in the most prominent guidelines [2, 3, 10].

Currently, up to 70% of kidney tumors are accidentally discovered before symptoms arise [11, 12]. The mean size of surgically treated tumors has decreased in the last two decades [13–15] and the absolute number of SRMs (≤4 cm) diagnosed has increased. Pathologic assessment of SRMs has evolved and the classical cut-off of 3 cm to distinguish a renal carcinoma from a benign adenoma is no longer valid. In addition to the established relationship between tumor size, RCC subtype, and grade, the increasing prognostic impact of grade is being considered, and new subtypes and RCC-associated entities are being recognized [16]. Conversely, evolving immunohistochemistry (IHC) techniques and molecular and genetic markers are emerging as promising diagnostic and prognostic tools to be applied to renal mass biopsy in the future [17–19].

Besides the fact that recent systematic reviews show that BRT is highly accurate when a diagnostic sample is obtained [8, 20], the introduction in the clinical practice of angiogenesis inhibitors and more recently the novel immunotherapy based on checkpoint block point out the capital of determining RCC subtype to apply for the most adequate treatment strategies [21, 22].

When cross-sectional imaging is reviewed, the problem is not the differential diagnosis in the case of large renal masses but the differentiation and filiation of SRMs [23, 24]. Contemporary surgical series show a benign tumor incidence of 20–30% among SRMs and this incidence is inversely proportional to size [23, 24]. Although bias cannot cannot be ruled out in surgical series, because of the inclusion of different Bosniak categories, cysts, or inaccurate radiological assessment, the percentage of benign masses in this size range is clearly too high to justify an intervention without histologic confirmation of malignancy or a reasonable doubt that the mass is benign.

Among SRMs, subtype aggressiveness and grade increase its size and although the 2009 TNM classification still establishes a stage size cut-off of 4 cm for clinical or pathological definition of T1a, there is some evidence that a definitive cut-off for aggressiveness can be established at the 3 cm diameter [25, 26].

Partial nephrectomy or enucleation, the standard of treatment for SRMs, which is historically underused [9, 27],

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Companion website: www.wiley.com/go/smith/textbookofendourology

has increased in recent years, especially since the development of robotic assistance [28], and this has led to overtreatment of benign SRMs and small RCCs [29, 30]. At the other end of the management spectrum, a biopsy provides information for a decision on ablation or surveillance of an SRMs and further follow-up vigilance.

## Biopsy nomenclature

The nomenclature used for the results of a BRT deserves special consideration to avoid misdiagnostic and to properly frame the diagnostic performance of the test.

In basic terms, when a renal tumor is evaluated, a biopsy can deliver one of two results: diagnostic (benign or malignant) or nondiagnostic (Figure 124.1). When the biopsy is diagnostic, other characteristics, such as histopathologic type and subtype and grade, can also be assessed.

Pathological interpretation of "nondiagnostic samples" includes insufficient material, inconclusive results, and normal renal parenchyma, as well as inflammation, necrosis, or blood only [8, 10, 20].

There are various reasons for a nondiagnostic biopsy (Table 124.1). Conceptually a failed biopsy means that no tumor tissue is found in the biopsy specimen sample, although other types of tissue might be present in the sample. The reason for a failed biopsy could be a technical failure of the puncture method (e.g. misfire or malfunctioning of the biopsy gun) or an incorrect sampling. Incorrect sampling is sometimes unavoidable due to the nature of the renal tumors: these may contain necrotic and fibrotic tissue, or be mixed in nature with solid and cystic components. The presence of normal renal tissue also implies that the sampling is incorrect as very few renal masses are composed of normal renal tissue. The presence of fibrotic, inflammatory, fatty, or necrotic tissue in the specimen means that a diagnosis cannot be made from it.

In indeterminate (or inconclusive) biopsies, tumor tissue is present in the biopsy specimen but it is impossible to determine the biology of the cells. In this case, IHC or genetic techniques may be of help if enough tissue is available [17, 18].

Definitions in the literature are elusive and consequently there is overlap between failed, incorrect sampling, and indeterminate biopsies.

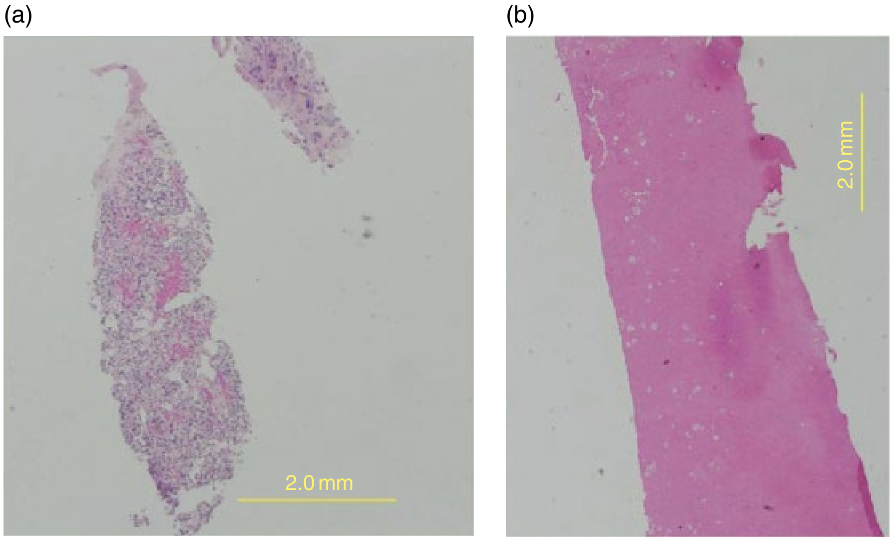

**Figure 124.1** (a) Diagnostic and (b) nondiagnostic (fibrin) core biopsy of a renal tumor.

**Table 124.1** Nomenclature of the nondiagnostic biopsies based on the sample findings, and reasons leading to a nondiagnostic result.

| Nomenclature | Tissue in the sample | Reasons |
|---|---|---|
| Failed biopsy | Absence of tumor cells (other types of tissue may be present) | Technical failure (e.g. misfiring)<br>Erroneous sampling (e.g. normal kidney, fibrosis, fat, inflammation, necrosis, blood) |
| Indeterminate (inconclusive) biopsy | Impossibility to differentiate benign from malignant cells | Insufficient cells<br>Morphologic overlap<br>Cellular heterogeneity |

Diagnostic yield is the rate or percentage of all biopsies with a definitive diagnosis. Diagnostic biopsies can also give false results, both positive and negative, and the sum of these is the rate of inaccurate biopsies. Accuracy is then calculated from the total number of diagnostic biopsies.

In addition to technical failures and indeterminate biopsies, benign nontumoral conditions (e.g. normal renal parenchyma, fibrosis, granulomatous tissue) found in the biopsy specimen are classed as diagnostic by some and nondiagnostic by others. Variations in results are conditioned by the lack of standardization of the taxonomy but also by the well-proven interobserver variability among pathologists. Interobserver variability may be responsible for up to 11% difference in the rate of nondiagnostic biopsy for both core biopsy (CB) and fine needle aspiration (FNA) [6, 31–33].

## Renal biopsy technique

Two aspects should be considered when assessing the technique of percutaneous renal biopsy: the type of image guidance and the type of biopsy performed (CB or cytologic aspiration (FNA)).

### Image guidance

Currently, most renal mass biopsies are performed percutaneously and supported by image guidance using computed tomography (CT) or ultrasound. Biopsies are normally performed under local anesthesia in an outpatient setting. When performing biopsies during surgery or *ex vivo*, direct vision can be used. Compared with *ex vivo* renal mass biopsies, recent studies with imaging-guided percutaneous renal mass biopsies have shown better outcomes in terms of failed or indeterminate biopsies [8, 10, 20, 34]. The outcomes of biopsies performed using ultrasound, CT or magnetic resonance imaging (MRI) are similar and therefore the choice between the radiologic modalities should be made on grounds of availability, location of the tumors, and ultrasonographic appearance [10, 35–38]. MRI-guided biopsy is not widespread as it entails the use of more costly, nonferromagnetic needles [35].

#### Ultrasound

Ultrasound guidance has several advantages over CT-guided renal mass biopsy. It is generally available and less costly, results in less radiation, can be performed by the urologists during the initial workup, provides real-time and multiplanar imaging, and the device is portable and user friendly [39]. However, not all lesions are visualized on ultrasound and anatomy may limit access to the tumors (e.g. rib shadow and gas obscuring visibility). In addition, performing ultrasound-guided renal biopsies requires a significant learning curve. Visualization of the needle tip on ultrasound can be improved by several methods [40]. Biopsies can be performed either using a guide or "freehand."

#### Computed tomography (Figure 124.2)

Among the advantages of CT guidance are the fact that most renal masses can be identified after contrast injection and that the puncture of intratumoral features that may be prone to a nondiagnostic results (e.g. hemorrhagic zones that can result in necrosis or cystic component) can be avoided, optimizing the results of the biopsy. Adjacent organs can also be optimally identified and the technique is easier to master. These advantages are even more significant in obese patients. However, real-time CT imaging is potentially hazardous for the investigator and patient due to radiation exposure and iodine injection is contraindicated in patients with allergy or severe chronic kidney disease. It is possible, due to manipulation of the needle, that the biopsy is performed outside the selected target, leading to a false negative result.

### Type of biopsy

Two types of biopsy can be performed under radiological guidance: fine needle aspiration (FNA), which provides cells for cytological analysis, and core biopsy (CB), which provides a cylinder of tissue of variable dimension depending on the caliber of the needle used.

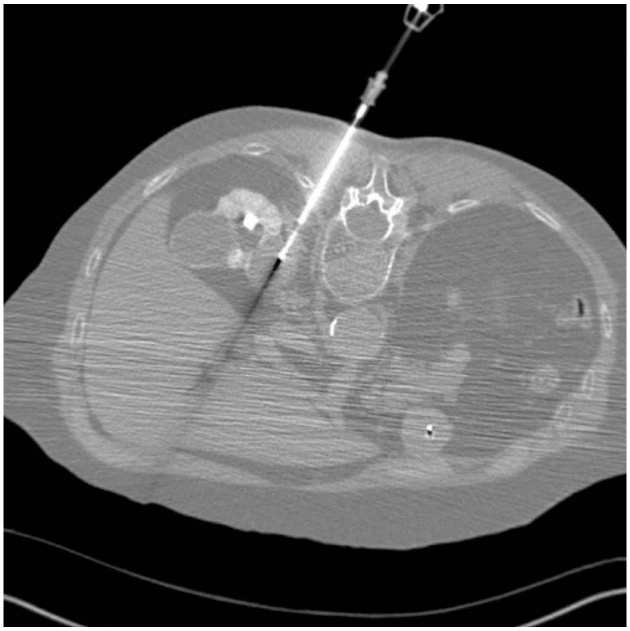

**Figure 124.2** CT-guided biopsy of a renal mass in the right kidney (patient in the prone position).

### Fine needle aspiration

FNA or cytologic aspiration is performed under image guidance. When the patient is properly positioned, the most suitable needle path is chosen. A guiding cannula is advanced onto the tumor surface and the needle is passed through the cannula into the tumor, trying to avoid possible necrotic areas. The cannula is used to avoid direct contact between the tumor and surrounding retroperitoneal tissue, decreasing the risk of tract seeding [40, 41]. The needle is then moved back and forth within the tumor to collect the cells. Traditionally, negative pressure with a syringe is applied on the needle in order to collect more cells. Another method that does not use negative pressure is Zajelda's fine needle capillary technique. This tends to reduce the amount of blood in the sample, but may result in fewer cellular smears [35]. If a CB and FNA are to be performed in the same session, the FNA should be performed first, to reduce the amount of blood in the cytologic specimen [35]. The aspirate is placed on slides and smeared directly. An onsite cytotechnologist can immediately determine the quality of the specimen, which should increase the rate of diagnostic FNAs and subsequent CBs since correct needle placement is ensured [35].

Cytologic examination can provide cytologic detail that is sometimes superior to the features in CBs (Figure 124.3). FNA samples can be used to prepare cell blocks which are helpful to identify specific histoarchitectural features and to perform IHC studies. A recent study has shown excellent results with an improved agar microscopy, which entails processing the aspirate of FNA by centrifuging it in agar. This technique results in concentrated cell blocks composed of fragments and loose cells that are suitable for slicing and subsequent histologic interpretation with IHC [42]. Additional

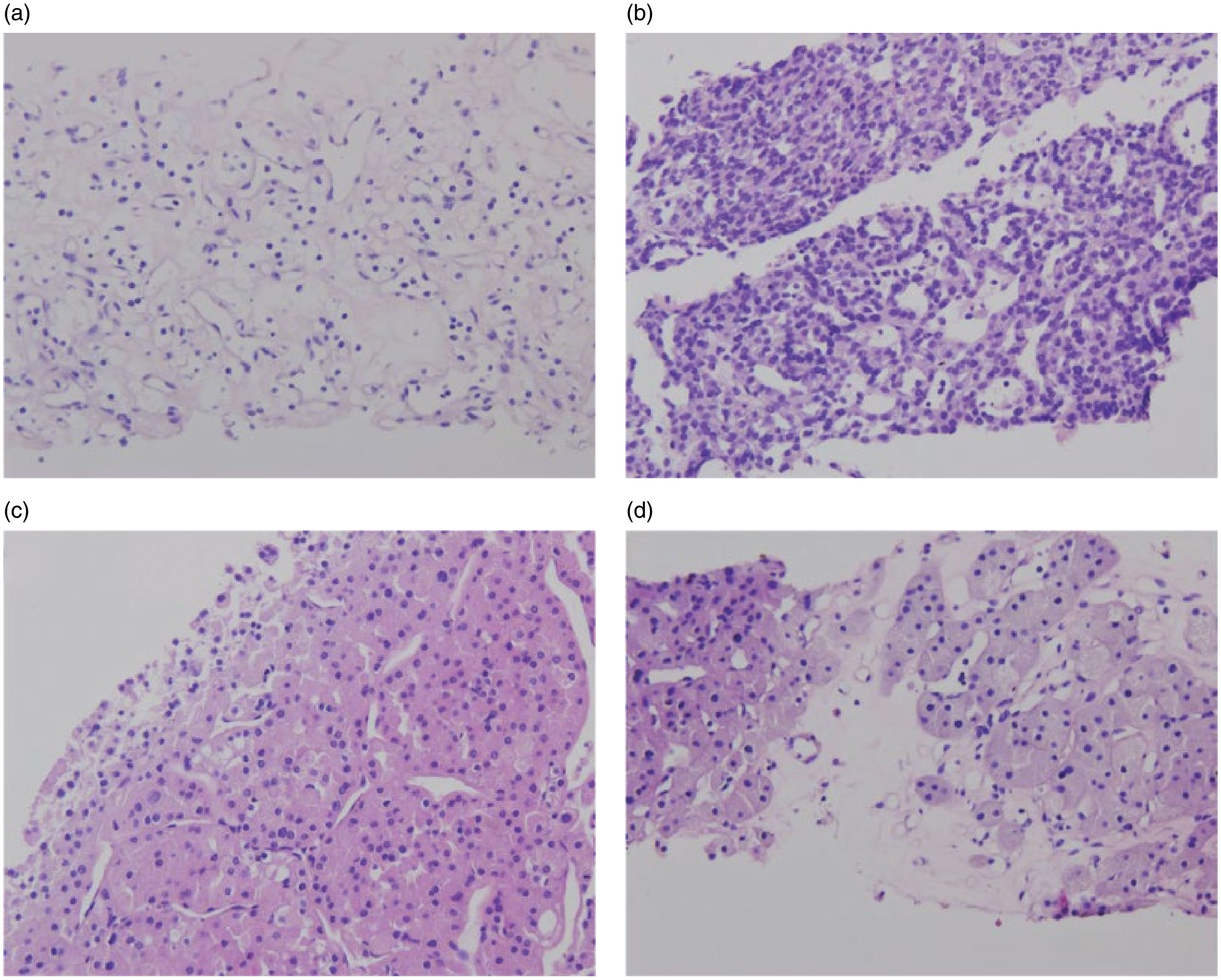

**Figure 124.3** Histopathologic core biopsy samples (H&E staining) of different subtypes of renal cell carcinoma and oncocytoma: (a) clear cell renal cell carcinoma; (b) papillary renal cell carcinoma; (c) chromophobe renal cell carcinoma; (d) oncocytoma.

testing, such as flow cytometry, fluorescent *in situ* hybridization (FISH), apoptosis assays, and picrosius red F3BA staining, are also possible with FNA [35].

### Core biopsy

CB is performed with a hollow needle, allowing it to remove small but solid samples of tissue suitable for fixation and histologic examination (Figure 124.4). The needle has a cutting edge that allows tissue samples larger than 1 cm in length to be removed. Thicker needles than for FNAs are used (17G or 18G). The risk of complications does not increase with the use of these needles [17, 18, 37, 43–50]. Usually, 18G or 17G needles are used with an automatic biopsy gun to obtain tissue samples of 15–22 mm in length. The quality of the core should be checked at the time of the biopsy, in order to repeat it if there are doubts about its quality [51].

## Technical considerations

Some technical considerations on FNA and CB may improve the quality of the sampling and maximize the results.

The choice of radiologic imaging depends on tumor location, size, access feasibility, visibility and individual preference. Imaging is used to avoid areas suggestive of pathologic necrosis or cystic areas. The same considerations apply to the choice of biopsy type (FNA or CB). In general, higher accuracy has been shown for CB, although experienced groups achieve the same results with FNA [52]. The combination of both biopsy techniques during the same procedure increases the diagnostic yield [53].

Larger needles have shown better results in terms of sample quality, and there is no increased risk for complications when comparing 18G to 22G needles [35, 37, 42,

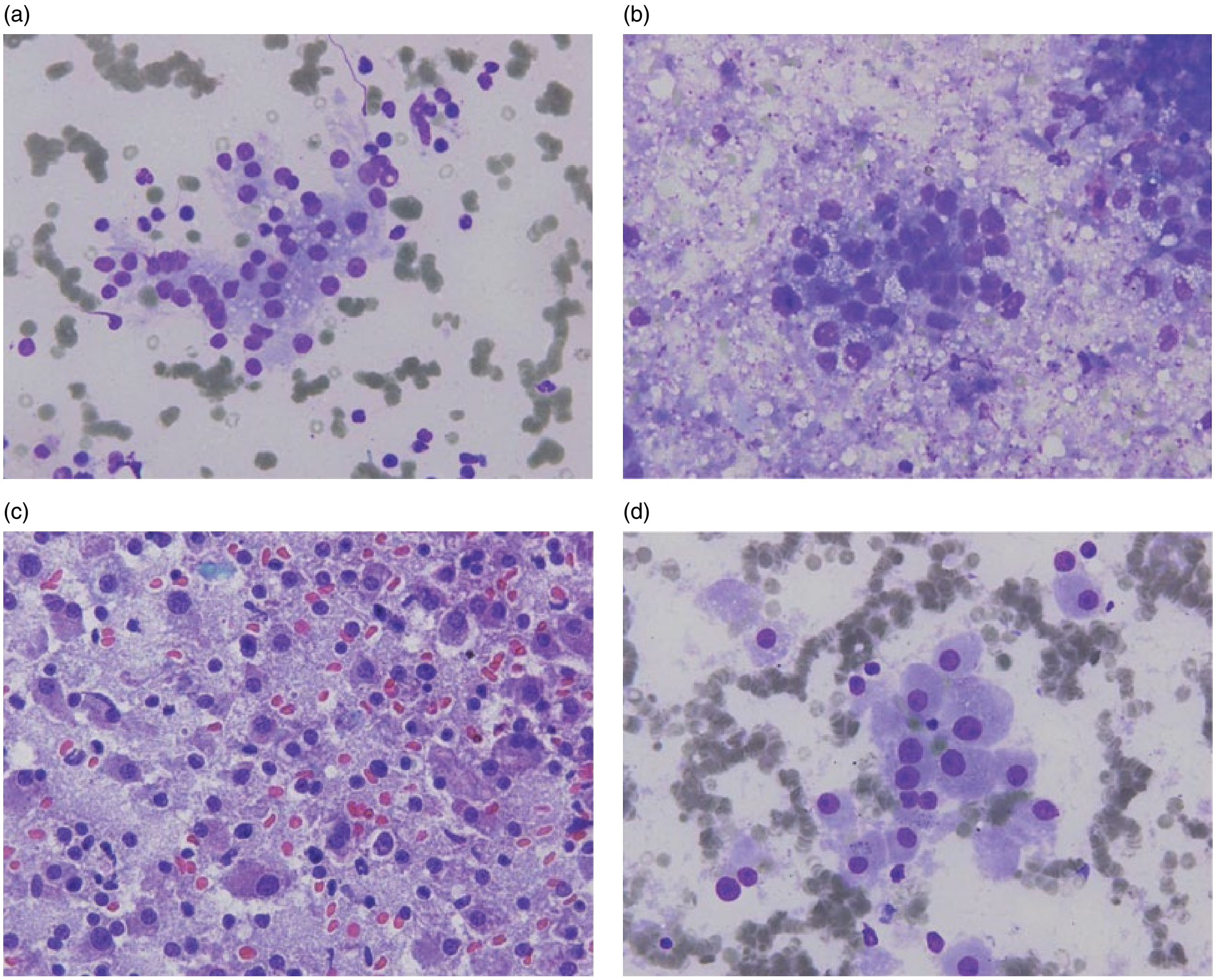

**Figure 124.4** Fine needle aspiration biopsy samples (Giemsa staining) of different subtypes of renal cell carcinoma and oncocytoma: (a) clear cell renal cell carcinoma; (b) papillary renal cell carcinoma; (c) chromophobe renal cell carcinoma; (d) oncocytoma.

47–50] (Figure 124.5). The *ex vivo* performance of three distinct needle calibers (14G, 18G, and 20G) has been compared in a blinded study [54]. One core biopsy (H&E and standard IHC panel) was obtained with each needle from 31 tumors. All biopsies performed with the 14G and 18G needles provided sufficient tissue for diagnosis, whereas the technical failure rate for the 20G needle was 14%. Sensitivity to distinguish between benign and malignant tumor was high for the three needle calibers, but specificity was lower for the 20G needle. Histologic accuracy was 92%, 97%, and 81% for 14G, 18G, and 20G needles, respectively. Grade accuracy was consistently low for the three needles (40–56%) and it was concluded that one core biopsy with an 18G needle offers the highest accuracy in histology diagnosis [54]. The widespread use of thick needles could be partly responsible for the current increasing accuracy and decreasing failure rate of the biopsies [34].

Different type of needles are available to perform a CB. Automatic Tru-Cut needles are easier to manage than the original manual Tru-Cut needles.

Tumor size influences the results of the biopsy. Since larger tumors more frequently have central necrosis, it is recommended to perform a peripheral and a central biopsy in tumors smaller than 4 cm and two peripheral biopsies for tumors larger than 4 cm [55]. The literature, including a recent consensus document, advises at least two CBs to be taken when a BRT is envisaged [10, 34, 35, 44]. For FNA, as many passes as necessary should be performed to ensure a diagnostic smear. Ideally, the cytologist should prepare the smear directly "on site" after puncturing and examine it to ensure the presence of cells and to give the opportunity to repeat the cytologic aspiration if necessary.

In both CB and FNA it is recommended to use a cannula that is wider than the biopsy needle to be used.

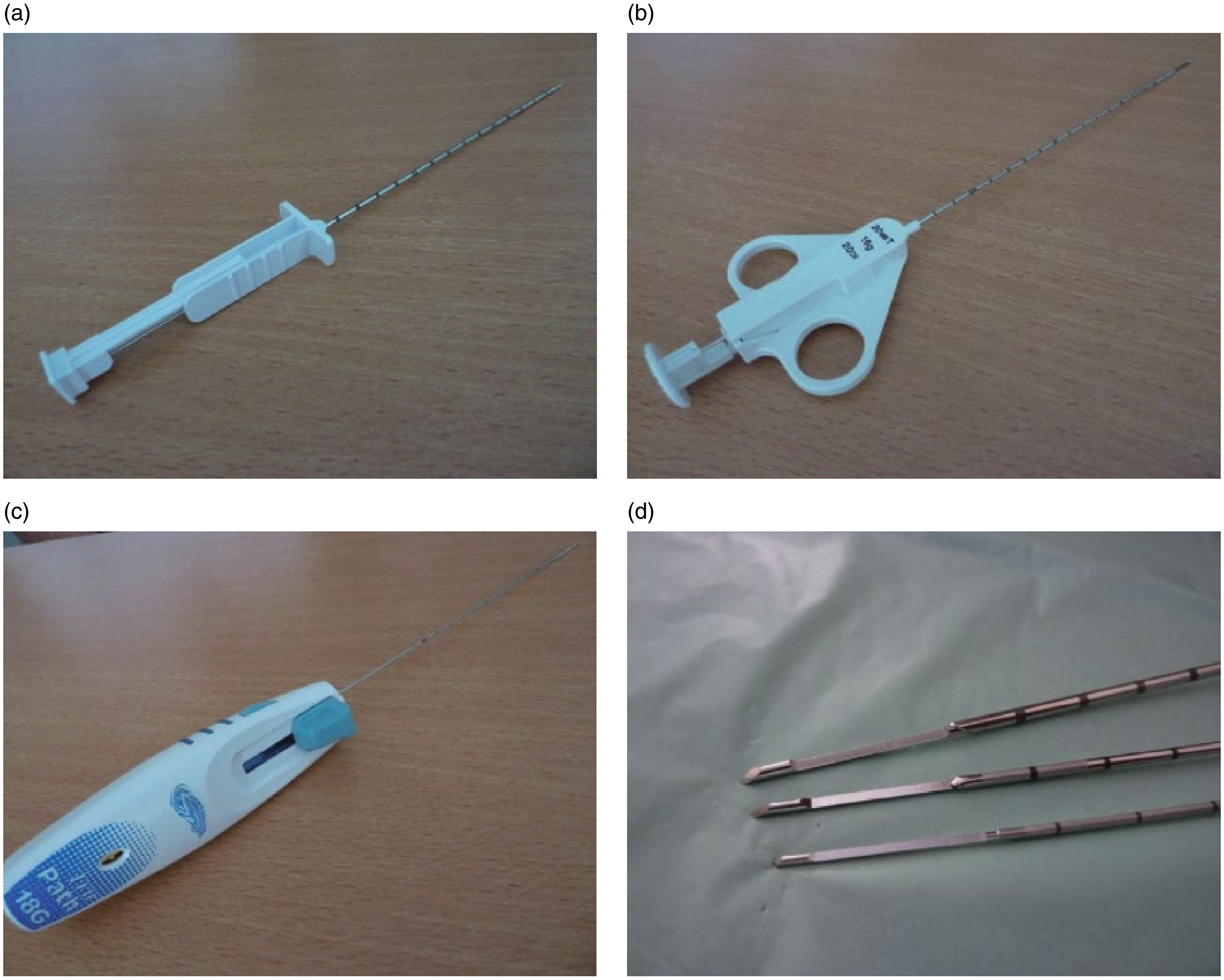

**Figure 124.5** Core biopsy needles: (a) manual 14G needle; (b) semi-automatic 16G needle; (c) fully automatic 18G needle. (d) Needle tips of the 14G, 16G, and 18G biopsy needles (top to bottom). All cores obtained are between 18 and 20 mm in length.

This cannula is advanced under imaging onto the surface of the tumor and remains stable during the whole procedure. The biopsy needle is advanced through the cannula, which allows a number of passes or biopsies to be performed without the risk of contamination or seeding, and avoids manipulation of the chosen tract.

Although bleeding complications are rare (see below), coagulation abnormalities should be corrected prior to biopsy, anticoagulants should be stopped when possible, and some hours of rest are recommended after biopsy.

## Complications

Complications of renal biopsy are rare. Potential complications of percutaneous renal biopsies are bleeding, tumor seeding along the needle tract, arteriovenous fistula, infection, and pneumothorax.

Overall, complications after BRT occur in 8.1% (2.7–11.1%) of patients [8, 20, 34, 51]. Most complications are Clavien grade I, and only few of grade II or more are described. Mortality has not been described in the recent literature [8, 20, 34]. The most frequent complication, perirenal hematoma, occurs in 4.3–4.9% of cases but less than 1% of the patients require blood transfusion. Self-limiting gross hematuria may present in up to 3% of patients and lumber pain in 1–3% of cases. The incidence of pneumothorax or need for embolization (Clavien III) is lower than 1% [8, 20, 34, 56, 57]. Reports on a possible correlation between needle size and rate of complications are controversial [50, 58, 59]. A correlation might be found when 15G needles are compared with 21G needles; however, no significant difference in complication rate has been found between 18G and 21G needles [59].

The most feared complication of renal biopsies is tumor seeding. However, in all recent series of BRT (from 1994 onwards) no cases of tract seeding have been reported in RCC. A possible explanation is the widespread use of a guiding cannula for BRT [35, 60]. Because tract seeding has been described in urothelial carcinomas, when urothelial cell carcinoma is suspected, a percutaneous biopsy for diagnostic purposes is not recommended [60, 61].

Other complications occur very rarely. Arteriovenous fistula should be ruled out in cases of persistent bleeding [62]. When the renal biopsy is performed through a posterior approach, pneumothorax has been reported in 14–29% of cases, although most of them not clinically significant [57, 61]. To further minimize the risk of a pneumothorax, the puncture should be performed in expiration and the needle positioned subcostally. Some upper pole tumors can be punctured using the paravertebral approach, which involves the injection of saline in the paravertebral space to displace the pleura laterally [63].

There is no evidence that a renal mass biopsy can complicate a subsequent partial or radical nephrectomy [50, 64, 65], although in case of hemorrhagic complications it seems reasonable to delay surgery, when possible, for some weeks.

## Results

A number of studies have assessed the diagnostic accuracy of renal mass biopsy, most of them retrospective. Early studies focused on cytologic aspiration with Chiba needles, but the incorporation of automatic fine CB needles minimized trauma and allowed core samples to be obtained that were easier to analyze.

The accuracy of a diagnostic test is measured by sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The results of a diagnostic test (index test) should be compared with the standard results (standard for comparison). In BRT, the ideal for comparison is the histopathological examination of the surgical specimen where histology, RCC subtype, and grade can be accurately characterized. Unfortunately, the literature shows that only a few series provide cohorts with a complete comparison between BRT histology and surgical specimen [8, 20, 34]. Comparison in 100% of the cases between BRT and surgical specimen is performed in a few series. This missed comparison is most prominent when a benign diagnostic is established by renal mass biopsy [8].

### *Ex vivo* biopsy

Several studies have evaluated the accuracy of *ex vivo* (in-bench) biopsy for the diagnosis of renal tumors [6, 17, 18, 32, 33, 54, 55, 66, 67]. The accuracy of biopsy taken directly from a surgical excision specimen (nephrectomy or partial nephrectomy) under direct vision was compared to the definitive pathological diagnosis of the surgical specimen in 100% of the cases. In most of the studies pathologists evaluating the biopsy were blinded to the definitive histopathological results.

*Ex vivo* CBs were sufficiently accurate to differentiate between a malignant and a benign renal mass (Table 124.2). Overall accuracy varied from 72% to 90%, and was not lower for FNAs [32]. The rate of nondiagnostic biopsies varied from 2% to 20% with a trend to be higher than in the modern percutaneous biopsy studies [34]. Using the same nomenclature as in the article by Lane et al. [34], Kummerlin et al. described a rate of failed biopsies (called “nondiagnostic”) between 8% and 16% for the five pathologists involved in the study, and a rate of indeterminate biopsies (called “nonconclusive”) between 0% and 8% [31]. This fact may be explained by the lack of visualization of the entire tumor, as can occur during imaging or in the

**Table 124.2** Results of *ex vivo* biopsies. Pathologic surgical specimen available in all cases.

| | Mean or median tumor size (cm (range)) | No. of tumors | Accuracy (biology) | Nondiagnostic biopsies (includes failed and indeterminate) | Accuracy RCC type | Accuracy RCC grade |
|---|---|---|---|---|---|---|
| Nurmi et al. (1984) [67] | – | 150 | 100% | 2% | – | 76%[a] |
| Dechet et al. (1999) [33][b] | 4.6 (1–18) | 106 | Overall 76–80%<br>Sensitivity 77–84%<br>Specificity 60–73%<br>PPV 94–96%<br>NPV 69–73% | 11–17% | NA | NA |
| Dechet et al. (2003) [6][b] | NR | 100 | Overall 72–77%<br>Sensitivity 81–83%<br>Specificity 33–60% | 20–21% | NA | NA |
| Wunderlich et al. (2005) [55][c] | 4.97 (2–20) | 50 | 98% (diagnostic yield) | 2% | 70% (diagnostic yield when tumor origin definable) | 83% (diagnostic yield when tumor origin definable) |
| Barocas et al. (2006) [17] | 5.3 (1.1–15.5) | 77 | Overall 90%<br>Sensitivity 87–100%[d]<br>Specificity 96.5– 96.5%[d]<br>PPV 96.4–96.9%[d]<br>NPV 87.5–100%[d] | 4% | 90% | – |
| Barocas et al. (2007) [18] | 4.5 (1.3–11.3) | 36 | 69–79%[e] | 14% | 87% | NA |
| Kummerlin et al. (2008) [31][f] | 5.5 (2–12) | 62 | Overall 77–90%<br>Sensitivity 79–100%<br>Specificity 100%<br>PPV 100%<br>NPV 29–100% | 8–19% | NA | NA |
| Kummerlin et al. (2009) [32][g] | 5.5 (2–12) | 66 | Overall 73–91%<br>Sensitivity 72–97%[h]<br>Specificity 63–100%[h]<br>PPV 93–100%[h]<br>NPV 24–75%[h] | 3–14% | NA | NA |
| Breda et al. (2010) [54][i] | 6.3 (0.8–17) | 31 | Sensitivity 96–100%<br>Specificity 67–75%<br>PPV 96%<br>NPV 75–100% | 0% (14G needle)<br>0%(18G needle) 16% (20G needle) | 92% (14G needle)<br>97% (18G needle)<br>81% (20G needle) | 48% (14G needle)<br>40% (18G needle)<br>56% (20G needle) |

[a] Grade as low, intermediate, and high.
[b] Two pathologists independently evaluated all samples.
[c] Five core biopsies per tumor.
[d] Addition of molecular diagnosis increased sensitivity and NPV.
[e] By adding FISH to conventional H&E staining.
[f] Core biopsy evaluated independently by five pathologists.
[g] FNA evaluated independently by five pathologists.
[h] For malignant tumors.
[i] Three different biopsy needle calibers compared (14G, 18G, and 20G).
NA, not assessed; NR, not reported; PPV, positive predictive value; NPV, negative predictive value.

absence of needle stabilization during percutaneous puncture. Subtype differentiation between oncocytoma and chromophobe RCC remains problematic (see Figures 124.3 and 124.4). Kummerlin et al. found a good overall accuracy for *ex vivo* FNA in differentiating between malignant and benign masses [29, 32]. However, again there was a substantial interobserver variation regarding the subtype differentiation, other than for clear cell RCC.

When interpreting the results of in-bench biopsy studies, it has to be taken into account that this *ex vivo* setting is only partially comparable to clinical practice, where percutaneous biopsies will be the standard.

## Percutaneous biopsy

In 2008 Lane et al. published an extensive review on the subject [34]. They divided the studies chronologically between those conducted before 2001 and those from 2001 onwards. Before 2001, 27 studies were considered, in two of which "*ex vivo*" tumor biopsy was performed. After 2001, seven clinical studies and three *ex vivo* studies were considered. Overall diagnostic accuracy of 88.9% was reported for the earlier period (including *ex vivo* biopsies). When *ex vivo* biopsies were excluded, clinical accuracy increased to 96% in the later period. These figures suggest an improving trend in the diagnostic performance of the biopsy. Furthermore, false negative and false positive rates both decreased between periods.

The accuracy of the biopsy was calculated based on the number of successful biopsies. Biopsy failures – defined as "the inability to obtain an amount of tissue sufficient for diagnosis" – were excluded from the accuracy assessment. In clinical practice, the physician should be aware that diagnostic yield is different from accuracy, as the biopsy failures still accounted for 9% and 5.2%, respectively, for the two periods. Indeterminate biopsies were included in the accuracy assessment in the review. However, an indeterminate biopsy is in fact a nondiagnostic biopsy. The sum of technical failures plus indeterminate biopsies ("no definitive diagnosis possible using the available techniques") was 19% and 10%, respectively, in the two periods [34].

Most recently, two systematic reviews have confirmed the results of Lane et al. [8, 20]. Although the number and chronology of the included articles differs, both reviews aimed to quantify accuracy and rate of adverse events. Accuracy of the biopsy was calculated in both reports excluding nondiagnostic biopsies. Essentially, the definition of nondiagnostic biopsy included any normal renal parenchyma, presence of blood, necrosis, inflammatory, fibrotic, or extrarenal tissue only and insufficient or nonadequate tissue for diagnostic.

The nondiagnostic rate in these two systematic reviews is reported as 8% and 14%, although it varies widely across studies from 0% to 26.6% for CB and from 0% to 36% for FNA [8, 20]. Sensitivity in distinguishing malignant from benign tumors is very high in both systematic reviews for CB (97.5% and 99%) and slightly lower for FNA (93.2%), and lower in cases of cystic masses (83.6%). Specificity was also very high in both reports (96.2% and 93.2% for CB) [8, 20]. However, NPV remains low when results are compared with the surgical standard (63.3%) [8].

These overall excellent results were reproduced when the analysis was performed exclusively in studies looking at SRMs [8, 20].

When considering these results, limitations common to the three reviews deserve mention [8, 20, 34]. First, the studies included in all these reviews compared the results of the BRT with several different standards. The index test varies from pathologic examination of the surgical specimen to radiologic follow-up in the case of non-extirpated tumors [7, 8, 20, 34]. For example, in the period before 2001, surgery, and consequently surgical specimen available for comparison, was noted in only 49.5% of the cases previously biopsied, excluding the *ex vivo* biopsy studies for which a surgical specimen was obviously available in all cases. The number of cases with surgical specimen available for comparison increased to 54% in the second study period [34] and is similar when RCC is diagnosed by BRT in the most recent reports [8]. The recent literature does not support the lack of radiologic growth as absence of malignancy [68, 69]. In short, old or new, the comparison of BRT histology to the pathology of the surgical specimen is available in less than half of the patients, with 100% of pathological specimens available in few series and thus the real PPV and NPV cannot be properly assessed.

Second, most of the series are retrospective and thus bias selection cannot be ruled out. Finally, heterogeneity among series in terms of selection criteria, technical issues (e.g. needle used, type of biopsy), and the different number of cases included precludes proof of sound statistical comparison.

All these reasons represent potential sources of bias in the interpretation of the analysis, and might lead to overestimation of the biopsy accuracy.

In an attempt to clarify the results, we further examined those series where pathologic confirmation was obtained in the form of a surgical specimen in 100% of cases, whether *ex vivo* or in the clinical setting, including with a preoperative percutaneous biopsy. Results of SRM biopsy are also considered separately, because it may not be possible to extrapolate results from general series to these masses.

## Percutaneous biopsy compared with 100% surgical specimens

The number of studies on the accuracy of percutaneous renal mass biopsy based on 100% comparison of the preoperative samples with the surgical specimen is very low. For example, only 17 of the 57 studies included in the systematic review of Marconi et al. provided this 100% comparison [20] and only 56.4% and 16.9% of the malignant and benign histology BRTs, respectively, received surgery in the systematic review of Patel et al. [8].

Accuracy in the diagnosis of RCC varied from 40% to 94% in the three studies before 2001 included in the review of Lane et al. [70–72]. The rate of biopsy failures varied from 0% to 22% and the rate of indeterminate biopsies from 4.3% to 36%. False positives were almost nonexistent (0–2.2%), but false negatives accounted for 0–24%. These results were clearly insufficient to justify the systematic use of percutaneous biopsy in the diagnostic setting. However, comparison with modern data is precluded as different needles, mostly 21G and 22G, were used, and in two of those studies biopsy was guided by old ultrasound devices.

After 2001, three more reports in the review by Lane et al. compared the percutaneous renal mass biopsy in all cases with the surgical specimen [66, 73, 74] (Table 124.3). The sensitivity of percutaneous core biopsy to detect malignancy proven at surgical specimen varies from 91.4% to 93.5% and the NPV varies from 50% to 81.3%. The rate of nondiagnostic biopsies was very low in these three modern studies, in the range of 2.4–7.1%, although in some cases a repeat biopsy was necessary to reach a diagnosis. Correct RCC subtype determination varied from 77.5% to 91% and correct Fuhrman nuclear grade from 51.5% to 76%, with the grade mainly being underestimated on CB.

## Biopsy in small renal masses

Because of the increasing diagnostic incidence of SRMs (≤4 cm), the high percentage incidence of benign masses among these kidney tumors [23, 75], and the difficulty of radiological distinction between malignant and benign in this size range, biopsy of SRMs has gained interest in recent years. At present, biopsy of SRMs is advised in major guidelines with the possible exclusion of those patients in whom watchful waiting or nonsurgical management is chosen [1–3, 10, 24]. In spite of the low biologic potential of small RCC, some may still exhibit a high grade [25, 29]. The clinical scenario becomes more complicated when considering that a large number of these SRMs are accidentally found in the elderly with comorbidity. In SRMs, a preoperative histologic diagnosis may lead to a change in management.

In general, sensitivity of renal biopsy in SRMs has been reported to be lower than in series including all tumor sizes. The recent literature challenges this result and reports show very high sensitivity and specificity of biopsy of small renal tumors, both close to 100% [8, 20]. However, biopsy failure rate and nondiagnostic rates should be expected to be higher in SRMs than in series including all size tumors. A rate of biopsy failure as high as 37% has been reported in renal masses smaller than 3 cm versus 9% in tumors larger than 3 cm [65]. The likelihood of biopsy success increases with every centimeter increase in the size of the SRM [76].

Table 124.4 gives an overview of published studies on biopsies in SRMs. As expected, biopsy of SRMs is less accurate than that in larger masses, with histologic confirmation by means of surgical specimen in 30–78% of cases [22]. The rate of nondiagnostic biopsies is also higher in SRMs, either because of technical failure or because of indeterminate results [10].

## Accuracy for histology and grade

Kidney tumors show intratumoral heterogeneity and therefore subtype identification can be misleading when biopsies are assessed. An overall accuracy of 94% in identifying the correct histologic subtype has been

**Table 124.3** Modern series on percutaneous renal mass biopsy with pathological confirmation (surgical specimen) in all cases.

| | No. of tumors | Mean tumor size (cm (range)) | Guidance/ needle | Type biopsy/ number of samples | Nondiagnostic biopsies (includes failed and indeterminate) | Accuracy | Accuracy histologic type | Accuracy grade |
|---|---|---|---|---|---|---|---|---|
| Schmidbauer et al. (2008) [74] | 78 | 3.9 (0.8–9) | CT/18G | CB/2–3 | 3% | Sensitivity 95.2%<br>Specificity 100%<br>PPV 100%<br>NPV 81.3% | 91% | 76% |
| Blumenfeld et al. (2010) [66] | 81 | 5.3 (1–17) | US–CT/18G | CB/at least 2 | 2.5% | NR | 88% | 43% |
| Sofikerim et al. (2010) [73] | 42 | 6.4 (2.5–14) | US/18G | CB/2 | 7.2%[a] | 90% for biology<br>Sensitivity 91.4%<br>Specificity 60%<br>PPV 94.1%<br>NPV 50% | 77.5% | 51.5% |

[a] Nondiagnostic rate lowered to 4.7% after repeated biopsy.

CT, computed tomography; US, ultrasound; CB, core biopsy; NR, not reported.

**Table 124.4** Results of biopsies in small renal masses. All included studies are on masses ≤4 cm with the exception of Shannon et al. [81].

| | Tumor size (cm) | Guidance | No. of tumors | Nondiagnostic biopsies (includes failed and indeterminate) | Pathologic confirmation (cases with surgical specimen available) | Accuracy |
|---|---|---|---|---|---|---|
| Neuzillet et al. (2004) [64] | 2.8[a] | CT | 88 | 9% | 70.4% | 90% |
| Rybikowski et al. (2008) [78] | ≤4 | CT | 66 | 18% | 78% | 91% for malignant<br>57% for benign |
| Thuillier et al. (2008) [79] | 2.5[a] | NS | 53 | 23% | 60% | Sensibility 96%<br>Specificity 100% |
| Wang et al. (2009) [80] | 2.7[a] | CT/US | 110 | 9% | 34% | 100% |
| Volpe et al. (2008) [77] | 2.4[b] | CT/US | 100 | 16% | 20% | 84% |
| Shannon et al. (2008) [81] | 2.9[b] (<5) | CT | 222 | 22% | 59% | 100% for biology<br>98% for subtype |
| Kummerlin et al. (2009) [32] | 3.5[b] | In bench[c] | 30 | 7–17%[c] | 100% | Overall accuracy 67–87%[c] (67–93% for malignant and 33–100% for benign)[c] |

[a] Mean size.

[b] Median size.

[c] Five pathologists' independent results.

CT, Computed tomography; US, ultrasound; NS, not specified.

Modified from Laguna et al. [7].

reported [34]. When the result of a biopsy is malignant, subtype determination is possible in 93% of the biopsies; however, IHC is necessary in a substantial number of cases. Concordance with the surgical specimen is high (91–100%) [77, 78].

In recent systematic reviews agreement of BRT with histologic subtype is good ($k = 0.683$) or substantial [8, 20].

Fuhrman nuclear grade is correctly assessed in biopsy in approximately 68% of cases, with a lower concordance than for subtype (60–100%) or otherwise fair agreement ($k = 0.34$) [8, 20, 77–79]. Fuhrman upgrade from low in BRT to high in the surgical specimen occurs in 16% [8]. Similar results for grade accuracy have been reported for SRMs, although IHC is necessary in a substantial number of cases [8, 20, 77–81].

One of the major problems in differentiating subtypes of RCC is the distinction between oncocytoma and chromophobe RCC, since hybrid tumors containing areas of benign oncocytoma and malignant chromophobe RCC exist [74]. This issue remains a challenge for the pathologist, especially when limited tissue is available, as is the case with biopsies. New auxiliary techniques, such as genetic profiling, polymerase chain reaction (PCR), and FISH are under development to distinguish chromophobe RCC, oncocytomas, and other subtypes of RCC with more accuracy [43, 44, 82, 83].

Heterogeneity of renal tumors also hinders correct determination of Fuhrman's nuclear grade by biopsy. In two large recent series, Fuhrman's nuclear grade was correctly determined in 70% [64] and 83% [55], respectively. In all the discordant cases, the actual grade found in postoperative pathology was within one grade of the grade found at biopsy. A higher accuracy (76–100%) is obtained when the nuclear grade of tumors is grouped into "low grade" (Fuhrman I–II) and "'high grade" (Fuhrman III–IV) [64, 65].

## Biopsy during thermal ablation

When performing thermal ablation of small renal tumors, such as cryoablation or radiofrequency ablation (RFA), information on the pathology of the ablated mass can only be gained through biopsy of the tumor, since the specimen is not extirpated. Because this information not only is useful diagnostically but also may impact follow-up policy, biopsy should be performed before or during ablation [2, 3, 10]. An additional use of biopsies in the frame of ablation therapy is in determining the presence of residual tumor.

Two recent meta-analysis have compared cryoablation with RFA [84] and percutaneous ablation with surgical ablation, including laparoscopy [85]. Biopsy of the mass was performed in 82.3% of the cryoablations, in 62.2% of the RFAs, in 84% of the percutaneous procedures, and in 88% of the surgically assisted ablations [84, 85]. Overall, between 54% and 64% of the biopsies confirmed RCC, 12.7% showed benign pathology, and 33.5% had unknown or undetermined pathology [84]. With the limitations derived from the lack of well-designed comparative studies, it becomes evident that biopsy of the tumors is widely adopted during ablation treatments, except in the case of RFA where 40% of the patients are still treated without information on tumor biology [10].

The rate of nondiagnostic biopsy varies from 0% to 23% in those series of percutaneous ablation [86–89] and from 0% to 30% when tumor biopsy is performed during laparoscopic ablation [90–95]. These figures are similar to the nondiagnostic rates described for SRMs (see Table 124.4) as the tumors treated by ablation are in this size range. At least during laparoscopy-assisted ablation, modification of the biopsy technique by activating the firing mechanism of the biopsy gun externally to the target tissue led to a higher diagnostic yield in a small clinical series [92]. The criteria classifying a biopsy as nondiagnostic or benign vary between groups, which may explain the broad range of nondiagnostic or benign results. For example, normal renal tissue, fibrotic tissue, or necrotic tissue are distinctly classed as benign by some and nondiagnostic by others [93, 95]. In fact, the stricter the nondiagnostic criteria are, the higher the nondiagnostic rate of the biopsy.

Tumor biopsies can also be taken immediately after ablation to minimize risk of bleeding or tract seeding. In this situation, the pathologist can identify RCC architecture both after RFA and cryoablation and the diagnostic yield of biopsies before and immediate after ablation is not statistically different [96–98].

Success after ablation therapy is mainly determined using cross-sectional imaging with contrast. Lack of contrast enhancement indicates absence of tumor recurrence [99]. However, the presence of viable tumors in the ablated area is not completely ruled out by the lack of enhancement on CT or MRI [100]. Therefore, some centers have performed an additional postablation biopsy to assess the success of the ablation. A study on the correlation of radiographic imaging and histopathology showed that in 24% of patients treated by RFA, the biopsy taken six months after ablation showed viable renal cancer cells even though there were no signs of radiologic enhancement at that time [101]. The biopsy taken six months after cryoablation was consistently negative in all nonenhancing masses. Therefore, the sensitivity of nodular enhancement at six months after RFA to detect a positive biopsy was only 38.4%, with a specificity of 91.3%. The results for cryoablation were superior, with a sensitivity and specificity of 77.8% and 95.1%, respectively. In contrast, a study on RFA lesion biopsy more than 1 year after ablation showed no vital lesion [102]. It is therefore advisable to use nicotinamide adenine dinucleotide (NADH) or other oxidative stress stains when assessing biopsy after ablation [103].

## Additional pathologic methods

RCC subtyping was originally performed using a light microscope and standard H&E staining. The diagnostic accuracy in differentiating benign from malignant renal mass is substantial, but for determining RCC subtypes the accuracy is lower, since complex and overlapping morphologic features exist. As described earlier, this results in interobserver and intraobserver variability of subtyping [31, 32].

For a long time research to improve subtyping of renal tumors had no priority because there were no clinical consequences. However, there has been interest in subtype determination of RCC following the incorporation in clinical practice of targeted therapies. Correct determination of RCC subtype can be of importance since paradigms for specific RCC subtypes may not apply to other subtypes. Therefore, a more accurate differentiation of RCC subtypes is desirable.

Differences among RCC subtypes at DNA, RNA, and protein level have been explored in order to improve the accuracy of subtype differentiation. Although different subtypes of RCC show overlapping histologic features they are biologically distinct. This is obvious when the cytogenetic abnormalities of different subtypes are observed: different subtypes have characteristic abnormalities, such as chromosome 3p aberrations in clear cell RCC and trisomy 17 in chromophobe RCC [104]. These characteristic differences imply that the different subtypes are distinguishable by mapping this genetic expression.

One method of performing molecular gene profiling analysis is DNA microarray. This has shown differences in gene expression profiles between subtypes of RCC and therefore differentiates between the histologic subtypes of RCC [105–107]. By analyzing the mRNA expression ratios of different genes in different subtypes of RCC, the individual subtypes can be differentiated. High *CA9* expression in clear cell RCC, *AMACR* in papillary RCC, and *CLCNKB* in chromophobe RCC and oncocytoma [108] facilitates a molecular diagnostic algorithm. It has been demonstrated that renal masses can be accurately classified on CBs using a combination of histopathology and molecular gene profiling analysis [17].

In order to obtain sufficient material for investigation, the genetic material harvested with percutaneous biopsy should be amplified by PCR [17, 35].

Another auxiliary technique for subtype differentiation is IHC, which localizes specific antigens or proteins in a tissue sample by binding the antigens with labeled antibodies. The formed antigen–antibody complex can be visualized by (fluorescent) staining and therefore the presence of the antigen can be demonstrated.

Several antigens have been found to be useful as a marker for subtype determination of RCC, and they are currently used in combination with histologic investigation to improve the diagnostic accuracy. It is likely that in the near future these techniques will contribute more to the diagnostic process [109–111].

## Conclusions and recommendations

At present, biopsy of SRMs is recommended in the major guidelines, particularly in case of SRMs, before or during ablative procedures, and when treatment depends on histologic subtype determination. CB is more commonly performed than FNA. Complications are rare and mostly of low grade.

Modern series on percutaneous biopsy of renal masses show a high accuracy and a lower rate of nondiagnostic biopsies than previous reports. Series with pathologic confirmation by means of surgical specimen support these results, although NPV remains low. The concordance between BRT and pathology subtype determination is good/substantial, while the concordance in terms of grade remains fair.

However, when considering a percutaneous biopsy in an SRM, there needs to be awareness that although accuracy may reproduce the figures reported for the general series on percutaneous biopsy, the overall rate of nondiagnostic biopsy – either failed or inconclusive – is still high in SRMs and size dependent.

Biopsies should be systematically performed during ablation therapy, although a similar rate of nondiagnostic biopsies is expected as for SRMs in general.

Current percutaneous renal biopsy is recommended when there is a suspicion of nonprimary RCC, when an infectious cause is suspected, during ablation therapy, to decide on treatment of SRMs, for therapeutic purposes in metastatic RCC, and for documentation and follow-up purposes when a RCC is submitted to active surveillance.

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# 125

# Radiofrequency Ablation of Renal Tumors

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## Introduction

With the increasing use of cross-sectional imaging, there has been a dramatic increase in the incidental identification of asymptomatic small renal masses (<4 cm in size) [1], the majority of which are renal cell carcinoma (65–80%) [2, 3]. The risk of metastases at the time of surgery for such masses is low [4], as is the development of *de novo* metastases [5]. Although active surveillance may be appropriate for many of these lesions, most tumors will grow with serial imaging [6], albeit slowly (mean 0.26 cm/year), and may require subsequent treatment.

Traditionally, renal masses have been managed by radical nephrectomy, but nephron-sparing surgery, namely partial nephrectomy, has been accepted more recently for most T1a (<4 cm) and in some cases T1b (4–7 cm) renal tumors with the recognition that chronic kidney disease after radical nephrectomy may lead to increased patient morbidity and mortality [7, 8]. Multiple studies have shown that partial nephrectomy has similar intermediate- and long-term cancer-specific survival [9, 10] with only mildly increased complication rates [11]. Although traditionally performed in an open fashion, other than at centers with an expertly trained laparoscopic surgeon, recent advancements in robotics and minimally invasive technologies have driven a shift towards increased utilization of laparoscopic nephron-sparing surgery. Technical considerations, including location, tumor depth/size, or proximity to the collecting system/renal hilum [12], may also impact the decision-making process as to the optimal treatment modality for each small renal mass.

Despite the advantages of partial nephrectomy, many patients will not be good candidates for extirpative surgery due to comorbidities, the need for ongoing anticoagulation, prior intra-abdominal or renal surgeries, or intolerance of positioning or procedure length. Others may simply prefer a “less invasive” alternative. For these patients, percutaneous ablation may be a suitable alternative. Radiofrequency ablation (RFA) of tumors was initially described in the treatment of hepatic malignancies in 1993 [13] and later in the treatment of a kidney tumor in 1997 [14]. Soon after, Walther et al. assessed the effectiveness of ablation by performing RFA followed by immediate tumor excision and noted effective cell death in 10 of 11 tumors [15]. Multiple cohort studies with increasing follow-up duration have since noted good oncologic outcomes, low complication rates, and short postprocedural recovery times with RFA.

Given the success and good procedural tolerance, RFA is now an accepted alternative treatment modality for small renal masses [16]. Although all of the above benefits make RFA an appealing option, it is important to continually evaluate long-term oncologic data and enhance technique to maximize surgical outcomes. In this chapter, we review the technical aspects of RFA, as well as its mechanisms of action, indications for the procedure, complications, and outcomes.

## Mechanism of action

RFA ablates tissue using a monopolar, alternating electric current into the target tissues, typically at a frequency of 450–1200 kHz. Application of a high-frequency alternating current causes ions, namely water, within the tissue to continually realign with the current polarity, leading to vibration and kinetic energy. This leads to molecular collisions, friction, and, invariably, heat production. Importantly, the heat is not directly supplied by the probe itself, as is the case with other ablative therapies (i.e. cryotherapy), and the probe is not heated by the current [17]. Once a critical temperature is surpassed,

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cellular protein denaturation and cell membrane disintegration occur, resulting in cell death.

Early reports assessing the critical temperature and duration necessary to induce tissue destruction identified irreversible cellular injury with >99% cell death when the tissue was heated to 55 °C for 30 minutes, 60 °C for 10 minutes, and 65 °C for 8 minutes in an *in vitro* model of human renal cell carcinoma [18]. Histopathologic analysis of treated lesions demonstrates coagulative necrosis, membrane disruption, protein denaturation, and vascular thrombosis [19], as well extensive cellular edema, localized tissue inflammation [20, 21], loss of nuclear detail and nonvisualization of nucleoli [15] within hours of ablation. Further nuclear degeneration and chronic inflammation will occur by 3–7 days post ablation, total loss of renal architecture with complete loss of cytoplasmic borders by 30 days, and near total resorption of necrotic tissue by 90 days [20, 21].

## Indications

Clinical indications for RFA are based on both patient factors and tumor characteristics. Initial reports suggested that RFA be reserved for patients at high risk for surgery due to comorbidities, compromised baseline renal function, and/or multiple tumors. Currently, the European Association of Urology (EAU) makes “no recommendation” on the use of RFA for small renal masses “owing to the low quality of [the] available data” [22], while the American Urological Association (AUA) recommends that RFA be considered as a first-line therapy for patients with major comorbidities or at increased surgical risk and a clinical T1a renal mass [16]. The AUA guidelines also consider RFA an option for healthy patients with a clinical T1a renal mass or patients with major comorbidities or at increased surgical risk and a clinical T1b renal mass.

At our institution, patients are considered candidates for RFA if they have a solid small renal mass with contrast enhancement (≥15 Hounsfield units [HU]) on computed tomography (CT) or magnetic resonance imaging (MRI), which is located >1 cm from surrounding structures, including the ureteropelvic junction (UPJ). In patients who meet this criteria, a thorough discussion is had regarding both ablative and extirpative treatment options, including both open and minimally invasive surgeries. The risks and benefits of the procedure are reviewed, including the good long-term outcomes of RFA [23, 24]. The typical recovery after both ablative and extirpative surgeries is also reviewed. The ultimate decision to proceed with RFA stems from shared decision-making. For those planning to pursuing RFA, the need for a more rigorous radiographic surveillance protocol and the possible need for repeat procedure (repeat RFA vs. extirpative surgery) if local recurrence were to occur is also reviewed.

## Contraindications

There are no absolute contraindications to RFA other than uncontrolled coagulopathy. However, there are a few relative contraindications that should be considered prior to proceeding with RFA. Patients unable to tolerate anesthesia or sedation can undergo ablation under local anesthesia but this is not as optimal given the difficulty controlling for patient movement and standardization of respiratory depth. Patients requiring blood thinners or with other coagulopathies should have these corrected prior to treatment [25]. Although some consider all T1 lesions to be amenable to RFA, T1b tumors have shown increased rates of recurrence and require multiple probes to be placed, thereby increasing the risk of complication. Thus, many, including the authors, would not advocate for the routine use of RFA for T1b lesions. Finally, hilar or centrally located tumors are at higher risk of complication after ablation due to the proximity to the renal pelvis and vasculature, as well as reduced ablative efficacy due to the “heat sink” effect of surrounding vasculature.

## Technical considerations

A thorough understanding of RFA equipment is critical to performing a safe and effective procedure. There are two types of RFA systems currently available: temperature-based and impedance-based systems. Temperature-based systems work by achieving a specified temperature for a preset duration based upon measured tissue temperatures at the probe tip during heating. Conversely, impedance-based systems work by delivering energy until a predetermined impedance level, or measured resistance to energy transmission, is achieved through surrounding tissues, thereby indicating tissue ablation. Incomplete ablation of tumors due to skip lesions has been identified more often with impedance-based technology, likely due to the indirect measure of impedance versus temperature [26].

Another consideration when selecting RFA technology is whether to utilize a wet or dry probe. If energy application is too sudden when ablating tissue, a charring effect can occur near the probe tip, leading to increased tissue impedance and limiting the ablation zone. This primarily occurs with a dry probe. Wet RFA probes infuse a constant stream of saline into the probe to minimize the chance for charring adjacent to the probe tip, allowing for a larger zone of tissue desiccation. Although the treatment area can be larger with the wet probes, the wider zone may provide less control over the targeted area and increase the chance of damage to normal adjacent parenchyma.

Varying array diameters (2–5 cm) and probe lengths are also available with each system. Given the inverse relationship between the induced tissue temperature and distance from the RFA probe (temperature ≈ 1/radius) [27], careful probe size selection, particularly in large T1a lesions, is crucial. In the end, the type and size of probe utilized should be tailored to each individual tumor.

Several devices are currently approved for RFA. The RITA device (Angiodynamics, Albany, NY, USA) utilizes an umbrella-shaped, multi-tine, dry probe with a temperature-based system controlled by thermistors embedded in five of the nine electrodes. Each electrode modulates energy delivery based upon the measured temperature, as well as the mean electrode temperature. The LeVeen system (Boston Scientific, Natick, MA, USA) is an umbrella-shaped, multi-tine dry probe with impedance-based system. The Valleylab system (Mansfield, MA, USA) uses an impedance-based system composed of a single, 17G ("cool tip") wet probe electrode. Although randomized human trials between these systems do not exist, a direct comparison in a porcine liver model demonstrated larger zones of ablation with the wet RFA probe systems, more spherical ablation with the 12-tinned electrodes, and better reproducibility with nine-tine electrodes [28].

## Tumor considerations

Circulating blood near the ablative site can act as a "heat sink" and remove energy (heat) from the surrounding tissues, thereby reducing the efficacy of the ablation. This is an important factor to consider given that the kidneys receive 20% of the cardiac output. Prior studies have found that vessels greater than 3 mm in diameter can produce a heat sink effect [17]. Temporary clamping of the renal hilum during RFA negates this effect, leading to an increased size in the procedural ablation zone and reduced time to target temperature, but no difference in ablation zone size after four weeks [29]. Thus, hilar clamping is not currently recommended due to increased risk (arterial thrombosis, ischemia–reperfusion injury) without added benefit. Some have advocated selective arterial embolization with RFA to achieve the same effect [30]. This may provide added benefit, particularly when ablation is to be utilized for a centrally located or large (≥4 cm) tumor.

Tumor location is critical to consider given the risk of injury to surrounding organs, namely the liver, spleen, bowel, and collecting system. Thus, any tumors within 1 cm of these structures or on the anterior portion of the kidney should be approached laparoscopically for ablation or with extirpative therapy. Alternatively, hydrodissection [31] with saline injection can develop a space for ablation, but this depends on surgeon familiarity and comfort. Posterior and lateral tumors, which are often far removed from these structures, can be ablated percutaneously under image guidance [32], although proximity to the body wall may also lead to postoperative complications.

## Procedural details

### Percutaneous radiofrequency ablation

Percutaneous treatment can be performed with either conscious sedation or general anesthesia depending on patient and surgeon preference. The authors prefer general anesthesia as it is safe for the majority of patients, enables control of respirations during probe positioning, and generally does not preclude same-day patient discharge when desired. Intravenous prophylactic antibiotics are administered prior to the procedure, with culture-directed antibiotics for anyone with a history of urinary diversion or preoperative evidence of urinary tract infection. Following urethral catheter placement, the patient is positioned on the CT gantry, being sure to properly pad all pressure points. The choice of position is largely dictated by the tumor location and patients may be placed completely prone or in a modified flank position.

Identification and treatment of the tumor proceeds in a repetitive, step-wise process. Due to the cumulative risk of radiation in this population of patients, it is essential to be mindful of each step in the ablative procedure [33]. Tumor localization is performed using an initial helical scan incorporating the entire region of the kidney with settings of 100–150 mAs and 120 kV. Once identified, the tip of the probe is placed up to the edge of the tumor along the expected trajectory required for treatment. For more anteriorly located tumors, a 5% dextrose solution in water is infused into the perinephric space to increase the distance between the renal lesion and closely neighboring structures, such as bowel. Probe placement is then performed utilizing repetitive CT scans at lower settings of 70–100 mAs and 120 kV, limiting the number of images to 3–6 per scan. At the authors' institution, a 14G Starburst XL (Angiodynamics) probe is then deployed and its position is adjusted to ensure complete lesion coverage plus a peritumoral margin of at least 5 mm. A confirmatory helical scan is then performed in order to confirm adequate coverage for the targeted treatment area. Depending on renal function, intravenous contrast is administered in order to define the deep renal margin (50% total normal dose). If no preoperative biopsy is available, an 18G TruCut biopsy may be performed by inserting the biopsy needle parallel to the ablation probe, with confirmation based on repeat imaging. Although the vast majority of our patients undergo preoperative biopsy, for those requiring an intraoperative biopsy, it is our preference to perform the biopsy after probe placement so that any bleeding from the biopsy does not obscure probe positioning. If there is bleeding from the biopsy site, ablation can proceed as planned as bleeding will be rapidly mitigated by the subsequent treatment.

Ablation cycles of 5, 7, and 8 minutes at a target temperature of 105 °C are delivered for tine deployments of <2 cm, 2–4 cm, and ≥4 cm, respectively, with two cycles delivered per treatment. During the brief intervening period between treatment cycles, the passive tissue temperature in each quadrant should be at least 70 °C. Once the ablation is complete, a final helical scan at 100–150 mAs and 120 kV can be utilized to look for perinephric bleeding and procedural complications. Depending on renal function, contrast may be administered to define a lack of enhancement (50% total normal dose) and determine early procedural success. If inadequately treated areas are identified, the radiofrequency probe is repositioned and the treatment is repeated. The probe tract is then ablated during probe withdrawal, maintaining a temperature of 70 °C up to the level of the fascia.

See accompanying Video 125.1 .

### Laparoscopic radiofrequency ablation

Laparoscopic RFA may be used for ablation of anterior or centrally located tumors. A transperitoneal approach is generally used. The kidney is mobilized, Gerota's fascia is entered and the lesion is exposed. The radiofrequency probe is inserted percutaneously through a separate stab incision and is deployed under laparoscopic ultrasound guidance, ensuring that the treatment tines extend beyond the tumor edge and the deep margin. At conclusion of the treatment cycles, a 5 mm toothed forceps may be used to obtain a biopsy of the mass, followed by reapproximation of Gerota's fascia prior to port removal and closure.

## Postoperative surveillance

The National Cancer Center Network (NCCN) recommends surveillance with a history, physical exam, and comprehensive metabolic panel every six months for 2 years, then yearly until 5 years post ablation. Surveillance imaging should include yearly chest X-rays for 5 years, initial abdominal imaging 3–6 months post ablation, and yearly abdominal imaging for 5 years [34]. At our institution, we follow the above NCCN protocol with the exception that a contrast-enhanced CT or MRI is performed at six weeks post ablation to look for early success and in order to define recurrence versus incomplete ablation. All images are reviewed by both a radiologist and urologist to evaluate for any remaining tumor or recurrence.

It is important to note that during ablation, along with coagulative necrosis and tissue desiccation, significant localized inflammation will occur around the ablation bed. Thus, immediate post-RFA imaging will show circumferential high attenuation around the ablation zone, which is a normal finding that can be mistaken for persistently viable tumor [14, 35]. In actuality, this area corresponds to a hyperemic inflammatory response of surrounding normal parenchyma, as shown on histologic inspection. True ablative effects cannot be fully appreciated until completion of coagulative necrosis at seven days after the procedure [15]. As mentioned above, complete destruction of renal architecture and cytoplasmic border loss may take weeks to occur; thus, waiting for six weeks to perform initial imaging allows sufficient time to accurately assess for incomplete versus successful ablation.

## Defining treatment failure

Any enhancement within the ablated zone on the initial imaging or enlargement of the lesion regardless of enhancement is considered an incomplete ablation. The most common finding when incomplete ablation is identified is a crescent-shaped area of enhancement on the medial margin of the ablated zone (Figure 125.1). This should be differentiated from recurrence, which is defined as enhancement within the ablated zone after a normal initial CT or MRI. Although incomplete ablation is typically found on the periphery, recurrence can occur at any location within the ablation zone. Importantly, lesions treated with RFA will demonstrate a characteristic fibrotic halo or circular demarcation around the treatment zone representing a foreign body giant cell fibrotic response [36]. This should not be misinterpreted as persistent or recurrent disease (Figure 125.2). Unlike cryoablation, involution of ablated lesions may not routinely occur, and thus should not be used as a marker for success. The two most important requirements for determining radiographic success of RFA are a lack of growth within the ablated lesion and lack of contrast enhancement [37].

Although an imaging-based definition for success has been most utilized, some question its validity [38] given that post-ablation biopsies may show intact tumor cells on

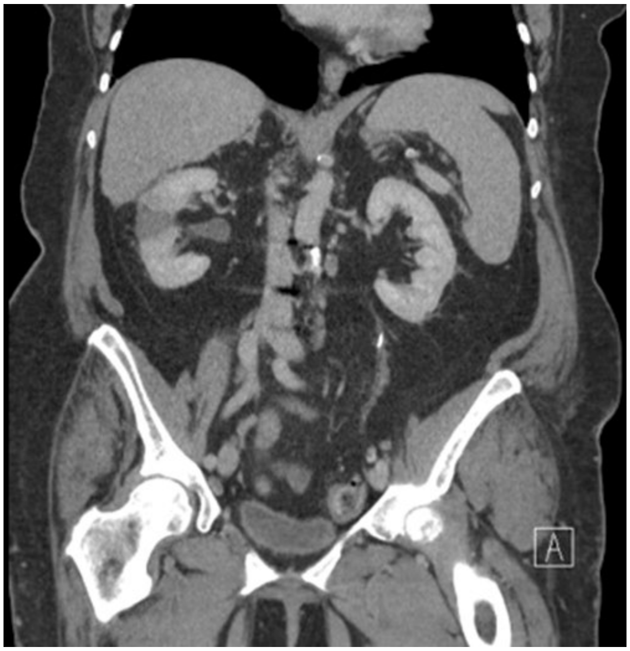

**Figure 125.1** A 75-year-old female 6 weeks after right percutaneous radiofrequency ablation showing incomplete ablation with nodular enhancement at the superior aspect of the ablation zone. The patient underwent a secondary ablation with no evidence of enhancement at subsequent six-week follow-up.

hematoxylin and eosin (H&E) staining. However, cellular viability as determined by nicotinamide adenine dinucleotide (NADH) diaphorase staining routinely demonstrates a lack of cellular viability [39, 40] in light of maintained architecture. In addition, Anderson et al. found that 14% of biopsies done within 150 minutes of ablation showed viable tissue in a porcine model, while no lesion biopsies after 3 hours showed viability, suggesting that biopsies performed too close to the time of ablation do not accurately characterize the full RFA ablative effect. Therefore, the timing of biopsies and method of staining after RFA are essential when evaluating for cellular viability and should be interpreted carefully. Given the difficulty in interpreting immediate post-RFA biopsies, we do not currently recommend postoperative biopsy in patients with good radiographic response to RFA.

## Complications

The overall complication rate following RFA is 8–11% [41–43], with a 4–6% rate of major complications [16, 43–46]. Multiple studies have also suggested a higher rate of complications with laparoscopic ablation [46, 47], as compared to percutaneous, due to laparoscopic technique [41], but rates remained lower than those for extirpative procedures [16]. Importantly, with increasing experience complication rates, regardless of surgical approach, decrease [41, 46].

The two most common complications of percutaneous RFA are bleeding and postoperative pain. Perinephric, subcapsular, or retroperitoneal hematomas can be seen in 3–6% of all patients and are typically managed conservatively. Tumors >3 cm in size are noted to have higher complication rates, primarily due to hemorrhage [48]. Pain and/or parasthesias at the probe site occur in up to 8% of RFA patients [42, 49], although the incidence has decreased over time. Evolution of ablation probe design with an insulation sheath, careful grounding pad placement, and maximizing the renal-body wall distance with positioning or hydrodissection [50] can help avoid damage to posterior abdominal wall cutaneous nerves [50, 51]. Transient hematuria and increased serum creatinine are also commonly reported and can typically be managed conservatively with spontaneous resolution.

With respect to major complications, significant blood loss [46] and urothelial injury are the most common [43, 45] but constitute less than 3% of all complications. Hemorrhage requiring transfusion may occur in 1.4–4% of patients treated with RFA [16], but the need for selective angioembolization is quite rare. The main risk factor associated with significant hemorrhage is the placement of multiple probes for larger renal masses. Bleeding during percutaneous needle placement can be controlled by proceeding with the ablation given the coagulative nature of RFA, while bleeding during laparoscopic ablation can be managed with hemostatic agents and/or direct pressure. Abdominal wall bleeding, namely from the intercostal arteries, can also occur and is typically identified as an expanding hematoma during routine imaging at the conclusion of the procedure. Bleeding at this point in the procedure should be evaluated for severity by performing serial scanning at 10 minutes after the ablation and prior to awakening the patient from anesthesia. If the hematoma is rapidly expanding or the patient becomes unstable, angiographic embolization may be required. Urothelial injury most commonly presents as a urine leak and may require ureteral stent placement with or without percutaneous drain placement depending on the severity of the urinoma. Other urothelial-related injuries, including ureterocutaneous fistula [52] and ureteral/UPJ stricture formation [43, 45], understate the need for careful tumor selection when in juxtaposition to the UPJ or upper ureter.

Damage to surrounding organs, including liver, pancreas, spleen, colon, and pleural cavity are exceedingly rare and can be minimized through appropriate patient selection, preoperative planning, and good surgical technique. Often these injuries occur in patients with anteriorly located tumors, tumors in close proximity to the collecting system, or tumors without a suitable access

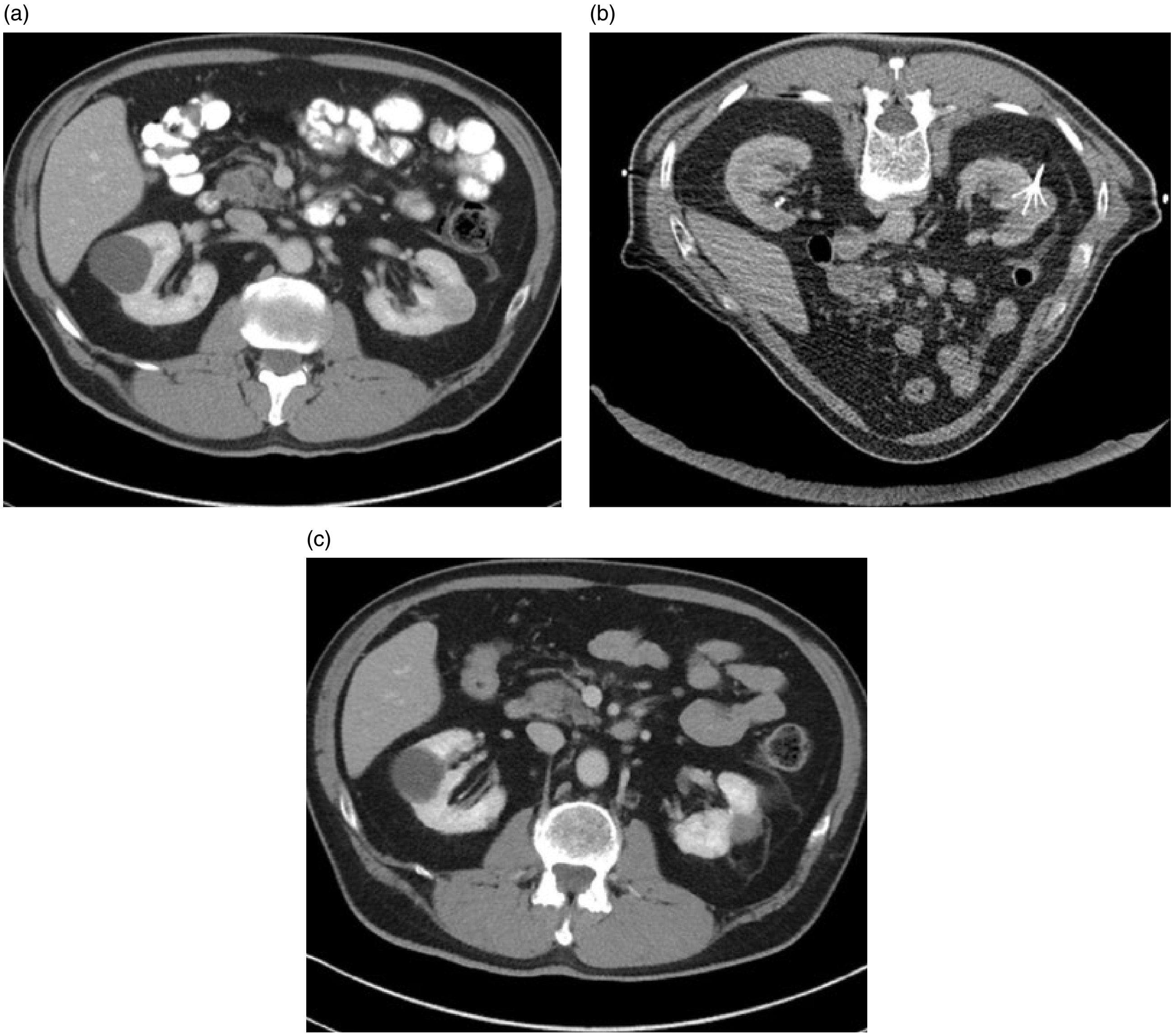

**Figure 125.2** A 63-year-old male with biopsy-proven 2.5 cm left renal cell carcinoma (R.E.N.A.L. nephrometry score = 8). (a) Preoperative axial CT. (b) Intraoperative tine deployment. (c) Postoperative CT at six months showing hyperdense area with lack of contrast enhancement and characteristic peritumor "halo."

tract for needle placement on preoperative imaging. Recognition that such injuries can occur and early identification of these injuries is paramount.

Injury to the pleural cavity, most often a pneumothorax or hemothorax, can occur with probe placement above the 12th rib. These complications are typically recognized during the procedure as either ventilation difficulties or, with percutaneous access, on routine imaging (Figure 125.3). If a simple pneumothorax is identified, it can be treated by aspiration using a small needle inserted into the pleural space at the conclusion of the case. If a large or persistent pneumothorax or large hemothorax is noted, placement of a chest tube should be performed. Postoperative chest pain or dyspnea should trigger suspicion of such an injury and prompt an upright chest radiograph.

Colonic injury should be managed in conjunction with a general surgeon given the spectrum of injury that can occur. In the setting of a frank colon perforation with signs of peritonitis, prompt surgical exploration should be undertaken. Colonephric fistulas can form and can be managed initially with placement of a ureteral stent. Patients with a persistent fistula or colocutaneous fistula may require surgical diversion or a trial of total peripheral nutrition. In tumors with close proximity to bowel, hydrodissection by injection of saline into the plane

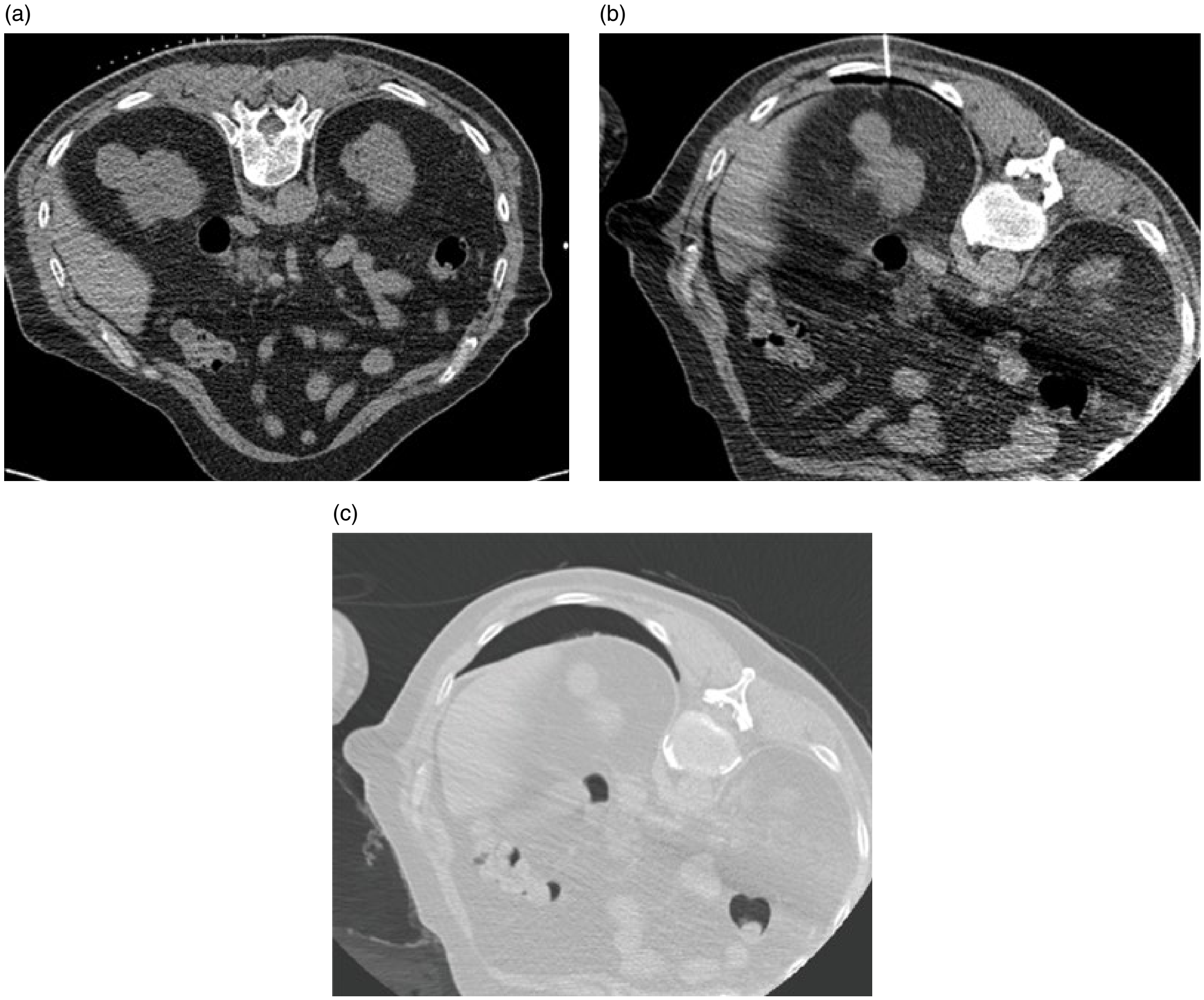

**Figure 125.3** A 71-year-old with 3 cm right renal cell carcinoma. (a) Initial imaging does not indicate the presence of the pleural space. (b) During placement of the probe intraoperatively, the needle is seen to be traversing the pleura. (c) Lung windows demonstrate expansion of the pneumothorax, which prevented percutaneous ablation at this setting. The pneumothorax resolved spontaneously and the patient subsequently underwent percutaneous ablation with a more inferior needle placement three months later.

between the tumor and colon can develop a safe working space around the tumor [31, 50] but ultimately depend on surgeon comfort and familiarity with anatomic landmarks.

Postoperative infection following ablation, in the absence of a large hematoma or urinoma, is exceedingly rare but may be lethal [53]. Patients most at risk for infection are those with chronic colonization of the urinary tract (e.g. ileal conduit) or active infection at the time of the procedure [52]. When infectious complications do occur, they typically present in a delayed fashion (1–6 months post procedure) as chronic drainage or a retroperitoneal abscess. Patients at risk for urinary tract infection should be screened by urine culture and treated appropriately prior to their ablation procedure. We routinely administer perioperative prophylactic antibiotics at the time of the surgery at our institution.

In an effort to objectively determine the risk of complications, several authors have attempted to utilize the R.E.N.A.L. nephrometry score [54], as has been done with extirpative therapy [12], to predict the risk and severity of RFA complications. Many conflicting studies have been reported and the debate is ongoing [53, 55].

## Overall outcomes

In considering the existing literature, there are multiple confounding factors that make interstudy comparisons difficult, including ablative technique (laparoscopic vs.

percutaneous), small cohort sizes, lack of uniform preablation biopsy, short-to-moderate follow-up, inclusion of patients with hereditary cancer syndromes, and variable definitions of recurrence. However, taken together, over intermediate-to-long follow-up, local recurrence-free survival can be expected in up to 88–95% of patients at 3–5 years [23, 24, 44, 47, 56–59].Both metastasis-free survival (87–100%) and cancer-specific survival (97–100%) [23, 45, 56, 57, 60] are excellent and similar to that reported for partial nephrectomy. Table 125.1 summarizes the most recent long-term series of RFA outcomes.

Although overall survival is an important metric in any study, its significance in the study of RFA tends to represent the patient population being treated rather than the oncologic nature of the cancer. Patients undergoing RFA tend to be older and have higher comorbidities than those undergoing extirpative surgery [16, 62]. Multiple large series have reported an overall survival of only 75–85% at 5 years [24, 60, 62], but with the recent shift to offer RFA to a less morbid population, along with refinement of the technique, excellent overall survival rates with medium-length follow-up have been reported (98–100%) [23, 56, 57]. Further assessment of these patients for long-term durability (10 years) will help to better shape the role of RFA in younger and healthy patients.

Comparison among ablative therapies is challenging for the aforementioned reasons, but, in experienced centers, there does not appear to be a difference in oncologic outcomes between RFA and cryoablation [16, 59, 63]. Furthermore, experience to date suggests that progression-free survival and disease-specific survival are similar for RFA and extirpative therapy (both exceed 90%). Two single institution comparisons have shown similar rates of local recurrence between RFA and PN [56, 62], but reached opposite conclusions regarding metastasis-free survival likely due to patient selection bias.

One other major advantage to ablative therapy when compared to extirpative surgery is the minimal impact on overall renal function after intervention. Most reports suggest a modest 2–10 $\text{ml/min/m}^2$ reduction in glomerular filtration rate (GFR) following RFA [57, 64] and a significantly lower number of patients with new-onset stage 3 CKD [65]. Improved renal function preservation has also been shown when treating tumors on solitary kidneys [66], likely due to not clamping the renal hilum and the precision of imaging guidance limiting the damage to adjacent normal parenchyma.

## Subgroup outcomes

As emphasized above, patient selection is very important when considering treatment options. The first parameter which should be considered is tumor size. While no specific cutoff has been established, RFA outcomes appear to be optimal in patients with tumors up to 3 cm. Best et al. noted a significantly higher 5-year disease-free survival for tumors <3 cm compared to those >3 cm (91% vs. 79%, $P = 0.001$) [67], while Psutka et al. identified a significant 5-year disease-free survival difference between T1a (91.5%) and T1b tumors (74.5%, $P = 0.003$) [60]. Although the AUA guidelines suggest that tumors greater than 4 cm may be treated by RFA [16], many centers avoid ablation of T1b tumors, regardless of comorbidity status, for these reasons. When RFA is reserved for smaller tumors, several studies report oncologic efficacy similar to that for partial nephrectomy [68, 69].

Other tumor characteristics beyond size are important in assessing RFA efficacy. Schmit et al. demonstrated that increasing tumor complexity, as measured by R.E.N.A.L. nephrometry score [54], is correlated with increasing treatment failure [53]. However, many patients undergoing RFA fall into the lowest or intermediate-risk groups based on tumor size cutoffs, making it difficult to discern risk between low nephrometry tumors in predicting procedural risk. Gahan et al. used a modified nephrometry score (adjusting the size scoring to be 1 point for <3 cm, 2 points for 3–4 cm, and 3 points for >4 cm) in 192 patients with moderate follow-up (32 months) [70]. No difference in initial ablative success or 3-year recurrence-free survival was noted with standard nephrometry scoring, but the modified score ("R-score") was significantly associated with both initial ablative success and 3-year recurrence-free survival. In addition to size and location, which are the primary measurements for the R.E.N.A.L. nephrometry score, preoperative tumor enhancement of >60 HUs has also been shown to be independently predictive of an incomplete initial ablation [71], potentially due to heat sink from highly vascular tumors.

Some authors have reported inferior initial treatment outcomes with the percutaneous approach compared to the laparoscopic approach but with similar effective treatment rates after a secondary procedure [46]. This is likely due to less aggressive initial treatments with RFA compared to those undergoing extirpative treatment, given the perception that percutaneous treatments are easily repeatable. Surgeons performing percutaneous ablation, therefore, may be more accepting of persistent disease on short-term follow-up, presuming that the tumor may be completely ablated with a second, minimally invasive procedure.

Other considerations include advanced age (>80 years old), which showed good efficacy and no major complications in a small series [72], as well as improved outcomes in patients with papillary disease (vs. clear cell) [73]. The latter has been postulated to be due to the less vascular nature of papillary tumors leading to less heat

**Table 125.1** Intermediate and long-term outcomes after radiofrequency ablation for renal tumors.

| Author | No. of patients (no. of tumors) | Follow-up (years) | Tumor size (cm) | Technique | No. of prebiopsy proven RCCs (%) | % Local recurrence-free survival | % Metastatic recurrence-free survival | % Disease-free survival | % Cancer-specific survival | % Overall survival |
|---|---|---|---|---|---|---|---|---|---|---|
| Tracy et al. 2010 [24] | 208 (243) | Mean 2.25 | Mean 2.4 | 172 Percutaneous<br>68 Laparoscopic<br>3 Open | 179 (79) | 5-yr 90[a] | 5-yr 95[a] | — | 5-yr 99.4[a] | 5-yr 85 |
| Best et al. 2012 [58] | 142 (159) | Median 4.3 | Median 2.4 | 102 Percutanous<br>57 Laparoscopic | 108 (72) | — | — | 5-yr 91% | — | 5-yr ~75 |
| Olweny et al. 2012 [56] | 37 (37) | Median 6.5 | Median 2.1 | 25 Percutaneous<br>12 Laparoscopic | 37 (100) | 5-yr 91.7 | 5-yr 97.2 | 5-yr 59 | 5-yr 97.2 | 5-yr 97.2 |
| Atwell et al. 2013 [61] | 222 (256) | Mean 2.8 | Mean 1.9 | 256 Percutaneous | 256 (100) | 5-yr 98.1 | 5-yr 98.1 | — | 5-yr 98.7 | — |
| Psutka et al. 2013 [60] | 185 (185) | Median 6.4 | Median 3 | 185 Percutaneous | 185 (100) | 5-yr 95.2 | 5-yr 99.4 | 5-yr 87.6 | 5-yr 99.4 | 5-yr 73.3 |
| Wah et al. 2014 [45] | 165 (200) | Mean 3.9 | Mean 2.9 | 200 Percutaneous | 183 (91.5) | 5-yr 93.5 | 5-yr 87.7 | — | 5-yr 97.9 | 5-yr 75.8 |
| Ramirez et al. 2014 [47] | 79 (111) | Median 4.9 | Median 2.2 | 111 Laparoscopic | 61 (77) | — | 5-yr 100 | 5-yr 93.3 | 5-yr 100 | 5-yr 72% |
| Lorber et al. 2014 [57] | 50 (53) | Mean 5.5 | Mean 2.3 | 29 Percutaneous<br>24 Laparoscopic | 53 (100) | 5-yr 92.5 | — | 5-yr 90.6 | 5-yr 100<br>10-yr 100 | 5-yr 98<br>10-yr 93 |
| Thompson et al. 2015 [62] | 180 (180) | Median 3.6[b] | Median 1.9 | 180 Percutaneous | 73 (41) | 3-yr 98.1 | 3-yr 93 | — | — | 3-yr 82 |
| Ma et al. 2014 [23] | 52 (58) | Mean 5 | Mean 2.2 | 34 Percutaneous<br>24 Laparoscopic | 55 (95) | 5-yr 94.2<br>10-yr 94.2 | 5-yr 100<br>10-yr 100 | 5-yr 94.2<br>10-yr 94.2 | 5-yr 100<br>10-yr 100 | 5-yr 95.7<br>10-yr 91.1 |

[a] Considered only patients with biopsy confirmed malignancy.

[b] Only considers patients still alive.

loss during ablation. Further evaluation is warranted to better highlight those patients who would optimally benefit from ablation.

## Conclusions

Given the currently available data, RFA is an acceptable alternative treatment modality to extirpative therapy for small renal masses (<4 cm). RFA has similar oncologic outcomes to extirpative therapies as well as low rates of morbidity and good preservation of renal function. With appropriate patient selection, oncologic outcomes with RFA appear similar to other ablative therapies, as well as partial nephrectomy. RFA is technically less challenging than partial nephrectomy, though learning curves exist for patient selection, tumor targeting, probe deployment, and generator use. Characteristics that have been shown to make a tumor particularly amenable to RFA include posterior location, <3 cm, enhancement less than 60 HUs, >0.5 cm from the ureteropelvic junction or renal pelvis, and >1 cm from surrounding bowel. Ultimately, the decision to treat a small renal mass with RFA should be decided on an individual basis taking into consideration tumor-related characteristics, patient demographics, patient comorbidities, and patient preference.

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# Percutaneous Cryoablation of Renal Masses

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## Introduction

Renal cell cancer (RCC) represents 2% of adult cancers and is the third most common urinary tract malignancy [1–3]. Disease epidemiology is poorly understood, although smoking, obesity, and acquired cystic renal disease have been identified as risk factors [1]. The natural history of renal cancer is typically one of a long period of indolent growth in asymptomatic patients. Clinical presentation on the basis of symptomatology usually indicates advanced disease, with metastasis likely, portending a poor prognosis. The advent of modern imaging, combined with changing diagnostic algorithms and practices, has led to a serendipitous increase in diagnosis of small renal tumors. It is estimated that as many as 70% of diagnosed renal tumors are stage T1a. Small renal masses within this size range have been shown to grow at an average rate of 0.3–0.4 cm/year and exhibit a very low rate of progression to metastatic disease [1–4]. Of small renal masses, 80% represent RCC, but approximately 20% are benign [1]. This raises the management dilemma of active surveillance or extirpative therapy; the more aggressive approach, while definitively treating the tumor, would lead to the treatment of many indolent tumors of uncertain malignant potential [5]. An important concept in the management of renal tumors is cytoreductive therapy. No matter how large or the extent of metastatic disease, there still appears to be benefit to treatment in most situations. The Southwest Oncology Group 8948 and European Organization for Research and Treatment of Cancer (EORTC) 30947 trials demonstrated superiority of nephrectomy + interferon-α over interferon-α alone with 3- and 10-month survival benefit [6]. Patient selection is important for optimization of therapeutic benefit and efficacy. Currently, in most settings, ablation patients are typically poor surgical candidates, or those require nephron sparing, usually on the basis of prior resections and/or renal insufficiency. Typical patients have tumors of TNM staging T1a (limited to the kidney and less than 4 cm) [1]. In addition, it is the opinion of the authors that based on the current data, even good surgical candidates with lesions less than 2.5–3 cm in ideal anatomical locations, are also appropriate candidates for cryoablation. Finally, efficacy has also been demonstrated in treating T1b tumors (limited to the kidney and between 4 and 7 cm) but there is no question that based on oncological outcomes, patients in this category, who are likely to tolerate surgery with general anesthesia, should undergo nephrectomy [5].

## Historical perspectives

The first account of the use of cryotherapy to ablate tumors was by James Arnott in the 1800s using combination of ice and salt applied topically to palliate breast and cervical cancer [7, 8]. Topical techniques were further refined in the early 1900s with the use of compressed air, and eventually compressed liquified $CO_2$ to treat dermatologic conditions [9]. By 1967 Ortved et al. published a report of 100 cases using intense cold from liquid nitrogen to ablate tissue from the obstructed prostate gland [10]. Renal cryosurgery followed in 1968 by Lymberopoulos [11]. A shift from liquid nitrogen-based systems to argon gas-based ones occurred in the 1970s and entered mainstream use by the 1990s. This enabled a substantial reduction in probe size, allowing for percutaneous applications [7]. While gaining traction in the treatment of liver tumors in the early 1990s, popularity declined soon after, which some have attributed to

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complications such as cryoshock or tissue “craking.” Cryoshock is believed to be a cytokine-mediated systemic response to cryoablation that results in hypotension, decreased renal function, coagulopathy, respiratory dysfunction, and multiorgan failure. Although this phenomenon was believed to be relegated to hepatic tumor ablations, usually during open procedures, it was not until the late 1990s that tumor cryoablation, in all organs, saw the resurgence in interest that has resulted in its routine use today.

## Physical principles of cryoablation

Cryoablation utilizes the Joule–Thomson effect, by which a high-pressure gas cools as it expands [7]. A closed circuit of high-pressure argon or nitrogen is passed through a metallic probe, resulting in formation of an iceball around the probe. In contrast, helium warms during expansion, enabling its use in some of the available systems for thawing and to facilitate probe removal [7].

The destruction of tissue is achieved via a number of mechanisms, both direct and indirect, which occur at various phases in the freeze–thaw cycle.

### Direct cellular injury

During the freeze phase, temperatures rapidly reach −165 °C to −190 °C in the region immediately surrounding the probe. Ice crystals form predominantly in the extracellular space. The resultant osmotic gradient draws water out of the cell, leading to cellular dehydration. The osmotic pressure that develops during freezing due to water flux is sufficient to cause rupture of cellular plasma membrane. As intracellular ice crystals form, protein denaturation damages organelles, leading to cellular death.

During the warming phase, ice crystals coalesce into larger crystals, which disrupt the cellular membrane. In addition, laboratory biochemical analyses suggest that decoupling of oxidative phosphorylation during this phase effectively halts the cellular machinery.

Warming initially affects extracellular ice, causing a reversal of the osmotic gradient, which causes an influx of water, increasing cellular volume and leading to membrane rupture and cellular necrosis. Histopathologic analysis suggests that lethal intracellular ice crystal formation predominates in the region closest to the probe, while osmotic effects predominate at the periphery of the freezing zone [12].

### Indirect effects

Indirect effects occur via microvascular occlusion during freezing, with subsequent glomerular congestion and tubular necrosis [12]. During freezing, vasoconstriction and eventual cessation of blood flow to the ablation zone damages the vascular endothelium. During warming, vasodilatation occurs, increasing vascular permeability. Platelet aggregation occurs due to activation by the damaged endothelial lining, triggering microvascular thrombosis, acute ischemia, and hypoxia [12].

These mechanisms result in local ischemia and necrosis of the tumor and surrounding margin. In the long term, scarring and fibrosis have been demonstrated in the ablation zone.

Successful tissue ablation requires close monitoring of many factors, including the number of freeze–thaw cycles, rapid cooling, lowest temperature achieved, duration of ablation, and slow thawing. The lethal temperature of normal tissue is −19.4 °C, whereas the fibrous nature of tumor enables it to tolerate lower temperatures. Studies of different tissue and tumor types have shown a range of −20 °C to −40 °C to be ideal for tumor lethality when used with multiple freeze–thaw cycles. The additional benefit of multiple freeze–thaw cycles is attributed to more rapid cooling during successive cycles and increase of the frozen tissue volume.

## Treatment and techniques

### Extirpative therapy

For over 50 years, radical nephrectomy had been the standard treatment for RCCs. As high-resolution cross-sectional imaging has gained widespread use, renal tumors are diagnosed at an earlier stage, which some have referred to as a staging migration. This staging migration of renal cancer diagnoses has been accompanied by a shift in the treatment algorithms to include minimally invasive and nephron-sparing techniques [13]. Guidelines from the American Urological Association (AUA) published in 2009 reflect this shift and recommend partial nephrectomy for solitary renal masses if technically feasible. Radical nephrectomy, ablation, or active surveillance are recommended as alternatives based on tumor characteristics or patient-specific factors or preference [14]. Huang et al. wrote in 2015 that the number of partial nephrectomies eclipsed radical nephrectomies by 2009 [15].

Although partial nephrectomy currently remains the treatment of choice, ablation has become an attractive alternative in patients with comorbidities. Cryoablation, when compared to robot-assisted partial nephrectomy, demonstrated somewhat lower 5-year disease-free, cancer-specific, and overall survival rates of 83.1%, 96.4%, and 77.1%, respectively, in the cryoablation cohort versus 100%, 100%, and 91.7% in robot-assisted partial nephrectomy [16]. Cryoablation offers practical advantages over more invasive treatments. One such advantage over surgery is reduced intraoperative blood loss and postoperative hematoma. This has been attributed to absence of a need for renorrhapy or dissection of the hilum with vascular clamping. Ablation probes can be placed under image guidance in a peripheral manner, thereby avoiding larger vessels. Other complications are also fewer, namely urinary leaks and requirement for ureteral stenting. Adverse effects on renal function following either partial nephrectomy or cryoablation appear to be equally rare [17]. Short hospital stays have also been reported of 72 hours on average for partial nephrectomy compared to the usual practice of cryoablation being performed on an outpatient basis [17]. Finally, cryoablation offers easier localization and access to endophytic and posterior lesions [1].

## Other ablative technologies

The most studied minimally invasive ablation technologies are radiofrequency and cryoablation, although newer technologies are gaining traction, such as microwave ablation and irreversible electroporation. Cryoablation differs from these less in its clinical efficacy, and more in practical matters, which affect the overall precision and risk profile of the procedure.

One such distinction between cryoablation and other ablative techniques is the relative imaging conspicuity of the iceball; and laboratory studies have confirmed that cryoablation provides superior imaging of the forming iceball with both CT and grayscale ultrasound [12]. Although we understand that the very peripheral aspect of the visualized iceball is nonlethal, the ability to see the applied energy as opposed to just predicting this from the probe geometry, as in other thermal ablation techniques, allows for better confirmation of accurate probe placement and therefore lesion coverage during the freezing process.

Another advantage of cryoablation is the reduced anesthesia requirements when compared to heat technologies. A retrospective clinical trial performed by Allaf et al., comparing anesthesia data for both radiofrequency ablation (RFA) and cryoablation in populations with similar demographic and tumor characteristics, showed an overall decreased need for nacrotics in the patients undergoing cryoablation [18]. A much larger retrospective study by Truesdale et al. also noted overall less sedation (midazolam) and narcotic (fentanyl) medications required for cryoablation compared to RFA [19]. This is thought to reflect partial anesthetic effects of cold. Some theorize that the microvascular occlusive effects of ice formation may also mitigate the heat sink effects of ablation of tumors near vessels. Both studies anecdotally mention the requirement for sedation reversal in the RFA groups, which may support a higher level of patient safety and comfort with cryoablation.

Ablation procedures are often performed with CT guidance. As mentioned in the Procedure description section, with each pass, the patient is moved in and out of the CT gantry. Vigilance is thus required to ensure that the cables connecting the needles, as well as the gantry itself, do not dislodge or deflect the probes from their intended trajectory. Cryoablation probes are equipped with a stick mode, which lowers the temperature around the probe just enough to provide traction, further securing it within the patient [20].

There is always concern for collateral injury during percutaneous ablation procedures. Cryoablation is advantageous over the heat-based ablative technologies, as even when included in the cryoablation zone, damage to or rupture of the collecting system is still unlikely [7, 21]. Studies have shown that indirect injuries to the collecting system were less common than when using heat-based systems [22]. There is no urothelial injury in cryoablation, which enables the cryodamaged collecting system to heal in a watertight fashion, virtually eliminating leak or urinoma formation as a complication [7, 21]. In a retrospective review of 67 cases, where imaging demonstrated overlap of the iceball with collecting system, no cases resulted in urinoma [23].

## Radiofrequency ablation

If any clinical difference in outcome exists between RFA and cryoablation, it would require a large, high-powered study to elicit such differences as studies have shown virtually no difference in progression to metastatic disease [2, 3, 24]. A laboratory comparison of needle-based ablation techniques in animal models demonstrated skip areas in impedance-based RFA, whereas heat-based RFA and cryoablation resulted in complete necrosis of treated lesions [12, 14, 25].

Although studies have demonstrated a reduced risk of tumor seeding of the needle tract in either modality, RFA allows cauterization of the puncture tract to minimize seeding as well providing as potential hemostatic effect [7]. Newer cryoablation systems, however, also allow this function, enabling more rapid thawing as well as tract ablation.

Differences in technical success also favor cryoablation over RFA. Studies that include long-term follow-up have suggested fewer retreatments required in cryoablation compared to RFA [2, 3]. Finally, cryoablation results in significantly lower rates of local tumor progression compared to RFA [2, 3]. Nevertheless, complication rates between cryoablation and RFA are less clear and some studies have shown slightly higher bleeding complications in cryoablation compared to RFA [21].

Overall, the role of cryoablation may edge out RFA on the basis of economics and cost-effectiveness. In an economic analysis, patients undergoing RFA had a lower quality-adjusted life expectancy [13]. The cost of cryoablation is approximately US$3010, whereas RFA had costs of US$3231–6398 [13]. It is interesting to note that US-based cost-efficacy analysis showed active surveillance with later cryoablation to be the most effective approach [13, 26].

### Microwave ablation

Microwave ablation is a technology which has gained recent enthusiasm due to its success with liver masses. A form of heat-based thermal ablation, it utilizes electromagnetic waves, which are oscillated to cause polar water to vibrate, producing friction and heat. Cell death occurs from coagulative necrosis [27]. It is currently under investigation for RCC [13].

### Irreversible electroporation

Irreversible electroporation employs the use of electric probes to employ rapid alternating electric pulses to induce microscopic pores in the cell membrane, leading to tissue necrosis. Irreversible electroporation may allow for ablations closer to critical structures. This nonthermal technique requires close cardiac monitoring, general anesthesia, and neuromuscular blockade [7]. It is currently still under investigation [28, 29].

## Procedure description

Planning cryoablation of a renal mass depends on a multitude of anatomic and physical factors. At our institution, prone or slight lateral supine oblique positioning is preferred [30]. Moderate or deep sedation and a local anesthetic are administered prior to the procedure [29]. In prone patients in whom adequate ventilation and monitoring might be an issue, the authors have a low threshold for endotracheal intubation with general anesthesia, compared with the option of light or no sedation.

The lesion is localized with CT, and then a needle biopsy is usually performed with specimen provided to the pathologist or cytopathology technologist, who examines the specimen with touch prep within the procedure suite [29]. The lesion is localized with an initial unenhanced scan and intravenous contrast only used when it is unclear if the ablation zone is adequate to cover the tumor.

In planning a safe kill zone, attention to patient position and the consequent varying spatial relationships with adjacent visceral structures is required. Traditionally, a transperitoneal approach is utilized for anterior or anteromedial tumors and a retroperitoneal one for posterior and posterolateral tumors [1]. The ideal distance of the kill zone from the renal hilum is at least 5 mm, and from bowel is 10 mm. Different positions may also help with optimizing distance from surrounding critical structures [31].

Probe number and size are also important factors to consider. Smaller, multiple cryoprobes provide synergistic effects which expand the freezing and lethal zones between closely positioned probes [32]. Ideally, one probe should be used for every cubic centimeter of tumor [1].

A technique uniquely available to cryoablation probes is the use of “stick” mode available to enable the operator to distance the targeted lesion from nearby structures with the use of probe traction. The kidney is fixed via ligamentous attachments surrounding the hilum, however, no attachments exist around the capsule. As a result, the kidneys are mobile within the perinephric space. This can make penetrating the kidney difficult at times, as the kidney may move close to sensitive structures in the process of piercing the target lesion. Once the needle traverses the lesion, the probe is placed in “stick” mode. The needle is gently retracted and can be held in place with sterile folded towels placed between the needle hub and the patient (Figure 126.1).

Hydrodissection and pneumodissection are useful techniques to move adjacent viscera away from the ablation zone. We try to achieve the ideal distance of 15–20 mm from target tumor margin [5]. In both techniques, after the first ablation probe is placed and set to “stick,” a second needle is utilized to inject either air and/or saline or dilute contrast in an effort to displace the nontarget tissues from the ablation zone. Pneumodissection, or injection of air, is the preferred dissection medium, as it provides [33] spatial isolation and better thermal insulation than saline from the lethal isotherms (Figures 126.2 and 126.3) [33]. The dissected air also provides a natural negative contrast on CT imaging which is usually performed without intravenous contrast administration. Some advocate the use of 2% contrast-tinted saline when performing hydrodissection to achieve a similar effect [5].

During probe placement, avoidance of the collecting system should only be a concern during puncture and needle placement. Numerous studies have demonstrated safety of inclusion of the collecting system within the zone of the iceball. As long as the collecting system is not punctured with one of the probes, appreciable urine leaks, even in cases of significant collecting system compression by the iceball on CT imaging, have not been reported [30]. Pathological studies suggest that even

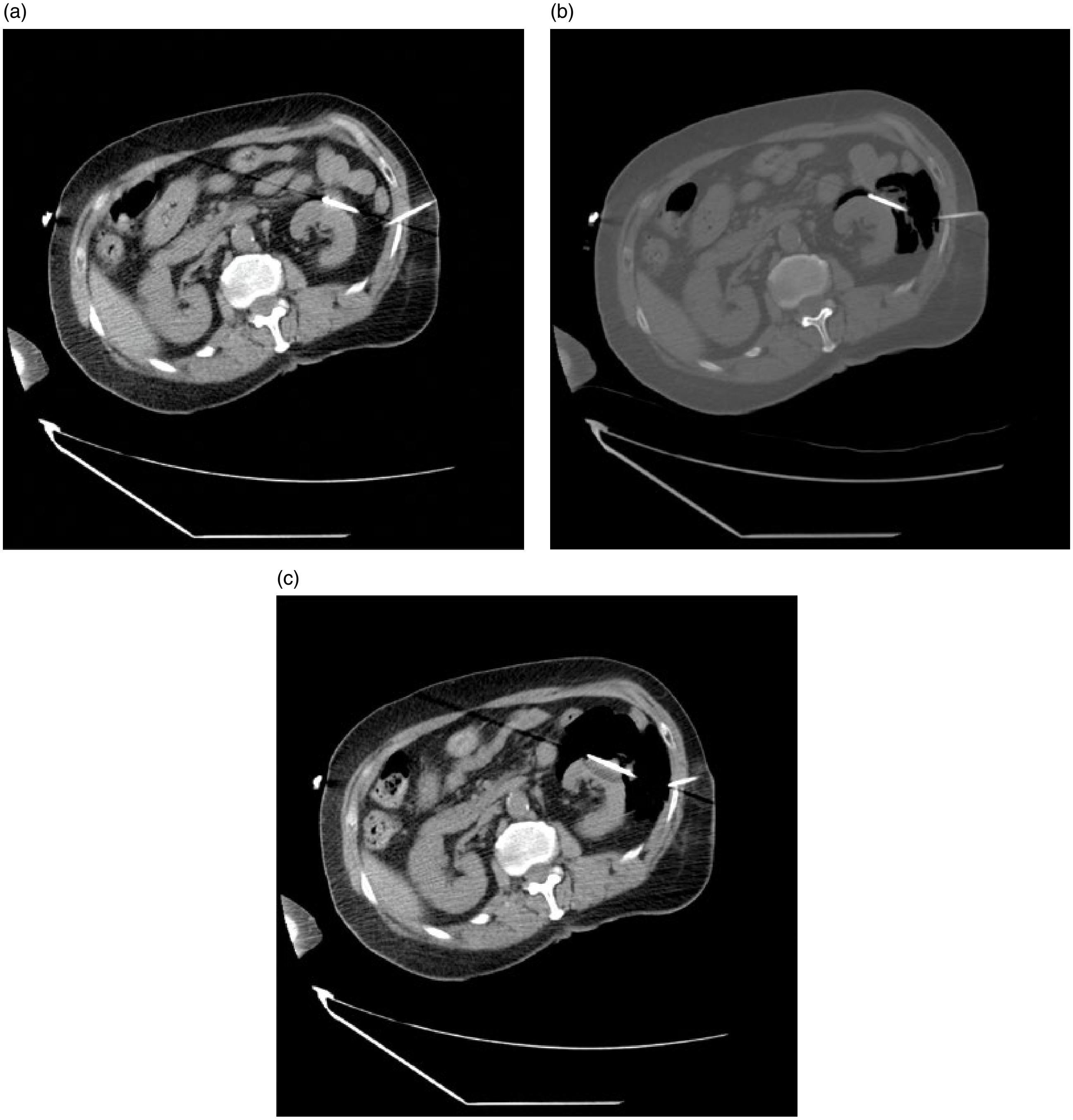

**Figure 126.1** (a) Soft tissue window: cryoprobe traversing lesion. Second needle partially visible, with tip in periephric space. (b) Bone window same level. (c) Bone window: mid-ablation. Layer of air provides distance and thermal insulation ot the adjacent bowel. Hypodense freezing zone is visible.

where partial necrosis is noted in the renal pelvis, structural integrity is preserved, suggesting relative resistance to cryotherapy [5, 7, 12, 34].

Successful ablation rests upon proper monitoring of ablation, rapid cooling, slow thawing, and repetition of the freeze–thaw cycle [7]. A temperature of −40 °C to −50 °C is thought to be required for absolute lethality during a single cycle, but −20 °C to −40 °C has been shown to be sufficient for most solid parenchymal tumors [7]. A distance from the outer margin of iceball to kill zone of 6 mm was demonstrated in animal models [7]. In practice, the targeted iceball should ideally extend at least 5–10 mm past the edge of the tumor [29].

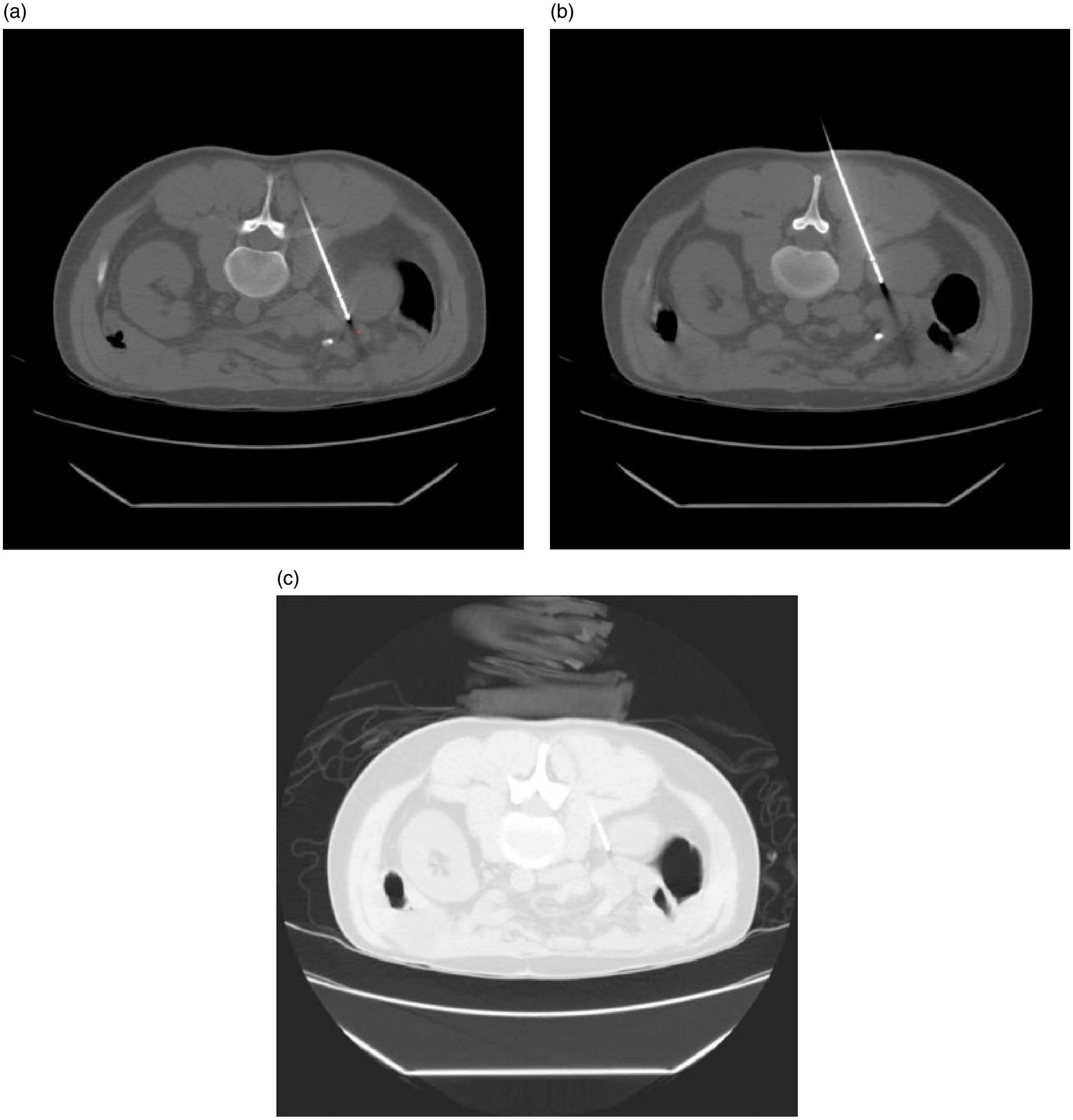

**Figure 126.2** Traction technique. (a) Bone window: cryoprobe traversing exophytic right renal lesion. Notice adjacent duodenum (red asterisk). (b) Using probe in stick mode, the lesion and kidney have been safely retracted away from the bowel. (c) Lung window: adjacent slice demonstrates a stack of towels placed in succession to safely distance the probe kill zone from vulnerable structures.

Some authors vary the length of freeze cycles according to tumor size, ranging from 3 to 12 minutes [30]. Other authors have discussed the use of active versus passive thawing between the two cycles. At our institution a 10-minute active freeze is used for both first and second cycles, with an active intervening thaw cycle [7, 29, 30]. We also recommend a review of intermittent CT to demonstrate iceball progression at approximately 4 and 9 minutes of each freeze cycle [30].

In the immediate postprocedure period, a completion CT is performed to check for bleeding [29]. Postprocedure evaluation of patients should focus on pain, vital signs, and evidence of hematuria on urination. After a brief period of observation, patients are instructed to resume

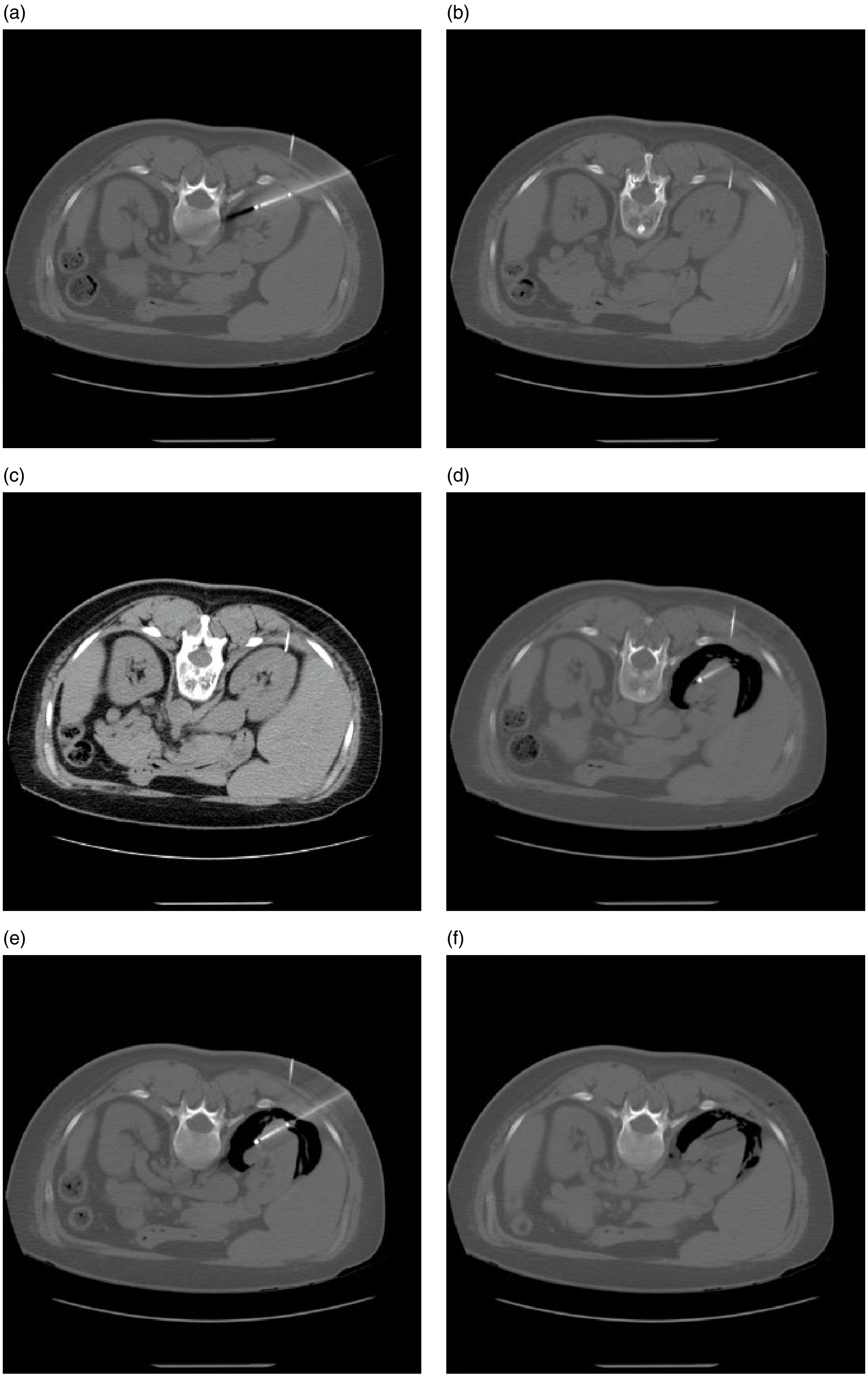

**Figure 126.3** Pneumodissection. (a) Bone window: cryoprobe traversing lesion. (b) Adjacent slice: an additional needle is placed at the renal capsule. (c) Soft tissue window: same level as (b). Air is subsequently insufflated. (d) Bone window: mid-ablation. Layer of air provides distance and thermal insulation to the adjacent diaphragm and abdominal wall, as well as the major nerves traversing the retroperitoneal space, the iliohypogastric, ilioinguinal, and genitofemoral nerves. A hypodense freezing zone is visible. (e) Adjacent slice. (f) Probe has been removed. Air is not evacuated.

activities, and then are discharged home [30]. Evidence of significant hematuria or pain warrants further observation, and in some cases, repeat imaging and admission [30]. Adverse outcomes of pneumothorax, flank paresthesias, and, in rare cases, urinary sepsis, have been reported. Small, self-limited pneumothoraces comprise the largest cohort of adverse immediate outcomes [5].

### Laparoscopic techniques

Cryoablation can be performed both percutaneously or intraoperatively via a laparoscopic approach. Studies have examined the relative efficacy and safety profiles of these two approaches. Although some have argued that laparoscopic approaches offer easier access to anteriorly located tumors, the percutaneous approach has been demonstrated to be safer than open or laparoscopic techniques and equally effective [28]. Similar oncologic outcomes have been repeatedly demonstrated between laparoscopic cryoablation (LCA) and percutaneous cryoablation (PCA) [29]. Percutaneous ablation also has the added benefits of shorter hospital stay, lower complication rates, and reduced overall cost [7]. The authors advocate for the use of a percutaneous approach for almost all renal cryotherapy, and feel that in most cases, if laparoscopy is undertaken, there should be no reason not to perform partial nephrectomy with its validated benefits.

## Outcomes

### Post-therapy monitoring

Evaluation of procedural success of cryoablation is based on intravenous contrast-enhanced CT or MR imaging, for which a number of follow-up protocols have been described [28]. A completion noncontrast CT performed immediately after the procedure is generally preferred for evaluating for immediate postprocedure complications. Following this, postprocedure contrast-enhanced MRI is generally considered a reliable method for screening for recurrence [1]. Three-month follow-ups are generally reserved for cases where there is concern for incomplete or inadequate treatment, with any distinct or nodular enhancement in the ablation bed representing incomplete treatment [5]. Surveillance is otherwise recommended at 6, 12, and 18 months, then annually, or at the discretion of the clinician for at least 5 years [5]. In subsequent examinations, nodular tumor enhancement is the hallmark of recurrence [29].

### Performance of cryoablation

Success of cryoablation has been encouraging. Overall 5-year survival numbers have been reported at 97% and cancer-specific survival 100%, comparable to partial nephrectomy [7]. Not all operators enjoy the same results, and studies suggest operator-specific and patient-specific factors which may affect outcomes. For example, a demonstrable operator experience effect has been observed, although in most cases this affects technical success, rather than safety of the procedure [5].

### Patent-specific factors

Tumor size has been cited as a factor influencing the success of cryoablation, with authors reporting an increase in recurrence following PCA in tumors greater than 3 or 4 cm [35, 36]. Location of tumor is also a factor in treatment success, with anterior tumors more likely to demonstrate recurrence [36].

Although not directly linked to treatment failure, other intrinsic factors which affect probe placement may impact the overall likelihood of successful cryoablation. Body mass index, for example can decrease quality of real-time CT imaging, potentially leading to decreased accuracy and operator confidence in probe placement [29].

## Conclusions

The continually evolving patterns of the diagnosis of renal tumors have accompanied an increasing need for minimally invasive therapies. Patients who cannot tolerate surgery or require nephron-sparing therapies with the proper size and tumor configuration can benefit from cryoablation. Cryoablation also offers factors which confer unique advantages over other ablative technologies and therefore, with time, will probably achieve widespread adoption for small, optimally positioned tumors in all patients. Given the economic and patient-related factors, as well as the safety profile and technical success rates, renal cryoablation continues to grow in importance as a modality for the treatment of renal masses.

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## Part 2 Angio-embolization in Urology

## 127

# Gonadal Vein Embolization

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## Varicocele

### Introduction/epidemiology

Testicular varicocele is a common condition of pampiniform plexus which is usually asymptomatic but may result in severe pain, discomfort, subfertility, and/or physical deformity. The incidence of testicular varicocele has been reported in as many as 23% of the normal healthy male population. Rates as high as 42% have been reported in the elderly population, suggesting a correlation with age [1]. A subset of patients (i.e. nutcracker syndrome, discussed later) may present with hematuria and links to subfertility have been reported as far back as the 1800s [2]. The etiology of the subfertility appears to be related to the quality of the semen, which is dependent on testosterone production [1, 2].

Varicoceles are predominantly unilateral, with the majority of cases occurring on the left side due to venous drainage anatomy (see later). Bilateral varicoceles are present in a subset of patients; however, the incidence is debated in the literature and has been reported to be as high as 80% when diagnosed with imaging [2]. Along with improvement in diagnostics, many treatment options have also emerged to treat these patients, with a trend toward less-invasive procedures. Herein, we describe the clinical presentation, imaging manifestations, treatment indications, and treatment options, with a focus on gonadal vein embolization.

### Etiology/anatomy/pathophysiology

The pampiniform plexus consists of three spermatic vein tributaries with interspersed anastomoses resulting in collateral circulation between the anterior, middle, and posterior pampiniform plexuses. Varicoceles result from a reversal of blood flow in the gonadal veins that drain the pampiniform plexus. Etiologies of primary or idiopathic varicocele appear to be multifactorial [1, 2]. Primary varicocele occur more commonly on the left as the left gonadal vein drains into the left renal vein (LRV) as opposed to directly into the inferior vena cava (IVC), as it does on the right. The left gonadal vein is thus longer than the right gonadal vein and makes an acute angle as it drains into the LRV. The increased LRV pressure, compared with the IVC, results in retrograde flow into the left gonadal vein. “Nutcracker phenomenon” or compression of the LRV as it traverses between the aorta and the superior mesenteric artery (SMA) is a common etiology of a primary varicocele [2]. Venous valves are present in 90% of patients; they are usually located at the junction of the gonadal vein and its draining vein (i.e. renal vein on the left and IVC on the right). Congenital absence of venous valves or valvular incompetence predispose patients to reflux and thus varicoceles [1].

Secondary varicoceles occur from extrinsic pathologic compression of the LRV or draining spermatic vein, most commonly abdominopelvic malignancies. Nonmalignant masses such as hydroureter and abdominal aortic aneurysms are also sources of compression. A rare cause of varicocele formation is a splenorenal shunt which may form in patients with portal hypertension. Accordingly, clinical examination and radiologic evaluation (detailed later) are crucial in the initial consultation of a patient presenting with varicocele to identify treatable secondary causes as treatment would be considerably different.

### Patient evaluation and selection

Preprocedural evaluation is imperative in patients who present with symptoms consistent with varicocele. A focused but detailed history must be obtained to rule out

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other causes of testicular pain and subfertility [2]. For example, patients with abdominal malignancies may present with abdominal pain or symptoms of mass compression (i.e. urinary or bowel obstruction). Patients with anemia or hypercoagulable states may declare malignancy on blood tests. As mentioned earlier, patients with nutcracker syndrome may present with hematuria, either macroscopic or microscopic on urinalysis. Patients with splenorenal shunts may present with signs and symptoms of portal hypertension.

Semen analysis should be obtained not only to confirm etiology of patients presenting for subfertility but also to gauge results post treatment. Physical examination is also important as it may elucidate alternate diagnoses for patients with secondary varicoceles. Classic physical examination finding includes a "bag of worms" scrotum. Patients should be examined in both the supine and standing positions. The supine position may reveal alternate diagnoses such as intrascrotal neoplasm or infection. Furthermore, varicoceles that do not resolve while lying supine may be secondary to an underlying cause (i.e. neoplasm). Varicoceles declare themselves in the standing position due to the effects of gravity on venous flow and may be accentuated by Valsava (Figure 127.1). A grading system based on physical examination findings is detailed in Table 127.1 [1, 2].

Radiologic evaluation of presumed testicular varicocele should begin with ultrasound using a high-frequency, high-resolution 7–10 MHz linear transducer performed in the standing position. As with history and physical examination, testicular ultrasound can help identify alternate diagnoses, especially in cases where a varicocele is not seen or palpated. Diameters of dilated vessels in the pampiniform plexus and the main draining vein can be measured (normal: up to 2 mm) [1]. Grayscale ultrasound should be accompanied with duplex imaging (color and pulsed). These techniques allow for real-time visualization of reflux into the pampiniform plexus, especially with Valsalva, which increases sensitivity and specificity (up to 95%). Multiple scoring systems have been developed to determine the presence of a varicocele on color Doppler ultrasound, the most commonly used being the Sarteschi's classification (Table 127.2) [3, 4]. Testicular ultrasound volume must be measured in children because testicular growth (usually of the left testicle) is affected by varicocele. Return of normal testicular development following treatment is achieved in up to 80% of patients [4].

Patients in whom a primary varicocele is diagnosed and have pain or subfertility issues should be referred for treatment. Large (grade III) varicoceles that cause cosmetic issues may also be considered for treatment. Patients with isolated right-sided varicoceles, bilateral varicoceles, or varicoceles that do not reduce with change in position (standing to supine) or do not demonstrate increase with Valsalva require further workup. A contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) scan of the abdomen and pelvis should be obtained to exclude malignant and benign masses causing obstruction. Furthermore, cross-sectional imaging may be of value in cases where

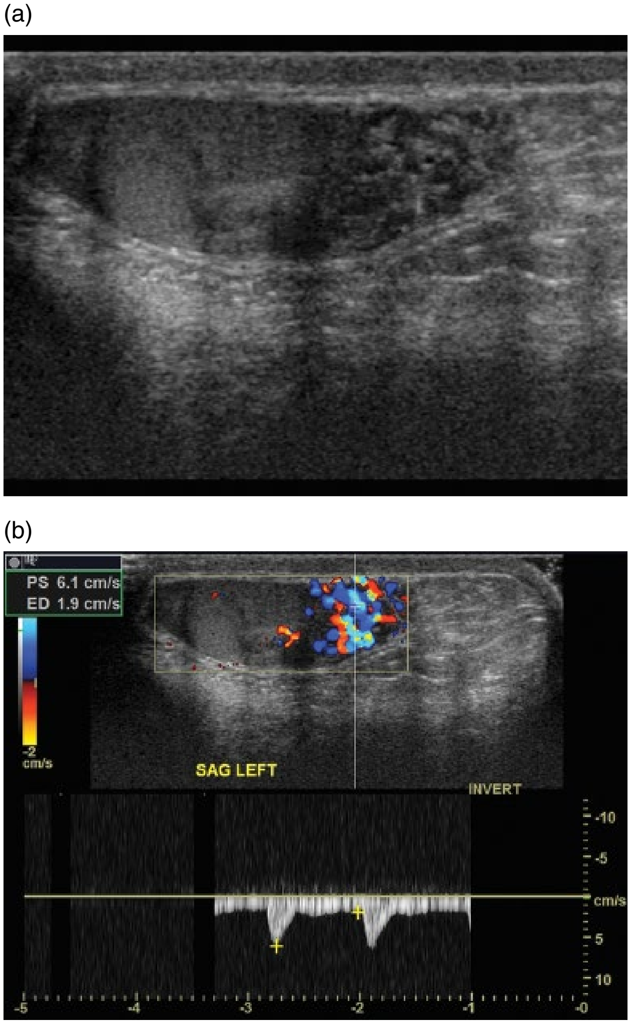


**Figure 127.1** Scrotal ultrasound evaluation for testicular pain. (a) Grayscale ultrasound image demonstrates small round hypoechoic intrascrotal varicosities that demonstrate increased vascular flow on (b) duplex color and pulsed Doppler.

**Table 127.1** Varicocele grading system (physical examination).

| | |
|---|---|
| Grade 0 | No palpable varicocele – only seen on ultrasound |
| Grade I | Only palpable when Valsalva maneuver performed by patient |
| Grade II | Palpable at rest (i.e. without Valsalva maneuver) |
| Grade III | Visible to the eye |

**Table 127.2** Sateschi's varicocele grading system (ultrasound).

| | |
|---|---|
| Grade I | Reflux in the inguinal gonadal veins on color Doppler, only during Valsalva maneuver on color Doppler<br>Varicosities not seen on grayscale imaging |
| Grade II | Reflux into the supratesticular gonadal vein on color Doppler only during the Valsalva maneuver<br>Varicosities increase in diameter on grayscale imaging only with Valsalva |
| Grade III | Reflux into the peritesticular/intrascrotal varices on color Doppler, only during the Valsalva maneuver<br>Varicosities increase in diameter grayscale imaging in standing position (Figure 127.1) |
| Grade IV | Reflux into the infratesticular varices that increases in vascularity on color Doppler during the Valsalva maneuver<br>Testicular hypertrophy; possible visible varices; Varicosities increase in diameter on grayscale imaging in the standing position |
| Grade V | Reflux into the infratesticular varices that do not increase in vascularity on color Doppler during the Valsalva maneuver<br>Testicular hypertrophy; possible visible varices; varicosities increase in diameter on grayscale imaging in the standing position |

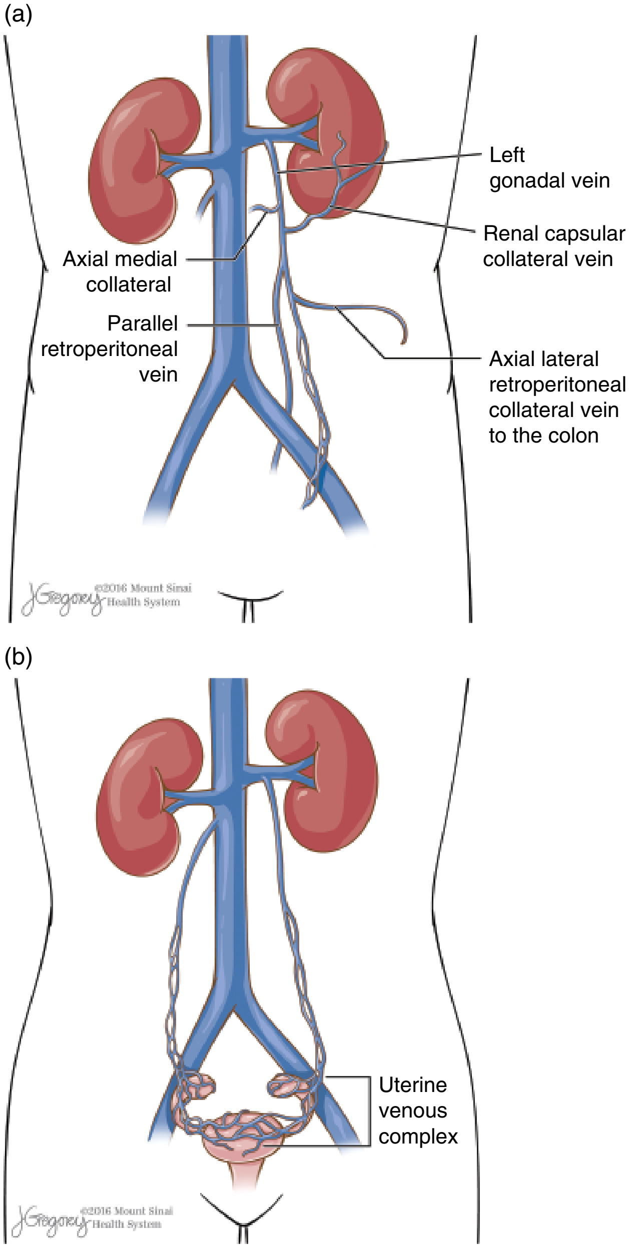

(a)
Left gonadal vein
Renal capsular collateral vein
Axial medial collateral
Parallel retroperitoneal vein
Axial lateral retroperitoneal collateral vein to the colon
J Gregory ©2016 Mount Sinai Health System
(b)
Uterine venous complex
J Gregory ©2016 Mount Sinai Health System

**Figure 127.2** Left gonadal vein collateral circulation. (a) Retroperitoneal collaterals of the left gonadal vein. (b) Cross-collateral between the right and left gonadal veins, mostly seen with pelvic congestion syndrome. Illustrations by J Gregory; printed with permission of ©Mount Sinai Health System.

there is atypical anatomy. For example, there are many congenital variations of the left and right spermatic veins, especially in cases of urogenital sinus and renal anomalies, which often occur together [2]. A wide range of pelvic anastomoses with pelvic veins must be identified to prevent persistence or recurrence of varicoceles (i.e. retroperitoneal, lumbar, iliac veins, etc. Figure 127.2a) [5]. These variations may present a dilemma to the interventional radiologist when attempting to treat the patient. Cross-sectional imaging for the evaluation of the varicose veins is detailed in the next section in patients with pelvic congestion syndrome.

Surgical options to treat varicoceles include open varicocelectomy, laparoscopic varicocelectomy, and microsurgical subinguinal varicocelectomy. Open varicocelectomy requires general or intrathecal anesthesia in order to make one of three incisions. The Palomo technique involves an open retroperitoneal approach for proximal ligation spermatic vessels. Smaller incisions using a low inguinal or subinguinal approach have been developed. Laparoscopic varicocelectomy also requires general anesthesia and utilizes a transperitoneal approach. Microsurgical subinguinal varicocelectomy is a less-invasive alternative to open and laparoscopic techniques that does not involve the abdominal fascia or musculature but still allows for identification of anatomy (including adjacent arteries) and can be performed under local anesthesia [2]. The first endovascular treatment of a varicocele dates back to 1978 [1]. Since then, advances in imaging and techniques have allowed for successful of gonadal vein embolization. Furthermore, radiation exposure is concerning for the pediatric population [6]. Gonad shielding and collimation is thus crucial. Accordingly, a multidisciplinary approach among interventional radiology, urology, and reproductive medicine should be undertaken to care for these patients.

## Interventional treatments

Percutaneous and endovascular treatments of varicoceles can be performed in the outpatient setting. The procedures can be performed under local and/or minimal intravenous sedation using midazolam and fentanyl. Appropriate monitoring equipment and staff are of course necessary. Appropriate shielding techniques must also be available to minimize radiation exposure to the gonads. For patients with iodinated contrast allergies, $CO_2$ digital subtraction angiography may be utilized [1, 2, 6].

### Vascular access

For the purpose of technical detail, the future discussion will pertain to a left-sided varicocele with mentions of nuances regarding treatment of a right-sided or bilateral varicocele. After sterile preparation and local anesthesia using 1% lidocaine, vascular access is most commonly obtained via the contralateral common femoral vein (i.e. right common femoral vein for a left-sided varicocele) using fluoroscopic and/or ultrasound guidance (Figure 127.3a). The contralateral approach allows for a favorable angle to catheterize the gonadal vein from the LRV. In addition, access to the right gonadal vein may be easier from a jugular or brachial vein approach due to a straighter course as its origin makes an acute angle immediately from the right anterolateral aspect of the IVC (Figure 127.3b) [6]. A short vascular 4 or 5 Fr (outer inner diameter) sheath is exchanged over a 0.035-inch guidewire (most commonly, a Bentson wire; Cook Medical, Bloomington, IN, USA) using the Seldinger technique. An angled 6 Fr Pinnacle Destination guiding sheath (Terumo Interventional Systems, Somerset, NJ, USA) can be used if the operator plans to use a vascular plug. An IVC venogram is performed to identify the origin of the renal veins (Figure 127.4a). A 4 or 5 Fr catheter is than placed into the IVC over the guidewire and used to catheterize the LRV. A hydrophilic system is preferred to help prevent vasospasm [2]. The 100 cm Cobra catheter (Cook Medical, Bloomington, IN, USA) is advantageous in this setting because its curved tip allows for easy catheterization of the left gonadal vein (Figure 127.4b,c). If the left gonadal vein proves difficult to catheterize, a coaxial system with guide catheters or guide sheaths can be used to stabilize the system [6]. In cases with extreme angulation or when high torquability is required, a braid-reinforced catheter may help [2]. A reverse curve catheter (for example SOS Omni Selective Catheter) may be used to catheterize the right gonadal vein directly off the IVC (see Figure 127.6a,b). A 2.8 Fr microcatheter can be introduced coaxially into the guiding catheter to assist in catheterization of the gonadal vein to the level of the inguinal ligament to study the pampiniform plexus.

### Venography

The catheter can be advanced into the distal gonadal vein just proximal to the origin of the pampiniform plexus. Pretreatment venography of the gonadal vein is performed at the level of the ischiopubic ramus to confirm the diagnosis as well as identify the highly variable collateral venous circulation [1, 2, 6]. Variant anatomy (i.e. duplicated gonadal vein) and collateral vessels, sometimes from the internal iliac vein, must be identified (Figures 127.4d and 127.5d) and embolized to

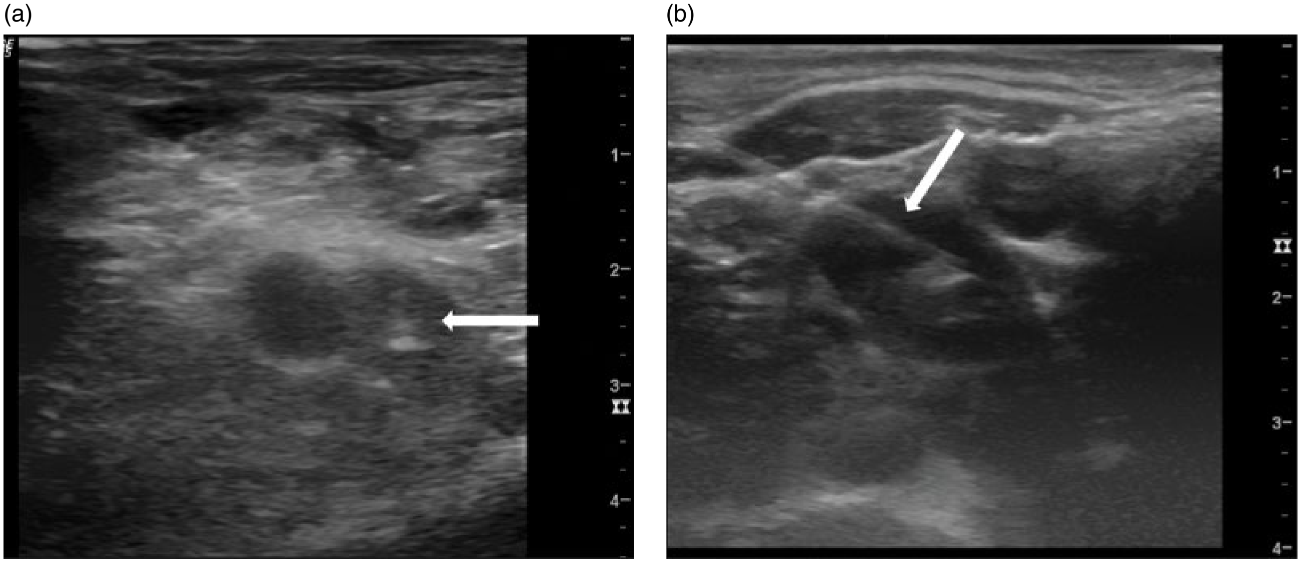


Figure 127.3 Ultrasound guided venous access. (a) Grayscale ultrasound image demonstrates a hyperechoic needle (arrow) in the lumen of the right common femoral vein and (b) the right internal jugular vein.

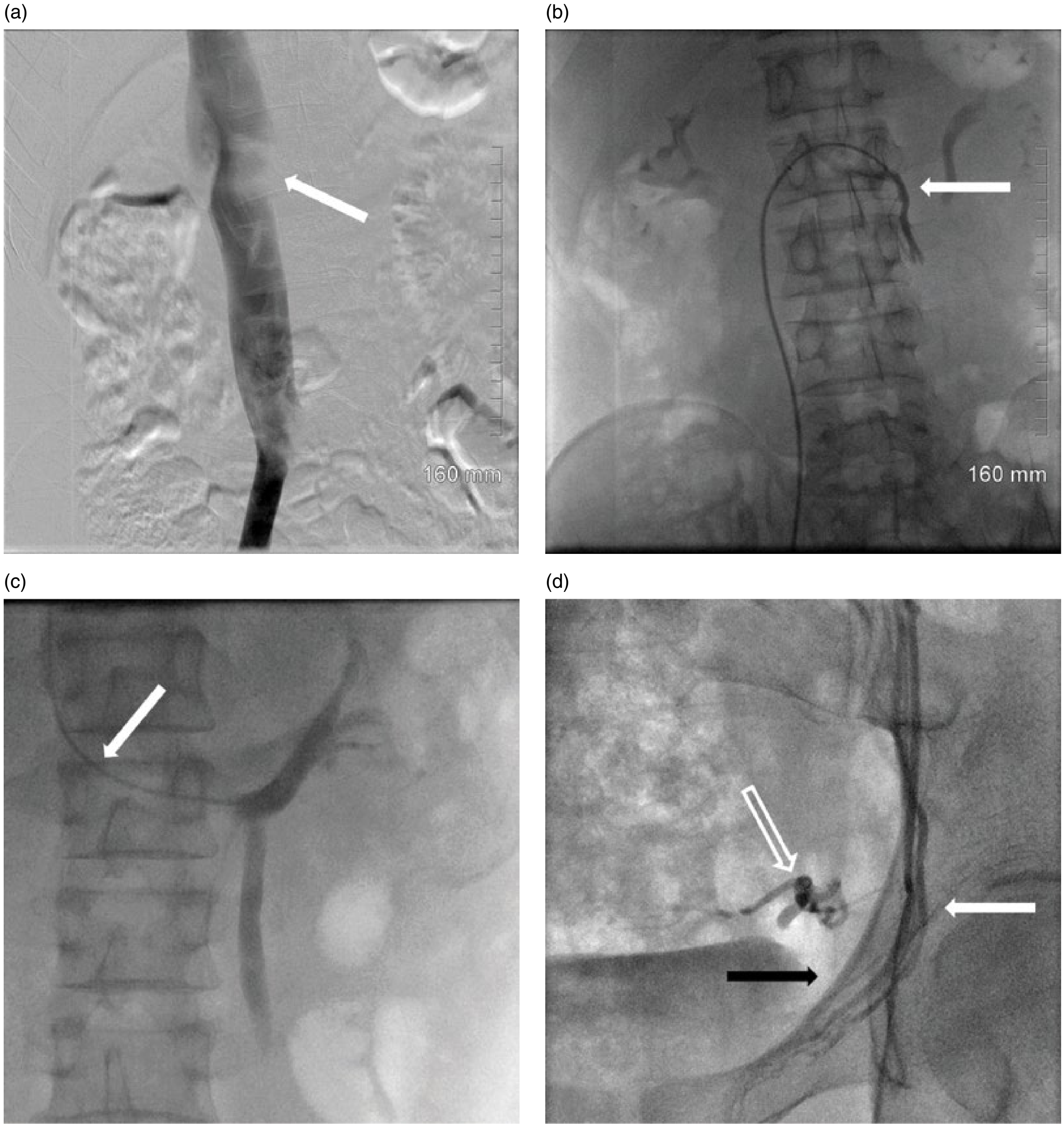


**Figure 127.4** Left gonadal vein access and venography. (a) Venography demonstrates bilateral flow voids at the level of the second lumbar vertebra (arrow showing dynamic filling defect related to inflow from the left renal vein). (b) Contrast injection of the left renal vein via a right common femoral vein approach. (c) Right internal jugular vein approach demonstrates the origin of the left gonadal vein. (d) Pretreatment left gonadal venography of the gonadal vein is performed at the level of the ischiopubic ramus (black arrow) to confirm the diagnosis as well as identify the highly variable collateral venous circulation (white arrow pointing to a parallel retroperitoneal collateral and white hollow arrow pointing to an axial medial retroperitoneal collateral).

prevent varicocele persistence or recurrence (Figure 127.5a,e). For optimal evaluation of the varicocele, the patient can be coached to bear down during contrast injection to demonstrate venous reflux. If the patient cannot adequately bear down, he can be positioned in reverse Trendelenburg to use the assistance of gravity. The classic venous drainage pattern is the medial and lateral branching of the gonadal vein at the

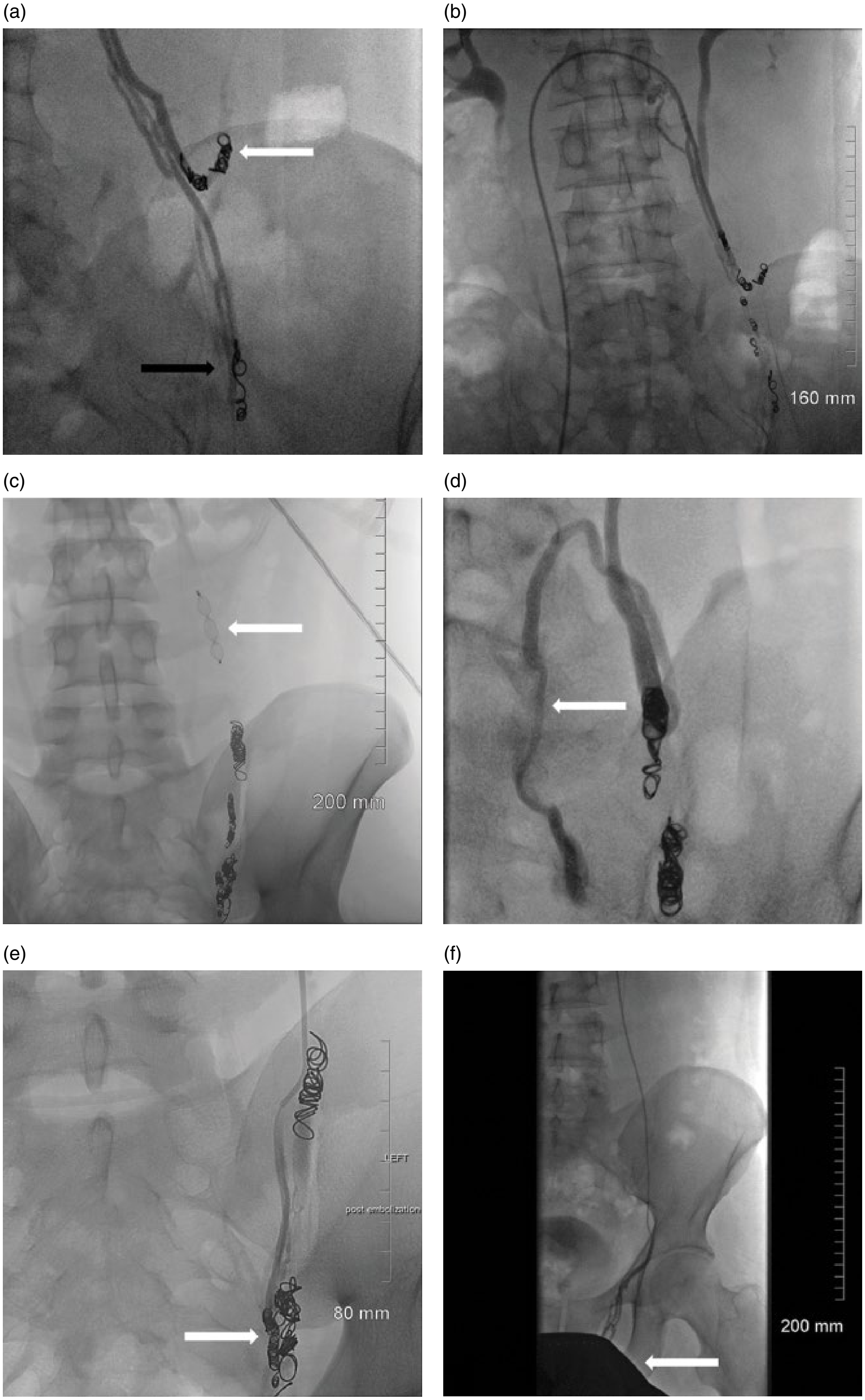


**Figure 127.5** Left gonadal vein embolization. (a) Contrast injection of the proximal left gonadal vein after coil embolization of the distal gonadal vein (black arrow) near the level of the pubic symphysis; below the level of the lowest axial lateral retroperitoneal collateral (white arrow). (b) Contrast injection of the proximal left gonadal vein after multilevel coil embolization of the gonadal vein. (c) Proximal gonadal vein embolization using an AMPLATZER vascular plug (St. Jude Medical, St. Paul, MN, USA) in a different patient. (d) Contrast injection of the left gonadal vein after coil embolization of the distal gonadal vein (black arrow) in a different patient demonstrating a medial parallel retroperitoneal vein which was subsequently (e) embolized with coils. (f) Radiation protection via gonadal shielding and collimation. Arrow points to gonadal shield used to protect the gonads from fluoroscopic radiation.

level of L4 [1]. If the plan is to use a sclerosant, subsequent small-volume contrast injection into the anterior pampiniform plexus is performed with Valsalva in the reverse Trendelenburg position while maintaining external pressure on the spermatic cord, either by hand or with a rubber band [1, 7]. This is to ensure that no reflux is seen into the posterior pampiniform plexus into the main draining gonadal vein. Careful manipulation of the catheter and wire is recommended as vasospasm and venous perforation may occur. Vasospasm tends to occur more frequently in children. A 0.016 inch guidewire and microcatheter system may be of assistance with technically difficult (i.e. tortuous) anatomy or to cross a perforated segment [1, 2]. In cases of persistent or large extravasation, the procedure should be terminated and rescheduled. Nitroglycerin (100–500 μg, dosed based on the patient's blood pressure) may be given through the catheter in cases of severe spasm [2, 7].

### Sclerotherapy

If no reflux is observed on contrast injection into the anterior pampiniform plexus or draining gonadal vein, the operator may proceed with injection of sclerosant with Valsalva in the reverse Trendelenburg position and external compression of the spermatic cord just as in the test bolus contrast injection [2]. While there are many different sclerosing agents that induce endothelial injury secondary to a thermochemical reaction, sclerosis is most commonly performed using a dilution of 3% Na-tetradecyl-sulfate (STS) [1]. Different dilutions have been reported to be effective; for example, a mixture 2–6 ml of STS and air in a 1:4 ratio is typically used to create a foam using the Tessari technique with a three-way stopcock [1, 7]. A small amount of contrast may be added to the mixture for visualization. Pressure on the spermatic cord can be released 1 minute after injection. If reflux is seen into the posterior pampiniform plexus or draining gonadal vein, additional sclerosant can be injected. Balloon occlusion catheters are used in cases of large draining gonadal veins or in cases of bidirectional flow [2]. After reflux ceases, gentle contrast injection into the gonadal vein is performed to confirm occlusion. When complete occlusion is obtained, results are considered to be equivalent to surgical ligation. An anterograde percutaneous sclerotherapy technique was employed in the early years of varicocele embolization. However, catheterizing the gonadal vein proved difficult due to complex anatomical variations. For this technique, an inguinal or subinguinal incision is made to isolate and access the pampiniform plexus. Anterograde venography is performed and sclerosis is performed as mentioned earlier.

### Gonadal vein embolization

Venous embolization involves occlusion of the draining gonadal vein and thus preventing reflux into the pampiniform plexus. Multiple embolic agents are available to the interventionalist. Coils are the most common embolic agents used for gonadal vein embolization. Fibered coils are surrounded by a thrombogenic fiber that facilitates occlusion of the gonadal vein, whereas hydrogel-coated coils expand to physically occlude the lumen. Detachable coils, with either mechanical or electrical detachment mechanisms, have a decreased rate of migration and vessel injury when compared to pushable stainless-steel coils, at the expense of added cost. Microcoils may be used if a microcatheter system is required to cannulate the target vessel. New detachable coils allow for accurate positioning of these embolic agents and thus increase the safety profile associated with venous embolization. The coils can be retracted into the catheter if inappropriately positioned/sized by the operator or result in venous perforation. Moreover, they also allow for a more distal occlusion [1, 2]. Embolization should begin below the lowest collateral vessel, which most commonly occurs near the level of the pubic symphysis (Figure 127.5a,d) to ensure no alternate circulation to provide flow to the distal refluxing gonadal vein (i.e. prevent persistence or recurrence) [1]. The catheter (or microcatheter) is then retracted proximally toward the draining renal vein (or IVC on the right) and multiple additional levels of embolization are performed (most commonly 3 or 4 levels) (Figures 127.5b and 127.6c). The gonadal vein should be measured at each level prior to embolization on the postprocessed digital subtraction venogram to determine coil size selection. AMPLATZER vascular plugs (St. Jude Medical, St. Paul, MN, USA, Figure 127.5c) have recently gained interest in the proximal gonadal vein as they offer a quicker alternative to coil embolization. Both coils and plugs are MRI compatible. Other uncommon options include detachable balloons and microvascular plugs [6]. Gonadal vein embolization is sometimes performed in conjunction with sclerotherapy. The sclerosant is delivered after the first (lowest) level of coils are placed. This so-called "sandwich technique" prevents reflux into the pampiniform plexus. The sclerosant can help occlude small tributaries which are too small to catheterize and may help in preventing recurrence [1].

*N*-Butyl cyanoacrylate (nBCA) glue is a liquid embolic agent that has been used for gonadal vein embolization. Glue as the embolic agent for varicocele embolization may be considered favorable in cases of recurrent or persistent varicocele to occlude small collateral veins. The ratio of nBCA to lipiodol is used to alter the polymerization rate of the glue and is determined by the capacity

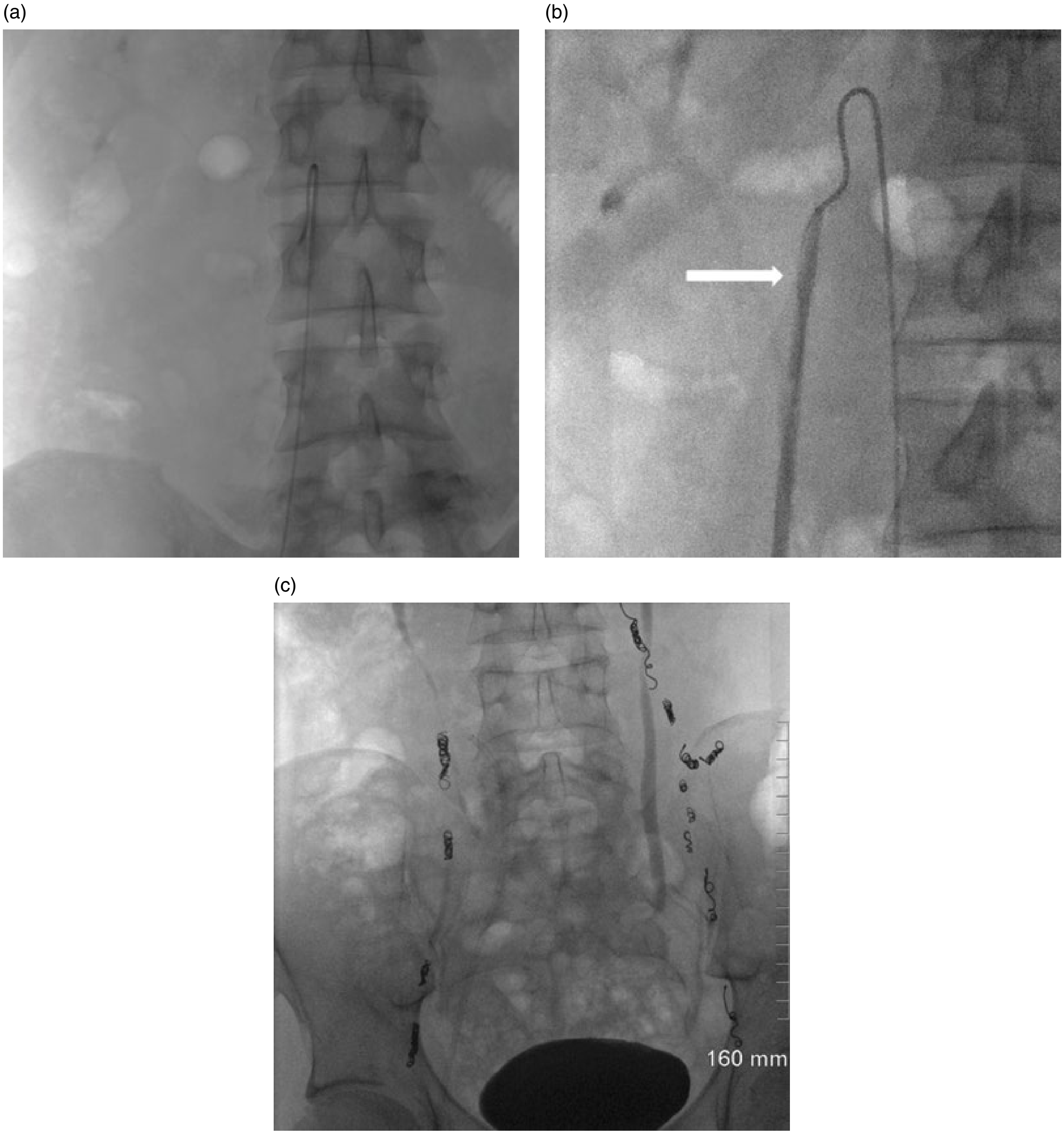


**Figure 127.6** Right/bilateral gonadal vein embolization. (a) Fluoroscopic image demonstrating a selective catheter in the inferior vena cava at the L2–L3 level in an attempt to (b) catheterize the right gonadal vein. (c) Fluoroscopic image demonstrating successful bilateral gonadal vein embolization.

and flow rate of the target vessel. It is especially difficult in venous embolization because there is a higher risk of gluing your catheter to the body due to the direction of flow. Operator experience with glue is necessary due to subtleties in the technique for glue delivery. For example, a coaxial microcatheter system is necessary for the delivery of glue. The glue must be delivered slowly and at a constant rate. An additional syringe of nonionic flushes (i.e. 10% dextrose) should be connected to the glue mixture via a three-way stopcock and should be delivered before, during, and after glue delivery. This prevents premature polymerization of the glue and thus occlusion

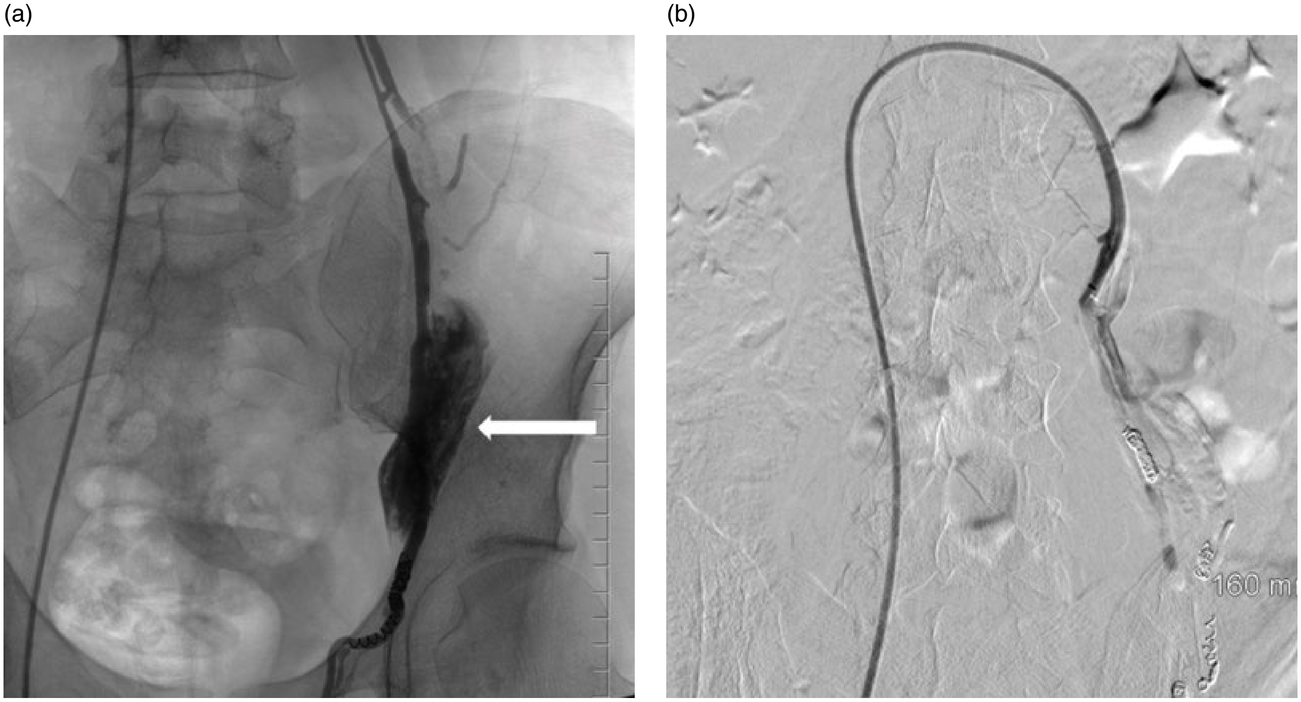


Figure 127.7 Gonadal vein extravasation. (a) Contrast injection of the left gonadal vein demonstrates active extravasation of contrast into the retroperitoneum. (b) Final digital contrast injection demonstrates no further extravasation after proximal and distal coil embolization.

of the microcatheter, reflux into the main catheter resulting in its occlusion, and gluing of the microcatheter or the system to the vein. The tip of the main catheter and delivery microcatheter can be soaked in silicone oil to also prevent sticking to the glue [2]. Detachable-tip microcatheters exist but are currently cost prohibitive for this purpose.

## Outcomes/complications

Technical success for gonadal vein embolization has been reported up to 96% with experienced operators [1]. However, many series have shown high technical failure rates with right-sided varicoceles [6]. A large meta-analysis demonstrated technical failure rate to be around 13% without attention to laterality [8]. Patients are generally discharged the same day with pain medications (i.e. anti-inflammatories) and a short course of oral antibiotic therapy (for example, 5 days of 1 g amoxicillin daily) [7]. Follow-up should occur in the clinic 1–2 weeks after the procedure to evaluate patients for symptom relief and complications. Nearly all patients that present with pain have resolution of symptoms within weeks. Patients receive ultrasound follow-up after three months and 1 year as well. Semen analyses can be repeated three months post procedure to follow up for subfertility.

Until recently, the jury was out in the success of gonadal vein embolization for the treatment of infertile secondary to varicocele. Recent literature suggests that the treatment not only improves semen analysis but increases pregnancy rates to nearly 50% within 3 years [9]. These findings are comparable to its more invasive surgical counterparts, including microsurgical subinguinal varicocelectomy [10]. Major complications including but not limited to nontarget embolization (regardless of complex collateral circulation), embolic migration, and/or renal vein thrombosis are rare [6]. Although gonadal vein perforation is common (Figure 127.7), it rarely leads to clinical sequelae. Postprocedure scrotal pain has been reported in many patients, especially with the use of sclerotherapy. A small subset of these patients may experience chronic pain. Epididymitis, scrotal hydrocele, and scrotal hematoma have also been reported. The minimally invasive nature of the procedure makes complications rare when compared to their surgical counterparts, which are similar to microsurgical subinguinal varicocelectomy; in contrast, complications have been reported to be as high as 30% with open and laparoscopic varicocelectomy.

For patients with persistent or recurrent varicocele, cross-sectional imaging should be obtained to evaluate the extent of venous obstruction. Rates of recurrence are reported to be at most 10% compared to their surgical counterparts, which are reported to be as high as 17% with open and laparoscopic varicocelectomy. Low inguinal or subinguinal techniques have reported rates of recurrence as low as 2% [11]. Duplicated gonadal veins and anastomotic pathways are usually the etiology for recurrence. Cross-sectional imaging allows evaluation of previous surgical or endovascular treatments which may hinder certain approaches. For example, prior proximal gonadal vein embolization may prevent accessing the gonadal vein distally to perform further treatment. Glue may be used in such cases [2]. Low inguinal or subinguinal techniques may also be considered in these patients.

### Future directions

Testicular pain and subfertility results in significant morbidity for patients with varicocele. Multicenter randomized controlled trials are needed to assess primary outcomes related to pregnancy rates and/or live births [12].

## Pelvic congestion syndrome

### Introduction/epidemiology

Chronic pelvic pain affects a third of women and is a common presenting symptom to gynecology. Pelvic congestion syndrome (PCS) is a diagnosis of exclusion first described in 1930 in patients where an underlying cause of pelvic pain was not found [13]. Patients present with nonspecific pelvic pain and can have associated constitutional symptoms (headache, gastrointestinal and urinary symptoms, or generalized pain/weakness) that may be related to the menstrual cycle. Patients can also report dysmenorrhea and dyspareunia. The pain is generally worse with situations that increase pelvic pressure, for example with pregnancy. A subset of patients also present with visible pelvic (i.e. vulvar) and/or lower extremity varicose veins. The etiology of pelvic congestion is not well understood; however, it is thought to be analogous to varicoceles in males and thus treatment parallels varicocele embolization. Ovarian varices are found incidentally in about 10% of patients, about half of whom have symptoms related to PCS. Herein, we describe the clinical presentation, imaging manifestations, treatment indications, and discuss treatment options with a focus on ovarian vein embolization [13].

### Etiology/anatomy/pathophysiology

The etiology of PCS is thought to be related to ovarian vein reflux secondary to incompetent or absent ovarian vein valves resulting in pelvic venous engorgement. However, patients with enlarged pelvic veins and/or reflux do not necessarily have PCS [13, 14]. PCS occurs most often in multiparous women and thus mass effect on the pelvic veins from a gravid uterus appears to be contributory. Longstanding pressure on the veins results in venous hypertension, which causes valvular incompetence and retrograde flow into the ovarian veins [14]. Furthermore, the effects of progesterone during pregnancy are thought to exacerbate venous dilation due to its inherent properties as a vasodilator. PCS is also seen commonly in premenopausal women, suggesting a hormonal influence. Patients with PCS often have polycystic ovaries without manifestations of the syndrome suggesting estrogenic effects. All of these factors weaken the structural integrity of the veins, resulting in refluxing valves. Some patients may have a genetic predisposition to developing PCS [14, 15]. In summary, the pelvic pain is secondary to stretch-activated pain receptors in the veins walls, which is proportional to the extent of dilatation and reflux [14].

Anatomy plays a large role in the pathophysiology of PCS. The pampiniform venous plexus resides in the broad ligament in female patients and drains into the gonadal (ovarian) veins bilaterally. Similar to the male patient, the left gonadal vein drains into the LRV and the right gonadal vein drains directly into the IVC. Variability in anatomy is common, with different collateral circulations [14]. In contrast to the male patient, many collateral pathways exist between the right and left venous circulation (Figure 127.2b) and thus patients benefit from bilateral treatment. Although PCS occurs bilaterally, valvular incompetence is usually unilateral and more common on the left [15]. Bilateral presentation is more common than in men, but an underlying etiology must still be excluded. Pelvic malignancies, uterine fibroids, and endometriosis may be culprits for secondary PCS in the female patient. Additional etiologies include IVC thrombosis and nutcracker syndrome (discussed previously) [14]. A variant of PCS that can also present with lower extremity varicose veins includes compression or valvular incompetence of the iliac veins, most commonly on the left. When the internal iliac vein is involved in isolation, lower extremity symptoms may not be present. May–Thurner syndrome is a condition in which the left common iliac vein is compressed by the right common iliac artery. These patients may present with deep venous thrombosis (DVT). Rare congenital conditions such as vascular malformations can also result in PCS [15]. Accordingly, clinical examination and radiologic evaluation are crucial in the initial consultation of a patient presenting with PCS to ensure that an underlying diagnosis is identified, as treatment would be considerably different.

### Patient evaluation and selection

Diagnosis of PCS is usually delayed in patients as the workup for pelvic pain is extensive and PCS is usually left as a diagnosis of exclusion. Visual analog scales (VAS) are typically used to grade a patient's pain, although these scores are subjective. Only a small subset of patients present with the physical deformities of varicose veins when compared to those who present with varicocele. Patients usually present with vulvar or perineal varicosities but may present with buttock and even lower extremity varicose veins. Lower extremity varicosities tend to be in the pudendal collateral distribution and appear visible on the superomedial thigh. The preprocedure workup is therefore crucial in patients presenting with pelvic pain. The diagnosis may be hidden in the details, for example within the social history as depression and relationship problems due to dyspareunia [13]. Because of the wide variety of symptoms, patients may present to different subspecialties for initial or follow-up evaluation, which adds to the complexity of the patient's care. For example, patients may be referred directly to urology for urinary symptoms of frequency and irritation with a discordant urinalysis for presumed diagnosis of recurrent urinary tract infections. Gynecologic examination may reveal adnexal tenderness, which is reported to have a reasonable specificity; however, this may lead to alternate differential diagnoses including, but not limited to, ovarian cyst or torsion [13–15]. Interestingly, pelvic pain and adnexal tenderness have been reported to be as high as 94% sensitive and 77% specific [16].

Findings suggestive of PCS are commonly made incidentally on imaging modalities for workup of a different diagnosis. Most patients who present with pelvic pain typically undergo transabdominal ultrasound using a low-frequency, low-resolution curvilinear transducer and transvaginal ultrasound using a high-frequency transvaginal probe to evaluate the uterus and adnexa to identify other potential causes of pelvic pain (i.e. ovarian cyst). If large dilated pelvic veins are identified, color and pulsed Doppler technique should be employed to evaluate these veins (Figures 127.8a). Reflux may be identified using transvaginal ultrasound in a patient with favorable anatomy and with operator experience. These veins should be evaluated with the patients standing up and performing the Valsalva maneuver, as described in the evaluation of varicocele earlier.

As mentioned, findings consistent with PCS are generally identified incidentally on cross-sectional imaging to evaluate patients for something other than PCS. CT of the pelvis requires the administration of intravenous iodinated contrast to identify enhancement of the veins and differential the conglomerate of venous structures from a pelvic mass or lymphadenopathy [13]. The CT must be performed in a venous phase of imaging, typically with a 90–180 second delay (Figure 127.8d–f). Early imaging may opacify the arterial vasculature of the pelvis which would limit the evaluation of the veins. MRI has the benefit of no radiation (Figure 127.8b,c). While there are nuanced exceptions, veins typically appear hypointense on T1-weighted images and hyperintense on T2-weighted images; gradient echo sequences provide the highest signal [13]. Intravenous gadolinium contrast-enhanced MR venography (MRV) provides great detail of the pelvic venous anatomy [13, 14]. Velocity-encoded phase contrast (VENC) imaging is under investigation for identification of reflux [14]. However, cross-sectional imaging may underestimate the degree of venous dilatation or reflux as it must be performed in the supine position (i.e. not standing) [13, 15]. Invasive methods of diagnosis such as laparoscopy are often used to identify the cause of nonspecific pelvic pain. Although these methods prove valuable to identify alternate etiologies of pain (i.e. adhesions), diagnosis of PCS is often missed due to supine positioning and pelvic insufflation [14].

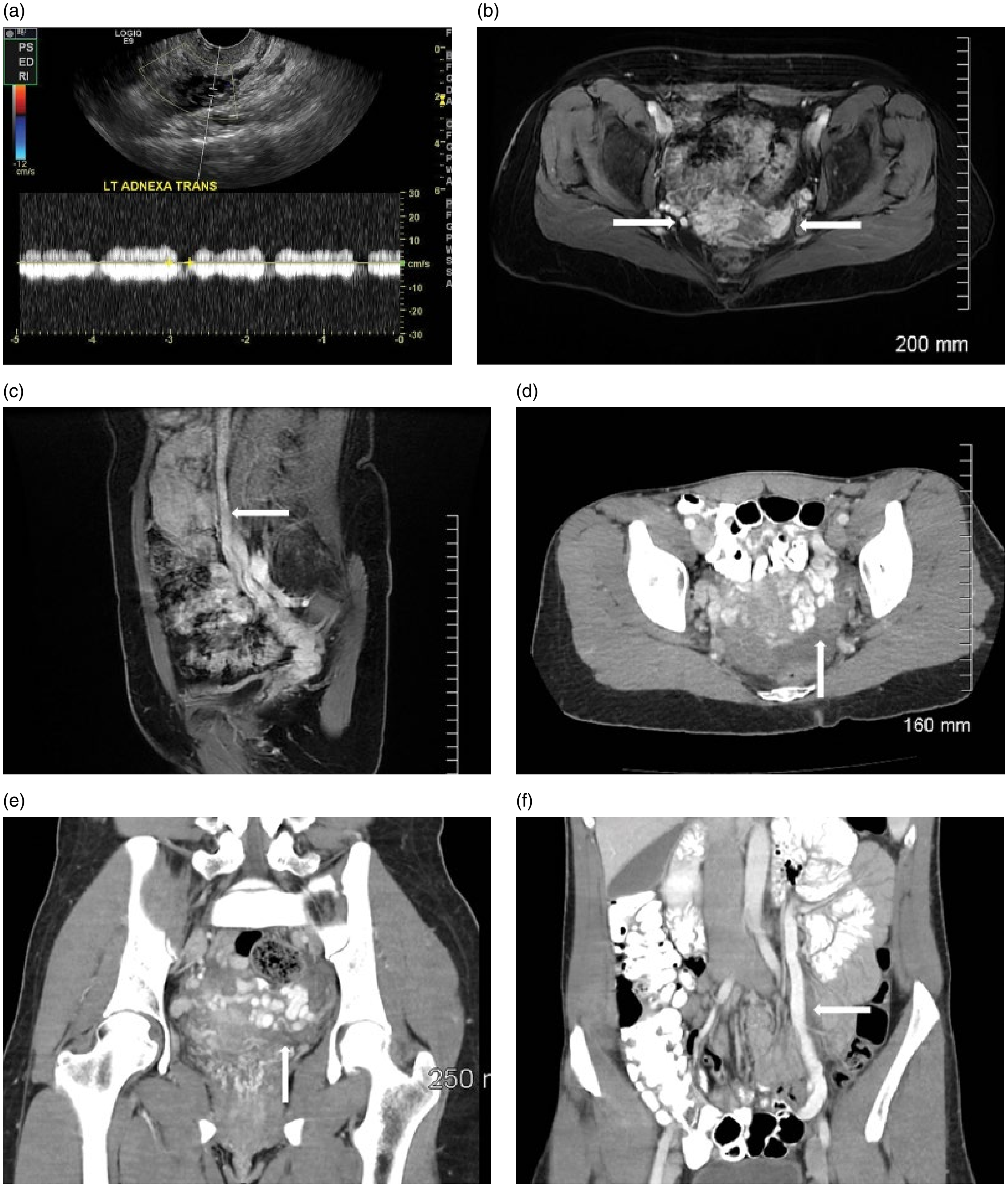
Patients with presumed primary PCS with symptoms should be referred for treatment. Ovarian vein size appears to correlate with amount of reflux and symptoms. Veins greater than 8 mm in diameter appear to have reflux and these patients present with pain [15]. However, many different classification systems exist due to the high variability of presentation and anatomy resulting in different treatment paradigms. Pelvic veins less than 4 mm in diameter are considered to be within normal limits [15]. Tortuous dilated veins measuring larger than 4–6 mm or dilated ovarian veins measuring larger than 8–10 mm are diagnostic criteria used by many for the diagnosis of PCS. Dilated myometrial veins, filling of varices, and/or polycystic ovaries may also be considered in the diagnosis [13–15]. PCS is diagnosed in 56% of patients who have polycystic ovaries [16].

Nonsurgical (i.e. medical) and surgical treatment options have been developed for the treatment of PCS. Hormone therapy using medroxyprogesterone acetate or gonadotropin-releasing hormone (GnRH) analog goserelin may be effective in a short-term period [14, 15]. Surgical options include laparoscopic ligation as well as total hysterectomy with oophorectomy [15]. Less-invasive interventional techniques described for treatment of varicocele in male patients have been employed to treat patients with PCS. The first endovascular treatment of PCS dates back to the early 1990s (27 in 1) [13]. Since then, technological advances have demonstrated favorable outcomes. A multidisciplinary approach among interventional radiology, urology, and gynecology should be taken to care for these patients.

## Interventional treatments

### Vascular access

Vascular access for the endovascular treatment of PCS is identical to that of varicocele treatment. However, dual accesses may be obtained (i.e. right common femoral


(a)
LOGIQ
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PS
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RI
-12
cm/s
LT ADNEXA TRANS
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-10
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-4
-3
-2
-1
-0
(b)
200 mm
(c)
(d)
160 mm
(e)
250
(f)

**Figure 127.8** Imaging in pelvic congestion syndrome. (a) Grayscale ultrasound image demonstrates small round hypoechoic left adnexal varicosities that demonstrate increased vascular flow on pulsed Doppler. (b, c) Axial and sagittal contrast-enhanced MRI of the pelvis demonstrates bilateral dilated veins and a prominent (>8 mm) left gonadal vein (on sagittal image). (d–f) Axial, coronal, and sagittal images demonstrate bilateral dilated veins and a prominent (>8 mm) left gonadal vein (on sagittal image).

vein access to catheterize the left ovarian vein via the LRV and right internal jugular/left common femoral vein access to catheterize the right ovarian vein). A brachial vein approach may also be used for selecting the right ovarian vein [17]. Bilateral treatments are usually performed in the setting of PCS due to cross-communication between the left and right pelvic venous circulation.

### Venography

Venography is also similar to that for varicocele embolization. Internal iliac venography may also be performed in select cases, for example in patients with thigh varices. In addition to Valsalva and reverse Trendelenburg positioning, a balloon occlusion test may be performed to visualize the pelvic veins. To assess for adequate Valsalva, the patient must maintain a pressure of 20 mmHg which can be assessed using the rubber tubing of a blood pressure cuff, if necessary [16]. Contrast venography is performed though balloon occlusion catheters that prevent rapid drainage of blood and fill deep collaterals [13, 15]. If contrast injection of the LRV demonstrates reflux into an ovarian vein measuring >8 mm, the diagnosis is confirmed [16] (Figure 127.9a).

### Gonadal vein embolization/sclerotherapy

These techniques are described in detail earlier in this chapter. After the diagnosis of PCS is confirmed angiographically, the treatment catheter is placed near the ovarian venous plexus and then techniques for embolization/sclerosing aforementioned are applied. The diagnostic catheter and/or microcatheter should be placed in the ovarian vein at the level of the pelvic brim to again identify the reflux and demonstrate filling of collateral veins. As mentioned, bilateral treatments are often performed, even in the setting of unilateral pelvic varicosities as vast communications exist between the left and right circulation (Figure 127.9). Single-side embolization would result in recurrence. If the plan is to use sclerotherapy, a balloon occlusion test injection of contrast may be performed to determine the amount of sclerosant necessary. Furthermore, the injection of sclerosant may also be performed with balloon occlusion in cases with large draining veins. Anastomosis from the internal iliac to gonadal circulation also exists. Balloon occlusion tests are generally performed in these cases to identify small tributaries of the internal iliac venous circulation that feed the varices. These small vessels can be subselectively catheterized prior to sclerosing to identify potential

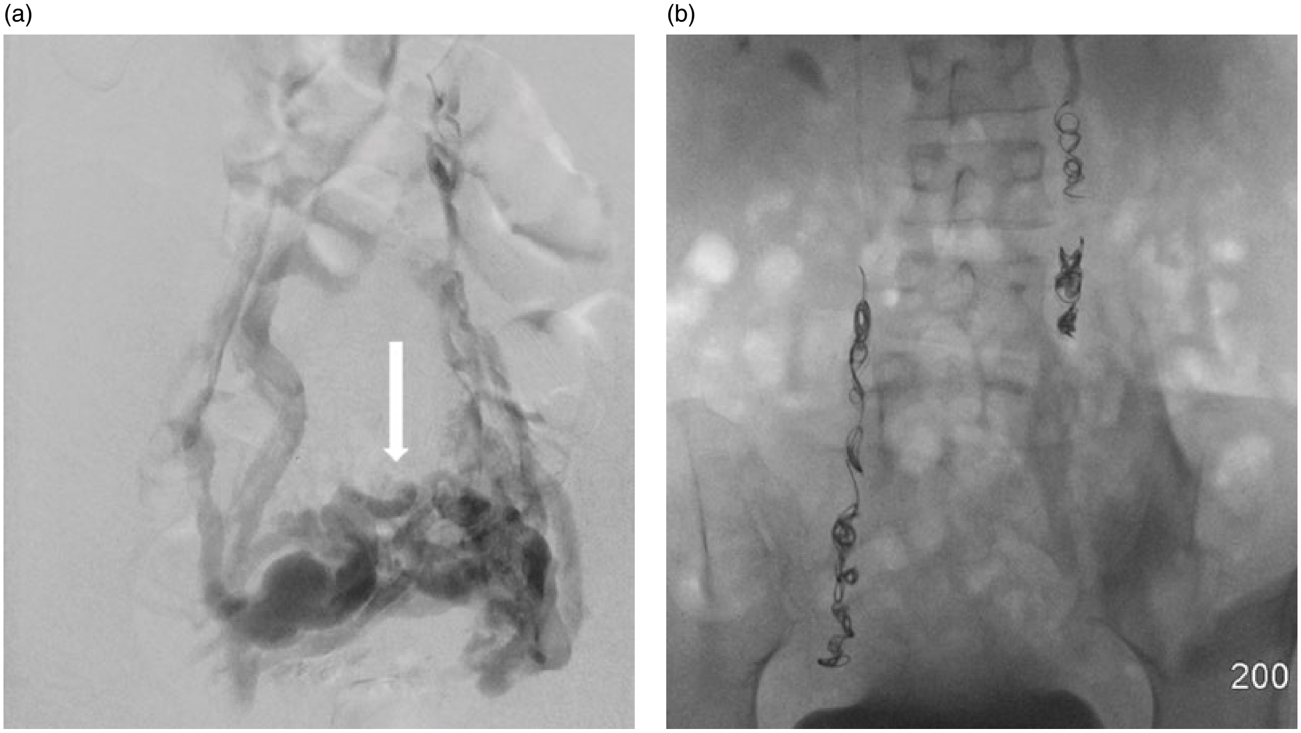

**Figure 127.9** Bilateral gonadal vein embolization for pelvic congestion syndrome. (a) Digital subtraction angiography (DSA) demonstrates enlarged and tortuous pelvic veins with cross pelvic collaterals that were subsequently (b) treated with bilateral gonadal vein embolization.

anastomoses that may result in nontarget embolization, for example reflux of STS into the common femoral veins. Furthermore, many patients demonstrate internal iliac venous insufficiency as the etiology of PCS and can be treated with proximal coil embolization or with sclerosant; however, flow in these vessels may result in migration resulting in nontarget embolization [15]. However, treatment protocols are debated among authors with respect to unilateral versus bilateral treatment, iliac vein treatment, collateral vein embolization despite lack of reflux, and embolization materials [16].

#### Outcomes/complications

With advancements made in technique, up to 100% of patients undergo successful embolization [14]. Postprocedure protocols and follow-up are identical to male varicocele treatment. Nearly 9 out of 10 patients who present with pain have resolution of symptoms within weeks [18, 19]. VAS scores have been reported to decrease from an average of slightly greater than 7 to slightly less than 1. Dyspareunia may be associated with a poor prognosis [17]. Results seem to be favorable when compared to total hysterectomy and oophorectomy. Recurrence rates are hard to quantify as changes in the VAS scores are typically used in patients without physical attributes of PCS; however, recurrence rates as high as 42% have been reported [17], although recent literature suggests that these were gross overestimates [18, 19]. A second embolization treatment may improve clinical outcomes in these patients [20]. Major complications including but not limited to coil migration, vessel perforation, and DVT are rare. An attempt can be made to retrieve migrated coils using a snare device. Patients may experience paraspinal and pelvic pain if sclerosants are used. This is usually self-limiting and controlled with anti-inflammatory pain medications [15]. No effects on menstruation or fertility have been reported [13]. Minimal long-term data are available for patients with endovascular treatments for PCS. Recurrence has been reported in up to 8% of patients up to 4 years after the initial treatment [13].

### Future directions

The cost of treating patients with chronic pelvic pain results in a considerable expenditure of healthcare funds each year [3]. Some consider minimally invasive endovascular therapies as standard of care for the treatment of PCS [20]. Multicenter randomized controlled trials are needed to compare patient outcomes with different treatment options patient with regard to technical success, recurrence rates, complications, and cost-effectiveness [14].

## Acknowledgments

The authors would like to acknowledge Jill Gregory, Certified Medical Illustrator for pictorial depictions of variant anatomy.

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# 128

# Renal Angiography and Embolization

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## Introduction

Renal angiography provides a significant diagnostic benefit in patients with a multitude of renal pathology, including trauma, neoplasm, and vascular malformations. In the acute setting, patients with life-threatening renal hemorrhage can benefit from nephron-sparing or total preoperative devascularization. Selective renal arterial embolization is also used for elective treatment of noncancerous renal tumors.

## Renal arterial anatomy

A familiarity with renal vascularity is paramount in order to efficiently perform renal arterial interventions. Bilateral renal arteries arise from the aorta at the level of 1st and 2nd lumbar vertebrae. Most kidneys are supplied by a single vessel (70%). The right renal artery is longer than the left, given the increased distance from the aorta. The kidneys have segmental anatomy as defined by their vascular supply; most commonly there are five segments: apical, upper, middle, lower, and posterior. Usually, the first branch of the renal artery is the posterior division which supplies the posterior segment of the kidney. The anterior division then trifurcates to supply the upper, middle, and lower segments. The apical segment vascular supply is commonly shared with the upper segment; however, there is a 10% incidence of shared vascularity with the posterior segment (Figure 128.1a). Smaller arteries arise from the main renal artery and its divisions to supply the renal pelvis and proximal ureter [1, 2].

Variant renal anatomy is present in nearly one-third of all patients. Most commonly, 30% of variants, there is an accessory, aberrant, or supernumerary renal artery. A vast majority of these vessels originate from the aorta. However, they rarely can stem from any artery within the abdomen and pelvis, such as the lumbar, colonic, pancreatic, gonadal, hepatic, adrenal, and inferior phrenic arteries. Most commonly there is an accessory vessel superiorly to supply the apical segment or inferiorly to supply the lower segment of the kidney. There is a slightly increased incidence of an accessory renal artery on the left than the right. A right-sided renal artery may course anterior to the inferior vena cava. In addition, there may be duplication of renal arteries in up to 10% or patients (Figure 128.1b) [2–4].

## Adrenal vasculature

The adrenal glands have varying vascular supply, and may be perfused by up to three arteries (Figure 128.2). The superior adrenal artery usually arises from the inferior phrenic artery, which may branch off the celiac plexus. The middle adrenal artery commonly stems directly from the aorta. The inferior adrenal artery usually originates from the main renal artery [5]. The adrenal gland may be supplied in part by combinations of this vascular supply; most commonly supply is from two vessels (61%) or three vessels (34%).

An understanding of adrenal vasculature is crucial to an understanding of renal vasculature and pathology. Given the likelihood of a shared vascular supply and regional proximity, disease of one organ may involve the other. Renal trauma or renal intervention may injure the adjacent adrenal gland or its vascular supply (Figure 128.3).

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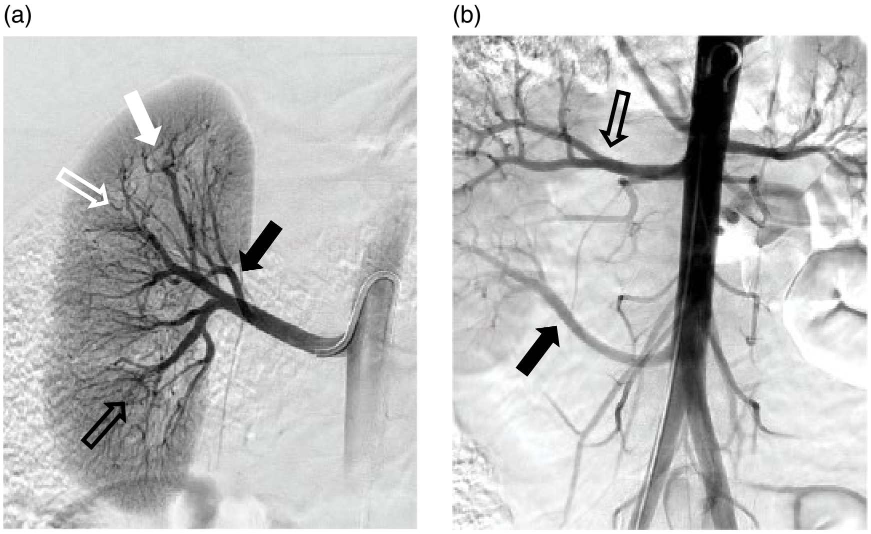

**Figure 128.1** Renal arterial anatomy. (a) Right renal digital subtracted angiography (DSA) depicts common renal arterial distribution. The first branch (black arrow) from the main renal artery descends posteriorly to supply the posterior segment. The anterior branch divides to supply the upper (white arrow), middle (white open arrow), and lower renal segments (black open arrow). (b) Aortogram of a different patient demonstrates a duplicated right renal artery (black arrow). Note the similar caliber compared to the more proximal right renal artery (black open arrow).

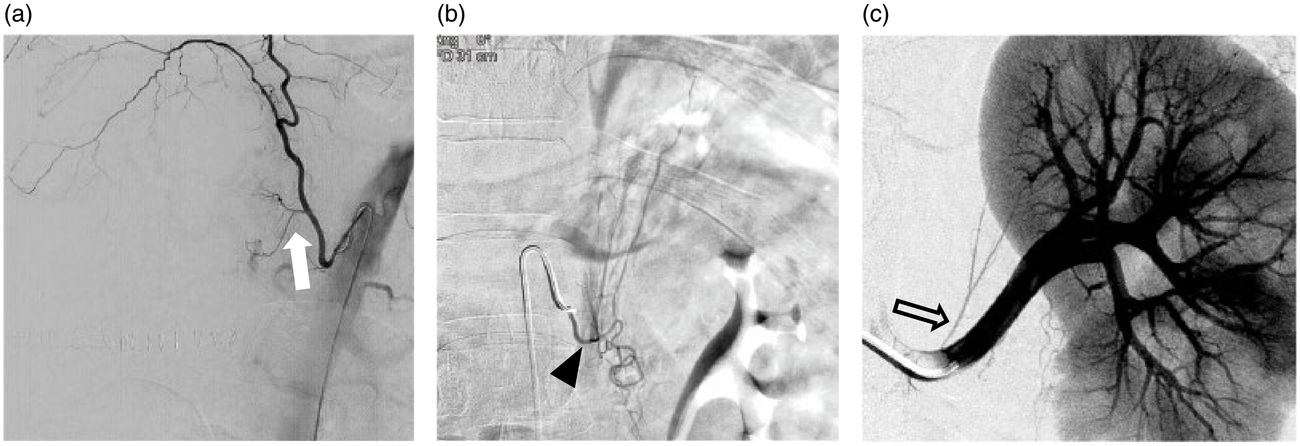

**Figure 128.2** Adrenal arterial anatomy. (a) Selective angiogram of the right phrenic artery demonstrates the superior adrenal artery branch (white arrow). (b) Selective angiogram of the left middle adrenal artery as a branch directly from the aorta (black arrowhead). (c) Left renal arteriogram demonstrates the inferior adrenal artery (black open arrow).

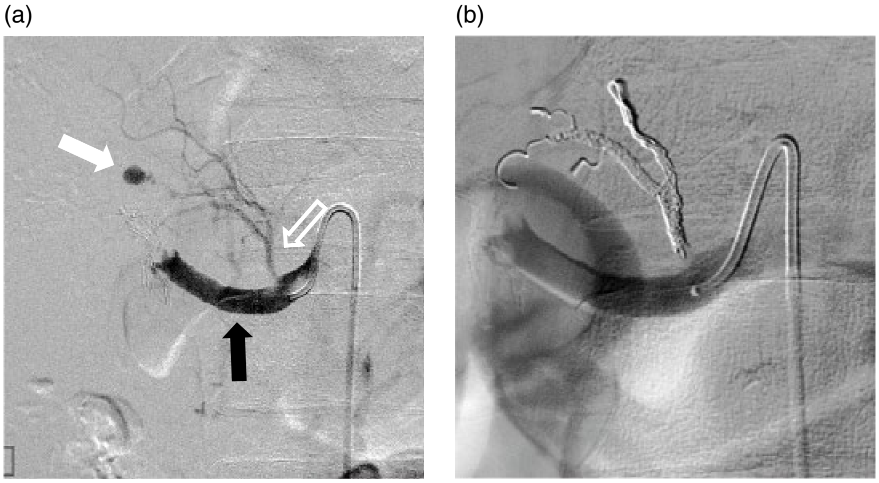

**Figure 128.3** Adrenal artery pseudoaneurysm. (a) Postnephrectomy right renal artery (black arrow). Inferior adrenal artery (white open arrow). Pseudoaneurysm of the right inferior adrenal artery (white arrow). (b) Post right inferior adrenal artery embolization right renal arteriogram demonstrates successful hemostasis.

## Horseshoe kidney

Formation of a horseshoe kidney is secondary to aberrant *in utero* renal development. Normally, during the first trimester of gestation, nearly adjacent bilateral metanephric buds of the pelvis are developing into the kidneys. As the gestation progresses the metanephric buds demonstrate external rotation and ascension into the retroperitoneum. As the metanephric buds ascend, their vascular supply arises from progressively more superior renal arteries from the aorta. The most common development aberration is malrotation of one kidney. If the lower poles of the metanephric buds fuse, their ascension halts at level of the inferior mesenteric artery, as the isthmus of this horseshoe kidney is bound superiorly by this vessel (Figure 128.4). Subsequent renal vascularity may vary as numerous adjacent vessels in the lower abdomen and pelvis may supply the organ [6].

Renal arterial interventions of a horseshoe kidney require thorough mapping of the vascular supply, as there may be multiple vessels which can stem from the aorta or the iliac arteries.

## Technical issues

### Vascular access

Every angiographic procedure requires a proper and skillfully established vascular access. Arterial access is commonly performed via the modified Seldinger technique, and can be aided with sonographic imaging in addition to physical exam. The common femoral artery is traditionally and most commonly used. However, radial, brachial, or axillary arteries may be utilized [7, 8].

Commonly, arterial access is achieved with a 21 gauge micropuncture needle under sonographic guidance. Serial dilatation of the puncture site is performed and followed by placement of a vascular access sheath over a wire. Sheath sizes commonly range between 4 and 6 Fr. Vascular interventions on small children or neonates may be performed with a 4 Fr system without the use of a vascular sheath. In rare instances, the umbilical artery can be catheterized in newborns.

### Renal artery catheterization

The renal artery may be targeted directly to reduce patient radiation and intravenous contrast dose, especially in cases where prior imaging is available to depict the patient's anatomy. Alternatively, an abdominal aortogram may be performed. Multiple catheters are available for arterial selection. Commonly, the catheter selection is based on the operator's preference. In certain instances, the short left or stenotic renal artery may be selected with a reverse curve catheter, as this catheter will provide a more stable access. Microcatheters are used in a coaxial technique to target smaller distal renal arterial branches. Selective targeting of renal vessels aids in increased clarity of regional pathology, and allows for nephron-sparing embolization.

### Embolization materials

Several embolic agents exist and demonstrate unique characteristics allowing for effective use in various clinical scenarios. The agents may be permanent or temporary.

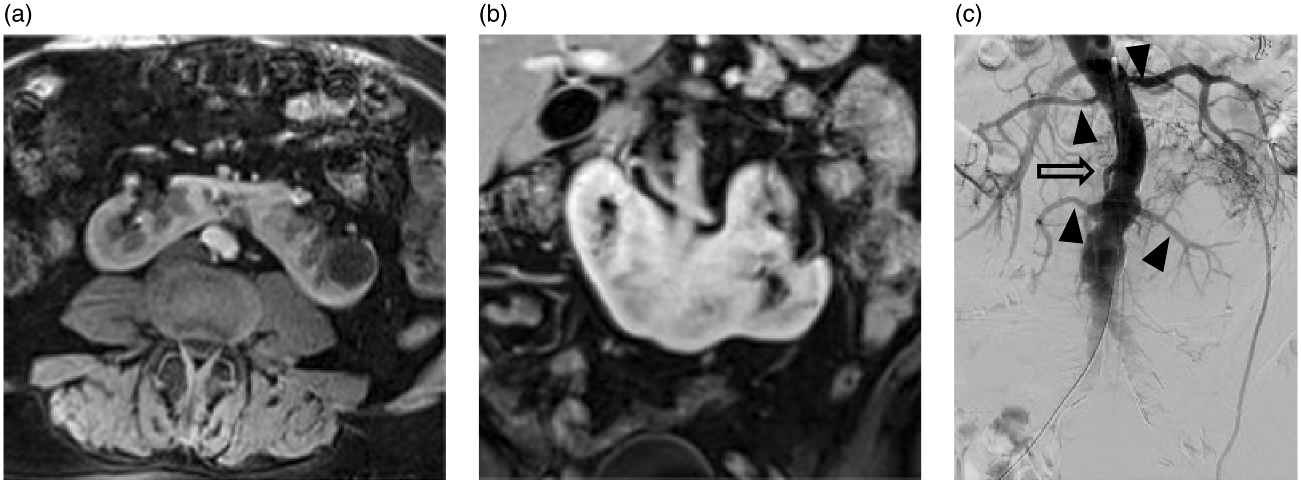

**Figure 128.4** Horseshoe kidney. (a) Axial and (b) coronal postcontrast MR images of a horseshoe kidney demonstrate renal fusion of the lower renal poles. (c) Aortogram demonstrates numerous renal arteries (arrowheads). Note the abnormally high location of the inferior mesenteric artery (black open arrow).

Temporary arterial embolization materials, such as microfibrillar collagen, gelatin foam, or biodegradable particles may be used in instances where delayed vessel reperfusion is appropriate. The occlusive effect varies and may last from 3 to 90 days depending on the agent used [7]. Permanent embolization agents include vascular plugs, coils, particles, sclerosing agents, and glue.

Coils are used quite commonly and may be detachable or nondetachable. The detachable coils remain attached to the wire until they are appropriately formed within the targeted vessel. Permanent embolization particles are produced in sizes ranging from 40 to 2000 μm. Small particles range from 40 to 300 μm and are commonly used to embolize distal tumor vessels to attain tumor necrosis. In certain tumors, such as angiomyolipomas, larger particles may be used to achieve tumor necrosis. In general, the larger particles provide a rapid vascular occlusion where tissue necrosis is not the primary goal. These large particles are commonly used as a means of preoperative embolization and to stop anastomosed arteriovenous shunting.

Several liquid embolic agents are available, including ethanol, glue, and several newer nonadhesive agents. The ethanol used ranges from 94% to 99% concentration, and causes endothelial damage which induces rapid vessel occlusion. Ethanol is commonly mixed with radiopaque iodized oil. The oil makes the injection visible on fluoroscopy. The oil also provides the added benefit of lengthening the vascular endothelial exposure to the ethanol. Ethanol injection is painful and appropriate pain management is advised.

*N*-Butyl-2-cyanoacrylate glue is a liquid embolic agent that polymerizes upon contact with blood or ionic substances. As with ethanol, the glue is mixed with radiopaque iodized oil. The glue consistency may be diluted to match target vessel flow and decrease the odds of nontarget embolization. This balance is rather precise and requires significant expertise and experience. Also available is an additional nonadhesive liquid agent composed of an ethylene vinyl alcohol copolymer combined with a radiopaque tantalum powder. This mixture hardens, forming a shapeable dense cast for several minutes, and is particularly useful when slow embolic delivery is required [7].

Postembolization arteriograms are always performed. It is important to perform a proximal renal artery injection following the angiogram of the occluded vessels. This allows for evaluation of the presence of additional arteries supplying the targeted area. Occasionally after target embolization is performed, additional feeding vessels to the area of interest are identified on aortogram, as vascular redistribution may occur.

Completion of the angiographic procedure involves removal of the access sheath or catheter. Hemostasis of the puncture site has classically been performed with manual compression of the vascular access site. However, multiple hemostatic patches are available which can be used with or in lieu of compression. If the radial artery was used for vascular access, then wearable compression-assisting devices are available to achieve hemostasis. In addition, vascular closure devices are also widely used. These devices provide added comfort to the patient and operating physicians when compared to manual compression.

## Postembolization management

Postembolization management involves prevention of arterial access site hemorrhage and management of the postembolization symptoms. For femoral access cases, strict bed rest with extension of the punctured extremity is employed. Common postembolization symptoms are rather nonspecific and include: nausea, emesis, fever, leukocytosis, as well as flank, back, and/or abdominal pain. These symptoms usually develop within 72 hours post procedure [9]. These symptoms are medically managed with use of antiemetic, anti-inflammatory, and pain medications with intravenous hydration. These symptoms are the result of the systemic inflammatory response, and a septic workup is not required.

## Treatment of traumatic and iatrogenic hemorrhage

Blunt force or penetrating injury are the most common etiologies of renal trauma [10, 11]. Blunt trauma is far more common and penetrating renal injuries are usually iatrogenic, following surgery, biopsies, or percutaneous urological procedures (Figure 128.5a–c).

Blunt renal injury is typically graded with computed tomography (CT) findings, and as per the American Association for the Surgery of Trauma which guides the need for surgical intervention. Low-grade I–II renal injuries are managed conservatively with hospitalization and blood transfusions as needed. High-grade III–V injuries are usually treated with either surgery and/or intervention. Renal angiogram and embolization may be performed alone or in conjunction with surgery. Preoperative embolization may minimize bleeding and facilitate nephron-sparing intervention.

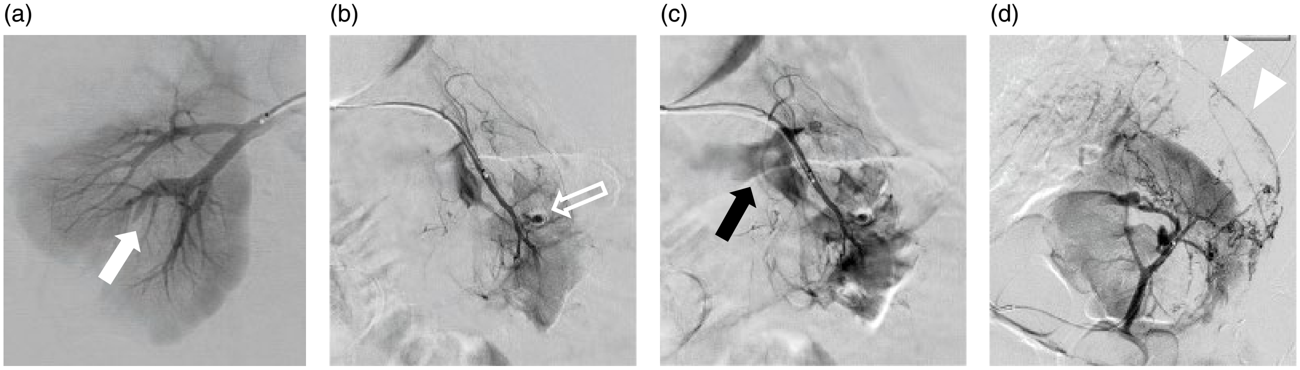

**Figure 128.5** Direct signs of vessel injury. (a) Arterial cutoff sign (white arrow). (b) Pseudoaneurysm (white open arrow). (c) Arteriovenous fistula (black arrow), early filling of the left renal vein. (d) Active contrast extravasation (white arrowheads).

Identification of hemorrhagic sources on angiography require a fundamental knowledge of the signs of bleeding. There are two types of angiographic signs of bleeding: direct and indirect. The indirect signs of bleeding are vascular spasm, hematoma, and displacement of the arteries from their usual course – usually by an underlying hematoma. The direct signs of bleeding include: abrupt termination of the artery (vessel cutoff sign), formation of a pseudoaneurysm, presence of an arteriovenous fistula and/or extraluminal contrast extravasation. Vessel cutoff sign or abrupt vessel termination represents arterial thrombosis as a result of complete or partial vascular transection. Pseudoaneurysms are areas of lobular contrast accumulation adjacent to the ruptured vessel confined by regional soft tissues. The pseudoaneurysms present with intermittent bleeding when the surrounding tissues periodically separate secondary to increasing pressures. Arteriovenous fistulas are an abnormal direct communication between the imaged artery and vein, and are identified angiographically with the presence of an early draining vein. Contrast extravasation reflects active hemorrhage (Figure 128.5) [11].

In patients with renal hemorrhage, renal angiography not only elucidates anatomic source(s) of hemorrhage but also allows for a minimally invasive treatment with a high rate of efficacy. Arteriography should be considered first line for recalcitrant and refractory bleeding in iatrogenic cases.

## Angiography and embolization of renal tumors

Identifying neoplasms angiographically requires knowledge of "tumor vascularity." These findings are similar for neoplasms in any part of the body. They include abnormal vascular tortuosity, luminal irregularities, aneurysms, pseudoaneurysms, hypervascularity, parasitized vessels, arteriovenous shunting, and early contrast opacification and delayed washout – also called the "mother-in-law sign" (Figure 128.6). Tumor vessels are more porous and lack the ability to control bleeding as normal arteries do, and as a result are susceptible to hemorrhage, especially as the tumors increase in size [12]. Not uncommonly, it is impossible to determine the nature of a tumor based on angiographic appearance, and using corresponding cross-sectional imaging is of the utmost importance.

### Renal angiomyolipomas

Renal angiomyolipomas (AMLs) are benign tumors containing fat, vascular, and smooth muscle components (Figure 128.7). They are sporadic in approximately 80% of patients. In approximately 20% of patients, AMLs are most commonly associated with a phakomatosis [13]. The sporadic tumors are more frequent in women and tend to be asymptomatic in approximately 75% of cases. Nearly 15% of patients with AMLs present with lesion hemorrhage. Multiple AMLs are seen in 15% of affected patients. The most common hereditary conditions associated with AMLs are tuberous sclerosis, von Hippel–Lindau syndrome, and neurofibromatosis type 1.

Clinical presentations of AML include palpable masses, flank pain, urinary tract infections, hematuria, renal failure, or even hypertension. Renal AMLs are prone to hemorrhage, and the risk of hemorrhage increases with the tumor size. At 4 cm or greater, the lesion has a significant bleeding risk (>50%) and preemptive embolization should be performed [12]. Surgical resection is an option, but this is generally reserved for rare cases where embolization cannot be performed.

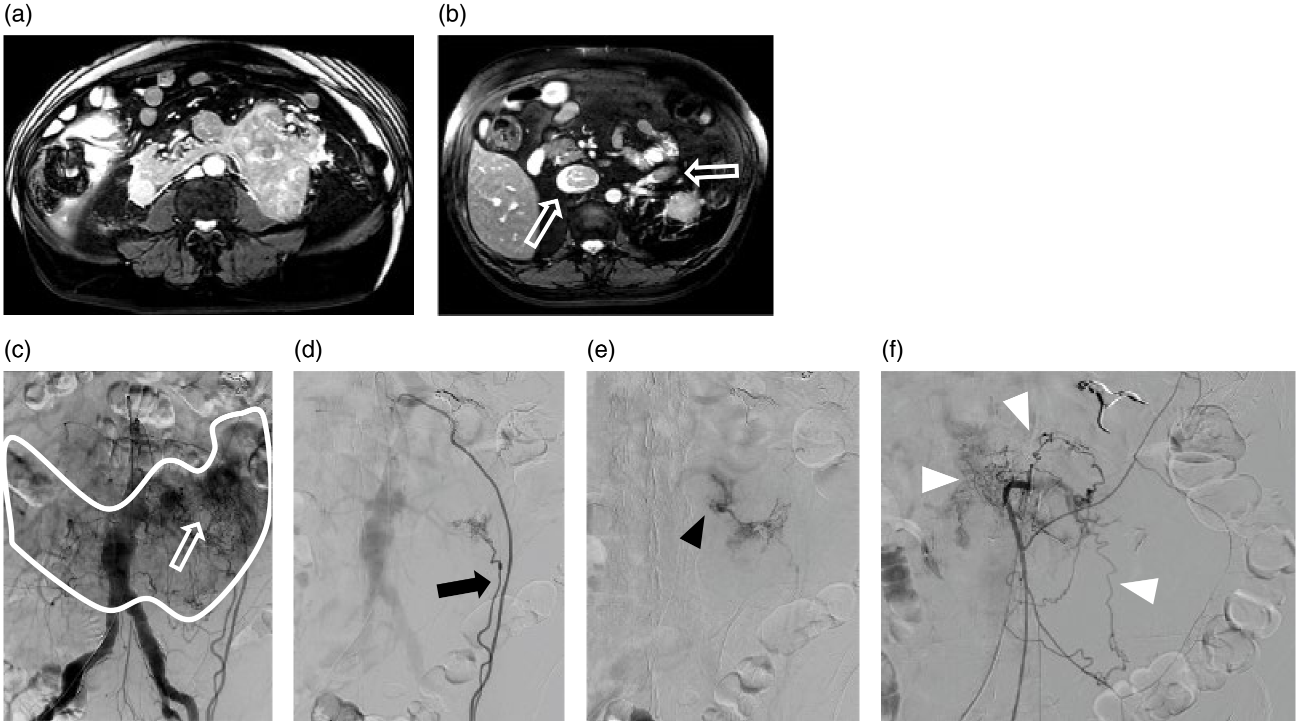

**Figure 128.6** Renal cell carcinoma, horseshoe kidney. (a) Axial T2-weighted MR images demonstrate a renal mass involving the left anterior aspect of the horseshoe kidney. (b) Tumor thrombus in the left renal vein and inferior vena cava (white open arrows). (c) Aortogram demonstrates hypervascular renal cell carcinoma (white open arrow) within the left portion of the horseshoe kidney (delineated). (d) Selective left gonadal arteriogram. Parasitic artery (black arrow) supplies the left renal mass. (e) Early left renal vein drainage (black arrowhead). (f) Selective inferior mesenteric arteriogram (IMA). Numerous parasitic vessels from the IMA (white arrowheads) supply the renal mass.

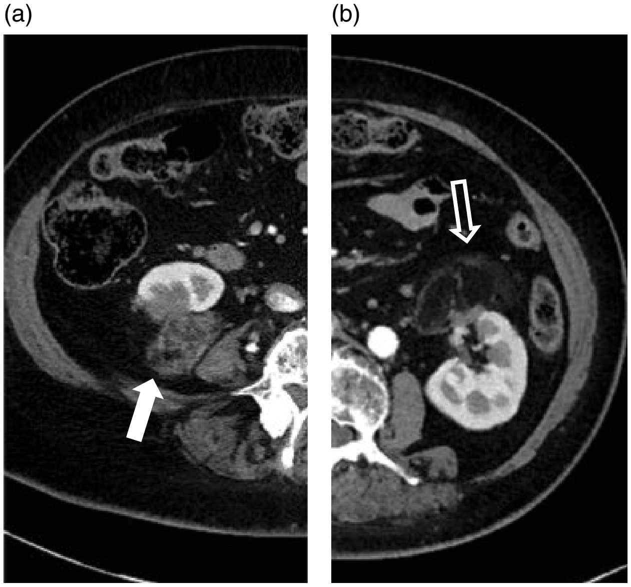

**Figure 128.7** Bilateral angiomyolipomas. Contrast-enhanced CT images of a patient with tuberous sclerosis. (a) Enhancing fat-containing lesion through the lower pole of the right kidney (white arrow). (b) Similar fat-containing lesion at the upper pole of the left kidney (white open arrow).

AMLs usually have well-demarcated margins, irregularly dilated vessels, aneurysms, and lack of arteriovenous shunting. Sporadic AMLs, compared to other renal tumors, typically demonstrate a single feeding artery. Particle embolization of an AML will decrease tumor vascularity, and will gradually lead to decreased tumor size and risk of hemorrhage (Figure 128.8). Embolized AMLs require follow-up, and approximately one-third of cases will require re-embolization. AMLs with acute hemorrhage can also be successfully treated with emergent embolization. AML arterial embolization is a well-tolerated, safe, durable, and effective kidney-sparing therapy [12, 14].

## Preoperative embolization for large tumors

Preoperative renal embolization can be helpful before radical nephrectomy for treatment of large renal neoplasms, such as renal cell carcinoma (RCC). It can minimize the intraoperative hemorrhage and decrease

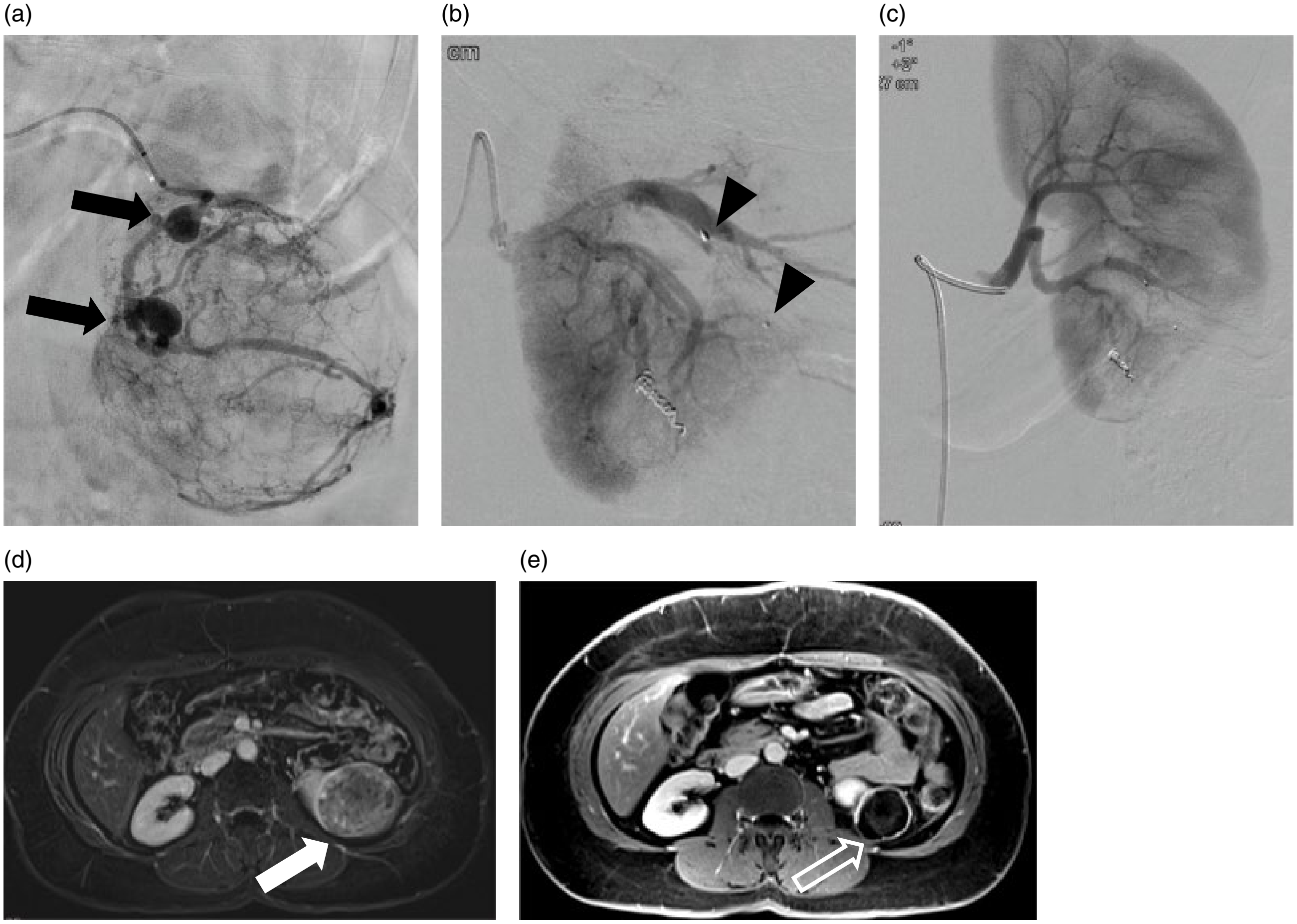

**Figure 128.8** Sporadic angiomyolipoma (AML) with interval treatment. (a) Subselective left renal arteriogram demonstrates irregularly dilated and tortuous vessels with saccular aneurysms (black arrows). (b) A microvascular plug (black arrowheads) and coils were used to devascularize the lesion. (c) Postembolization arteriogram demonstrates preserved vascular supply to the remainder of the kidney. (d) Preprocedural contrast-enhanced MRI demonstrates the large enhancing AML (white arrow). (e) Follow-up MRI demonstrates decreased size of the AML with absent internal vascularity (open white arrow).

the overall time of the surgery [15], which translates to a decrease in perioperative morbidity and mortality [7]. Arterial embolization of RCC is typically performed within 24 hours of the planned nephrectomy (as in previously mentioned Figure 128.6).

## Pediatric renal tumors

Selective renal arterial embolization can be helpful in the management of pediatric primary renal neoplasms such as Wilms' tumors, AMLs, rhabdoid, metanephric adenomas, etc. [16, 17]. For example, it has been used to stabilize patients who presented with active bleeding secondary to ruptured Wilms' tumors in order to bridge them to a complete nephrectomy (Figure 128.9) [18].

## Conclusion

Renal angiogram and embolization plays an important role in the management of urological patients. It can enhance the urological practice and improve clinical outcomes. These procedures can be used electively or emergently, preoperatively, or independently in patients with a range of urological diseases. Continuous advancement in digital technology, imaging, and material science increases efficacy and safety of these procedures and will continue to be an important asset in management of urological patients.

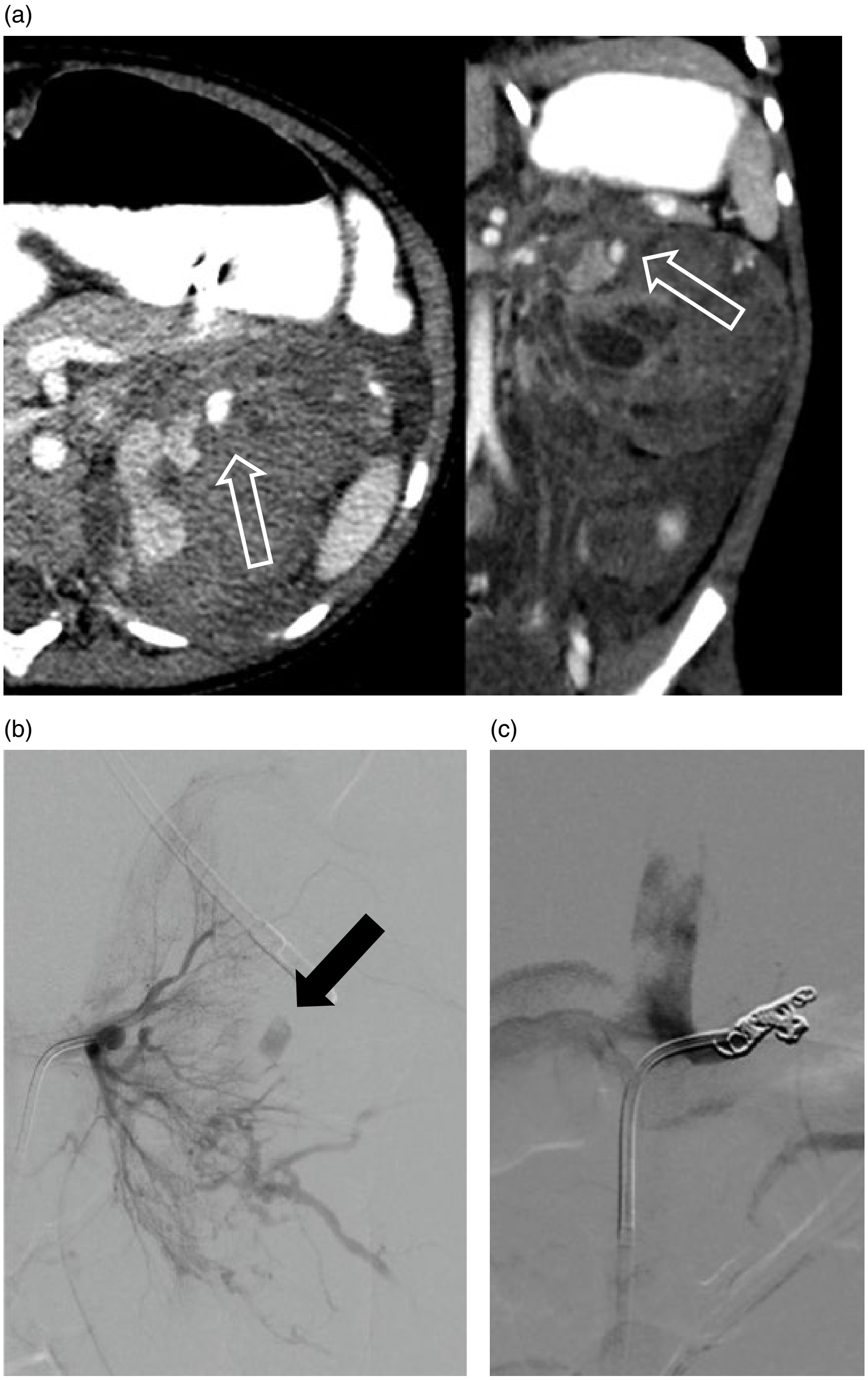

**Figure 128.9** Hemorrhagic Wilms' tumor. (a) (Composite) Axial and coronal reformatted contrast-enhanced CT images of the abdomen demonstrate a large vascular left renal mass with foci of hyperattenuation, compatible with pseudoaneurysms (white open arrows). (b) Left renal arteriogram depicts the pseudoaneurysm (black arrow). (c) Postembolization angiogram demonstrates successful preoperative devascularization.

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# 129

# Selective Arterial Prostate Embolization

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## Introduction

Symptoms of benign prostatic hyperplasia (BPH) affect a large number of middle-aged men, estimated to be more than 15 million in the United States, with an estimated cost to the healthcare system of US$3 billion annually [1]. Improving treatment of BPH therefore represents a major concern for the American healthcare system as an area for potential cost savings and quality-of-life improvements.

Symptoms related to BPH are commonly referred to as lower urinary tract symptoms (LUTS), and are broadly categorized into two categories: storage and emptying. The generally accepted standards for the evaluation of BPH symptoms includes the International Prostate Symptom Score (IPSS), which is used to assess changes in quality of life related to LUTS [2] and consists of a questionnaire covering symptoms of frequency, urgency, and nocturia among others. The first-line approach to treatment of LUTS commonly includes lifestyle changes such as management of fluid intake and output. Medical therapy with oral agents is the next step in symptom management and can include alpha-blockers (tamsulosin, terazosin, etc.), 5-alpha-reductase inhibitors (finasteride, dutasteride), anticholinergic agents, or a combination of these agents [2]. When patients can no longer be managed on one or more of the above medications, definitive management is generally offered with either minimally invasive or surgical therapy.

This chapter explores the technique and role of selective prostate artery embolization (SAPE) as a treatment for LUTS secondary to BPH as it compares to conventional definitive treatment options.

## Procedures for management of benign prostatic hyperplasia

Transurethral minimally invasive treatment options include transurethral needle ablation (TUNA) and transurethral microwave thermotherapy (TUMT). Both techniques involve using heat energy from either radiofrequency probes (TUNA) or a microwave probe (TUMT) to induce thermal necrosis of the adjacent prostate tissue. Criticisms of TUNA have centered around the lack of prospective randomized data on the technique and the apparently high lifetime retreatment rate (46% at 3 years in one study of 102 patients) [3]. Efficacy of TUMT has improved as technology has improved the ability of transurethral microwave probes to generate sufficient temperatures for prostate tissue ablation. It is estimated that around 80 000 TUMT cases are performed each year in the United States [2]. Similar to TUNA, concerns surrounding TUMT have focused on the lack of quality prospective data on the technique, especially given the technical differences in the devices available for the procedure over the years. Ultimately, the major benefits of TUNA and TUMT seem to be offering patients a lower rate of erectile dysfunction than conventional surgical management, with the major concern surrounding the treatments being the possible need for retreatment.

More recently, laser-based transurethral options have become a popular option for BPH treatment. Treatments include holmium laser ablation of the prostate (HoLAP), enucleation of the prostate (HoLEP), and resection of the prostate (HoLRP), along with photoselective vaporization of the prostate (PVP). All therapies use a transurethral laser probe to heat the periurethral prostatic tissue, with

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or without an additional mechanical component of resection. Use of laser therapies for BPH has been associated with decreased catheterization time and lower complications rates. Data on the techniques are limited by short follow-up and rapid evolution of device technology.

Surgical therapy for bladder outlet obstruction (BOO) related to BPH is defined as the mechanical debulking of tissue within the prostatic fossa. Techniques for debulking prostate tissues have evolved over the years, with options ranging from open prostatectomy to transurethral laser ablation and traditional TURP. Open (simple) prostatectomy represents the most invasive treatment option for BPH, and is generally reserved for patients with prostate volumes greater than 80–100 ml, bladder calculi, or bladder diverticula. It is associated with longer hospital stays and higher transfusion rates than TURP [4].

TURP remains the gold standard treatment option for LUTS related to BPH, and involves the use of a transurethral resectoscope to debulk the periurethral prostatic tissue. Short-term complications of the procedure include hematuria, while long-term complications can include urethral stricture, sexual dysfunction, and dilutional hyponatremia. The incidence of dilutional hyponatremia has decreased with the implementation of bipolar transurethral resection using normal saline as an irrigant compared to glycine. There has been only one reported randomized controlled trial comparing TURP and SAPE [5]. In the study, technical success rates for TURP and SAPE were comparable (100% and 94.7%, respectively). Patients were followed for 2 years. A compelling finding was the apparent trend toward greater improvement in IPSS, quality of life, peak urinary flow rate ($Q_{\max}$), and postvoid residual bladder volume (PVR) after one and three months in the TURP group, with the SAPE group ultimately reaching similar values at six months with sustained results for the remainder of the study period. The authors discussed the logical nature of this outcome, given that SAPE is not an instantaneous ablative technique. One advantage of SAPE appeared to be the relative safety of the procedure; two TURP patients required transfusion and another required intensive care unit admission, versus 0 in the SAPE group. Patients undergoing prostate artery embolization have reported improvement in erectile function, possibly secondary to an increase in blood flow to the pudendal artery following embolization.

## History of selective arterial prostate embolization

Embolization of prostate arteries has long been used to control serious bleeding after biopsy or prostatectomy. DeMeritt and colleagues described in their 2000 paper the first report of a patient experiencing decreased prostate volume following SAPE of the right inferior vesicle artery, which was used at the time for severe hematuria following prostate biopsy [6]. They discovered that prostate volume was reduced by 52% at 5 months and 62% at 12 months, suggesting that SAPE may be a clinically viable option for the treatment of BPH. SAPE has also been referred to as prostate artery embolization (PAE); this nomenclature is also used in uterine artery embolization (UAE). However, by using SAPE as an acronym we attempt to set it apart from UAE, which is technically less challenging.

Animal studies using triacrylic gelatin microspheres (Embosphere; Merit Medical, South Jordan, UT, USA) in dogs and pigs demonstrated the efficacy of embolization with spherical microparticles, resulting in decreased prostate volume with no apparent decrease in sexual function [7, 8]. Initial human implementation of SAPE for the treatment of BPH was described in 2010 by Carnevale et al. in two patients, both of whom experienced a steady decrease in prostate volumes up to six months [9]. A subsequent study by Pisco et al. demonstrated a mean improvement in IPSS of 6.5 points ($P = 0.005$) in a cohort of 15 patients treated with SAPE [10].

A single-center prospective study of 72 patients evaluated for possible SAPE, of whom 20 underwent treatment, revealed 19 of 20 patients with improvement in symptoms at 1, 3, and 6 months. Similar improvements in quality of life and sexual function were noted [11]. There were no major or minor complications in the study. Findings suggested that SAPE is a safe and effective option for treatment of BPH. A more recent meta-analysis examined the results of six studies of SAPE comprising a total of 481 patients revealed overall improvement in $Q_{\max}$, PVR, IPSS, and quality of life endpoints at 12 months, with a low incidence of serious adverse events (0.3%) [12]. They report a relatively high rate of minor adverse events (32.93%), with the most common being transient acute urinary retention and dysuria.

## Benign prostate hypertrophy workup and preoperative assessment

According to the 2010 AUA Guidelines for the Management of BPH, workup should follow an algorithmic approach as adapted from the 2009 article by Abrams et al. [13]. Assessment of LUTS may include a quality-of-life assessment using the IPSS, as well as quantitative measures such as PVR, prostate volume (either by ultrasound or MRI), urodynamic studies (generally $Q_{\max}$ and peak detrusor pressure ($P_{\text{det}}$) at $Q_{\max}$), and a urinalysis.

At our institution, we consider patients for prostate artery embolization with:

- LUTS for >six months
- IPSS score >13
- $Q_{\max} < 12$ ml/s and or urinary retention
- Prostate volume larger than 40 ml as assessed by MRI
- Negative screening prostate MRI (no lesions suspicious for cancer)
- Symptoms refractory to medical therapy or contraindications to medical therapy
- Baseline prostate specific antigen (PSA) <3.5 ng/ml.

In patients with baseline PSA >3.5 ng/ml, the patient must be counseled on risks and benefits of prostate cancer screening with their urologist. Furthermore, the subject must meet one of the following criteria:

- Negative prostate cancer screening (minimum 12 core prostate biopsy) within 2 years of the procedure
- No MRI visible prostate lesions suspicious for cancer: (negative prostate MRI)
- Negative targeted biopsy of any suspicious lesions on MRI along with a standard biopsy within the last 2 years.

Contraindications include:

- active urinary/prostate infection
- prostate cancer (clinically significant)
- neurogenic bladder
- urethral stricture or other urethral conditions contribution to BOO.

A conversation with the patient about future interest in fertility is warranted prior to therapy.

## Preprocedure imaging

Ultrasound and MRI are both able to provide estimates of prostate volume prior to embolization, providing a helpful baseline for later assessment of the treatment effect. Prostate ultrasound is operator dependent and relies on the ellipsoid volume formula to calculate prostate volume. MRI can provide a slice-by-slice volumetric assessment of prostate volume, making it superior to ultrasound in accuracy and the study of choice in our institution. In addition, MRI is able to identify unknown prostate cancers, thereby altering the course of treatment for a given patient. Efforts have been made to standardize reporting of prostate MRI findings, with the latest iteration from the American College of Radiology being PI-RADS v2 [14]. Patients with a suspicious MRI-visible lesion require discussion and most likely a biopsy before meeting criteria for prostate embolization. A prostate with characteristic findings of BPH is shown in Figure 129.1.

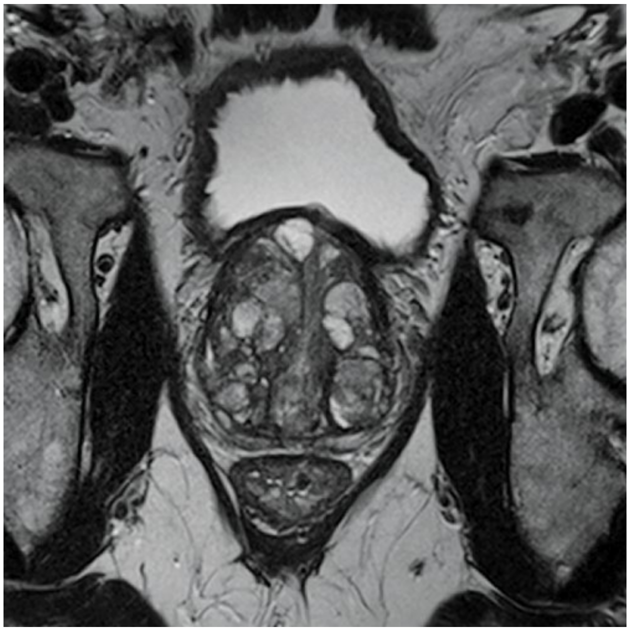

**Figure 129.1** High-resolution small field-of-view T2-weighted MRI of the prostate. Round high-signal foci within the central gland represent mixed-type BPH nodules with characteristic cystic and glandular components. Predominantly low-signal areas correspond to pure stromal-type BPH nodules. Expansion of the gland results in mass effect on the adjacent urinary bladder anteriorly.

## Technique

SAPE can be safely completed using moderate conscious sedation with midazolam and fentanyl. Preprocedure, we recommend placement of a Foley catheter balloon in the bladder, filled with 10–20% iodinated contrast, as a means to aid localization of the gland in its relationship to the bladder neck.

### Transradial approach

We typically perform SAPE via left transradial approach as previously described [15], though a transfemoral approach is also well-established. Assessment of palmar arch patency/presence of adequate collateral circulation is performed prior to access via the Barbeau test (modified Allen test) using pulse oximetry as previously described [16]. A type D waveform (i.e. lack of any ulnar artery collateral flow to the arch) is an absolute contraindication to radial access.

Initial radial access is obtained using ultrasound guidance and a micropuncture kit consisting of a 21-gauge needle and 0.021-inch nitinol wire. A 5 Fr hydrophilic sheath (Glidesheath™, Terumo Medical, Somerset, NJ, USA) is then advanced over the wire and secured using an adhesive bandage (Tegaderm™, 3M Medical, St. Paul, MN, USA). A solution of 2 mg verapamil, 3000 units of heparin, and 200 µg of nitroglycerin are then diluted in the patient's blood and administered through the sheath to prevent arterial spasm and thrombus formation.

Catheters used for transradial uterine artery embolization can generally also be used for SAPE given their similar technical considerations. We use a 130 cm 5F Select BER Catheter (Penumbra, Alameda CA, USA) and a 180 cm 0.035-inch Benston wire to advance the catheter up the left arm, over the aortic arch and down the descending aorta into the anterior devision of the left internal iliac artery. A 150 cm microcatheter (2.0Fr, PROGREAT, TERUMO, USA) is then used with an 0.016-inch hydrophilic wire (Fathom, Boston Scientific, MA, USA) to select prostatic artery branches. We sometimes find it helpful to use a smaller profile microcatheter, 1.7–1.9 Fr with a 45° angled tip microcatheter (Codman Neuro, DePuy Synthes, Wokingham, UK) in combination with a Silverspeed 0.014-inch hydrophillic wire (Medtronic, MN, USA), to navigate smaller prostatic vessels. Please take into consideration a patient's height when selecting catheters and patients for radial artery access.

## Transfemoral approach

If a transfemoral approach is preferred, catheters can again be selected from those used for uterine artery embolization. A 5 Fr cobra or vertebral artery diagnostic catheter can be used to select the anterior division of the internal iliac artery. A microcatheter and 0.018-inch hydrophilic wire are similarly recommended for subselection of prostatic artery branches. An alternative also includes the use of a pudendal artery catheter to allow for ipsilateral and contralateral access without the use of a Waltman loop.

## Angiography/selection of embolization site

Initial angiography is generally performed from the anterior division of the internal iliac artery using digital subtraction angiography (DSA). An ipsilateral 25–55° oblique view is used to assess the blood supply to the prostate, and can be maintained to facilitate catheterization of the internal vesicle artery [17]. Cranial angulation of 10–15° can also help with visualization of the prostatic vasculature. Figure 129.2 shows an example DSA image with anatomic labels.

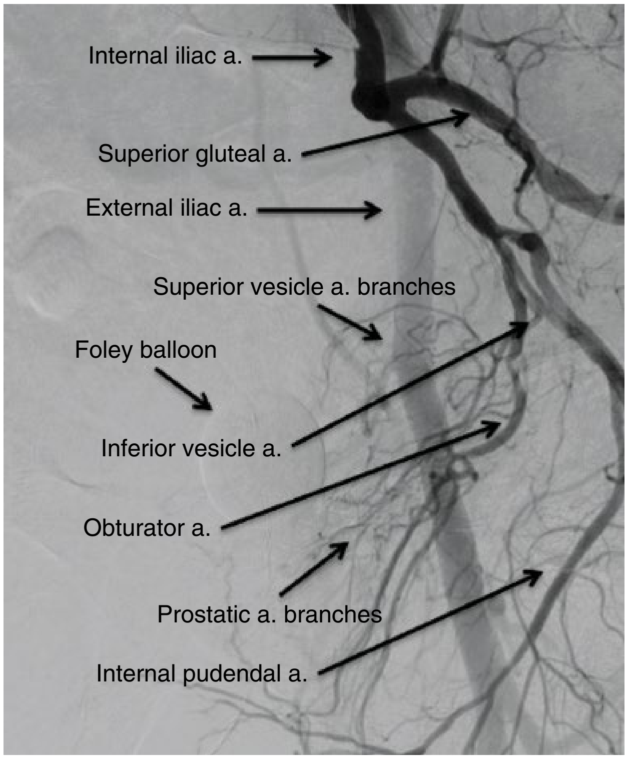

**Figure 129.2** Digital subtraction angiography performed from an ipsilateral 35° approach. Iodinated contrast was injected via a 5 Fr catheter positioned in the proximal internal iliac artery.

Numerous papers have described the benefit of cone-beam CT (CBCT) as a means for preventing nontarget embolization during SAPE [18, 19]. This can be performed prior to embolization from the prostatic artery. We agree, and furthermore if available prefer use of vessel detection software (EmboGuide, Philips Healthcare, Amsterdam, The Netherlands), which provides assistance with automatic feeding artery detection and live image guidance during the procedure. EmboGuide setup requires CBCT with an injection at the level of the anterior division of the internal iliac artery using approximately 3–4 ml/s for 10 seconds (total volume 30–40 ml) of contrast following a 5 second delay (Figure 129.3).

Further subselection of the prostatic arteries should ensure that any collateral vessels supplying the bladder, penis, rectum, or gonads have been passed, with the microcatheter ultimately stationed distally within the prostatic artery. CBCT angiography may be performed to confirm the vascular distribution within the subselected branch to help lower the risk of nontarget embolization. Figure 129.4 shows an example of a prostatic artery CBCT angiogram.

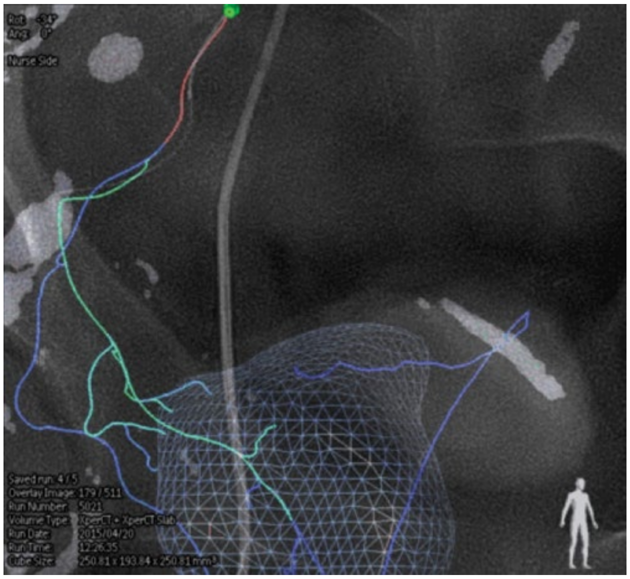

**Figure 129.3** Cone-beam CT angiogram using EmboGuide (Phillips) guidance software. A CBCT angiogram was performed using EmboGuide software with microcatheter positioned in the proximal portion of a right prostatic artery branch. Red, green, and blue lines indicate likely prostatic artery locations. Imaging is projected on the in-room monitors and correspondingly changes position as the operator manipulates the table and imaging angle.

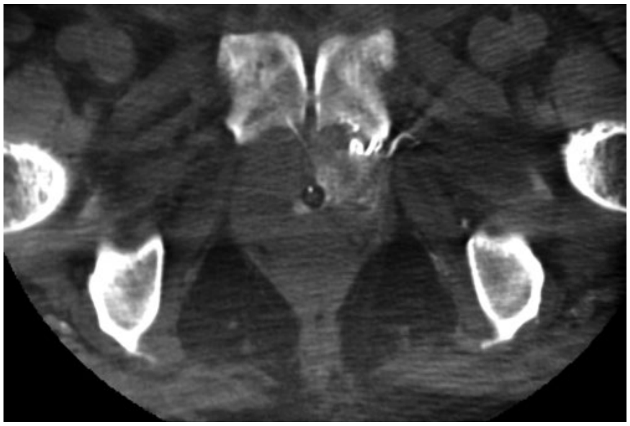

**Figure 129.4** Axial cone-beam CT angiography, mid-gland. Intraprocedural CBCT angiography was performed with contrast injection via microcatheter positioned in a prostatic artery branch. Parenchymal enhancement of the left lobe of the prostate gland is seen, along with opacification of the injected prostatic artery. A Foley catheter is seen in the prostatic urethra.

## Embolization

Arteries supplying the prostate gland generally measure between 200 and 400 μm. Among the generally accepted media for embolization are 300–500 μm Embosphere® Microspheres (Merit Medical, South Jordan, UT, USA), though other operators have described successful use of other spherical agents [11] (Embozene 100–400 μm, Boston Scientific) and non-spherical agents (PVA) [6]. A randomized prospective study comparing the use of smaller (100 μm) and larger (200 μm) PVA particles revealed greater reduction in prostate volume and PSA in the 100 μm group [20]. The rational is that smaller diameter particles achieve a deeper penetration within the prostatic vasculature, possibly down to the periurethral level, though these may cause more irritative voiding symptoms. Embolization particles as small as 40 μm have been evaluated without adverse side-effects [21].

Particles are diluted with equal parts saline and iodinated contrast medium and suspension is achieved via repetitive inversion. Embolization is performed to near-stasis.

## Vascular anatomy

In the setting of BPH, prostatic arteries will generally be hypertrophic, improving visibility during the procedure. Still some operators prefer that their patients undergo CT angiography (CTA) of the pelvis prior to SAPE. The utility of this technique was described by Bilhim et al. [22]. In their study of 21 male patients using DSA in all patients and CTA in seven patients, the most common site of prostate artery origin among patients was the internal pudendal artery (56% of sites), with a common gluteal/pudendal trunk origin representing the next most common site (28%). Two separate feeding vessels were identified in 24% of pelvic sides.

CTA was described by Bilhim et al. as "very useful as a pre-intervention tool allowing planning of the intervention, and was able to detect small vessels such as the prostatic arteries," allowing "definition of the iliac artery trajectory and atherosclerotic changes." We do not routinely perform CTA prior to SAPE, as we feel CBCT provides adequate procedural guidance. A helpful alternative could be MRA obtained as part of a preprocedural prostate MRI, however this method has not yet been validated as a tool for procedural guidance and may not have resolution yet to delineate this anatomy adequately.

A common complicating factor during SAPE is the presence of extensive atherosclerosis, which is expected given the average age of patients with LUTS from BPH. In previous studies, this was the most common reason cited as a cause for unilateral or bilateral technical failure in embolization [11].

On completion of the procedure, the sheath is removed. For transradial procedures, a compression band (TR Band®, Terumo) is used to achieve hemostasis as previously described [23], allowing patients to ambulate

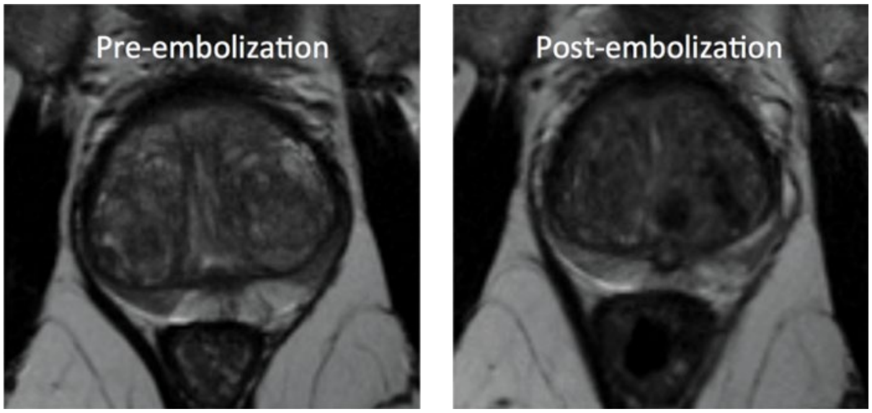

**Figure 129.5** Pre- and postembolization prostate MRI. Axial T2-weighted prostate MRI was obtained before and three months after SAPE. Prostate volume in the postembolization was 47 ml compared to 74 ml pre-embolization. Areas of low signal in the postembolization image represent areas of ischemia/infarct.

immediately after the procedure. Arterial closure devices may be used for transfemoral procedures at the operator's discretion.

## Postprocedure follow-up

Patients at our institution are seen for follow-up visits at 1, 3, 6, and 12 months. At each visit, the patient is asked to fill out the IPSS and quality-of-life surveys. At the 3, 6, and 12-month visits, $Q_{\max}$ and PVR are assessed.

Postprocedural imaging may be performed at the interventionalist's discretion; at our institution, prostate MRIs are performed at 1, 6, and 12 months to monitor for response, if the patients are on study. The primary goal of imaging is assessing change in prostate volume rather than parenchymal architecture, therefore ultrasound may be utilized as a cheaper, less accurate alternative as warranted. Examples of pre- and postembolization prostate MRI are shown in Figure 129.5.

## Conclusions

In summary, SAPE has the potential to play a larger role in the treatment of LUTS secondary to BPH, with published randomized trial data demonstrating comparable outcomes to TURP at 6, 12, and 24 months with the added benefit of improved erections and maintenance of normal ejaculatory function.

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## Part 3 Focal Therapy Lower Tract

## 130

# The Role and Methodology of Multiparametric MRI and Fusion-guided Biopsy in the Management of Prostate Cancer Patients

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## Introduction

The current standard for prostate cancer (PCa) diagnosis is transrectal ultrasound (TRUS)-guided biopsy to obtain 12 cores of tissue from the prostate in a systematic fashion. Systematic biopsy refers to standardized geographic sampling of regions, but this method is “blind” to specific areas that may harbor disease. Since the advent of prostate specific antigen (PSA), TRUS biopsy data have shown that a proportion of PCa diagnosed is low risk, clinically indolent, and portends an excellent prognosis [1]. Given the current lack of comprehensive understanding of PCa biology, such early detection may lead to the overtreatment of cancers unlikely to affect a man in his lifetime. This is compounded by the underdetection of high-risk cancers that may be missed given the current limitations of TRUS-guided biopsy. There remains a need for interventions to better distinguish between clinically actionable disease that contributes to prostate cancer-specific patient mortality and those that can be actively monitored safely. Unfortunately, there is no single modality that provides cost-effective, rapid, high-resolution imaging to define potential PCa targets. Targeted prostate biopsy, derived from regions of interest identified on magnetic resonance imaging (MRI) may provide such an opportunity. TRUS offers real-time imaging while sacrificing spatial image quality, whereas MRI offers high-resolution imaging to better delineate discrete lesions. Fusion of multiparametric MRI (mpMRI), which combines anatomic and functional sequences, with real-time TRUS now facilitates a more precise prostate biopsy resulting in improved PCa diagnosis, risk stratification, and staging.

This chapter reviews the general paradigm of mpMRI-TRUS fusion biopsy (FBx), its indications, and provides an overview of the workflow for this novel technology. Finally, we will review the commercially available mpMRI-TRUS FBx platforms on offer.

## Multiparametric prostate MRI

The initial and most critical step in the process remains image acquisition. “Multiparametric” MRI refers to the combined anatomic and functional phases obtained, which are: T2-weighted (T2W) anatomic sequences (T1 is also used as described later), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE) sequences (Figure 130.1) [2]. Magnet strength is either 1.5 or 3.0 tesla (T), with higher field strengths generally allowing for higher signal-to-noise ratios and spectral resolution, potentially facilitating higher spatial resolution. A body surface coil must always be used during image acquisition; although the images can be further augmented with an endorectal coil, this is not required [3]. The advantages of endorectal coil use are improved scan quality and improved PCa staging [3]. Yet coil use comes with associated costs, namely increased time of procedure, and significantly more patient discomfort. Dual coil use (surface and endorectal) has been shown to have a sensitivity of 76% and a positive predictive value of 80% for PCa detection, as compared to surface coil alone with a sensitivity of 45% and a positive predictive value of 64% [4].

Image interpretation relies on findings noted in corresponding locations across mpMRI sequences that

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Companion website: www.wiley.com/go/smith/textbookofendourology

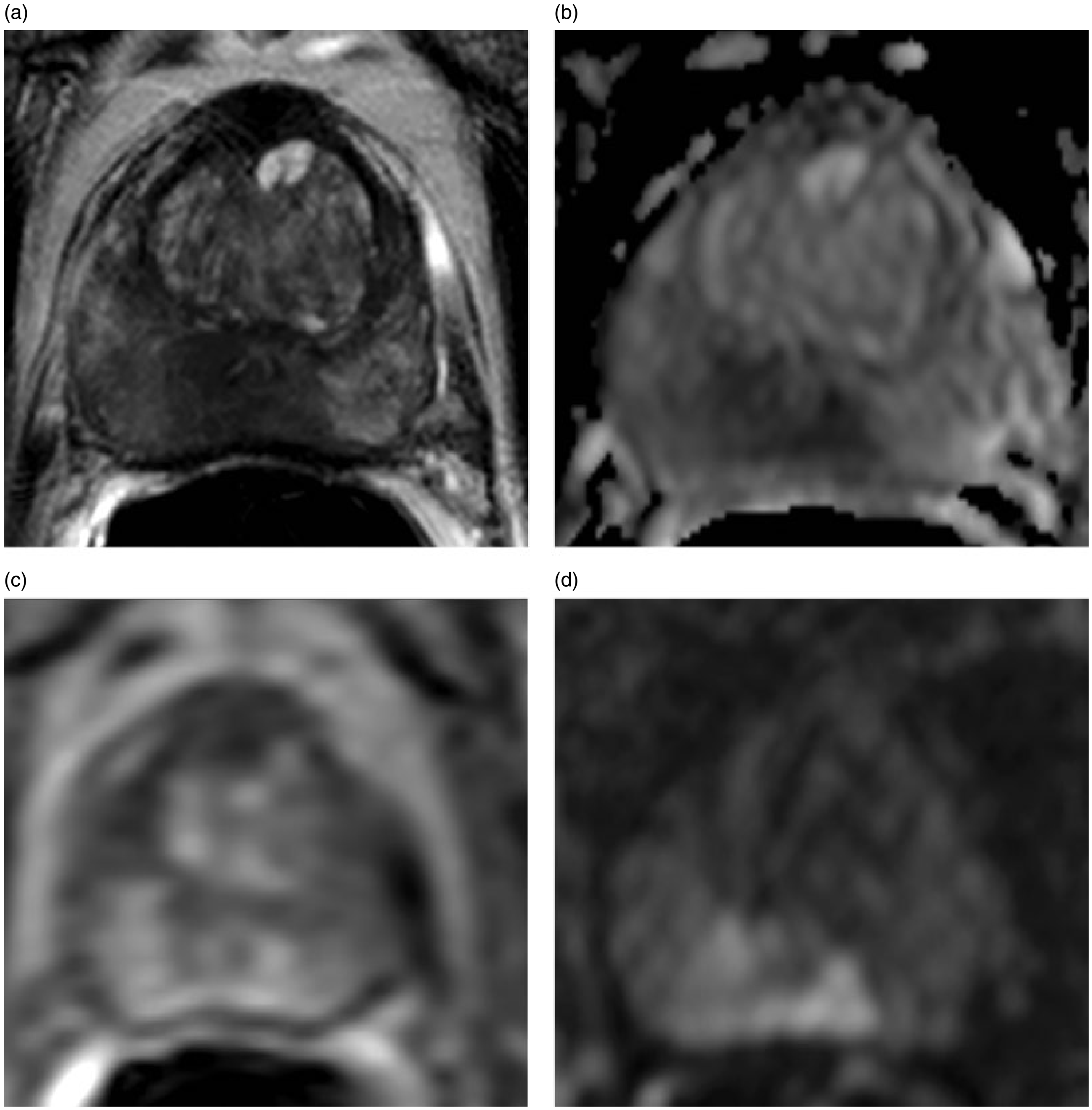

**Figure 130.1** Representative multiparametric MRI images. (a) T2-weighted axial; (b) apparent diffusion coefficient maps of diffusion-weighted imaging; (c) dynamic contrast-enhanced; (d) high *b*-value diffusion-weighted imaging. Patient was 66 years old, PSA of 14.61, and history of negative standard biopsies. A large lesion is seen in the right to midline mid-base peripheral zone (2.5 cm). This lesion has slight capsular bulge and a broad capsular base but no direct extracapsular extension. Seminal vesicles (SV) show possible invasion. Fusion-guided biopsy confirmed Gleason 4 + 5 (9), with SV invasion.

are integrated to provide a diagnostic impression [5]. T1-weighted imaging, which is a basic pulse sequence that produces images in which water-filled compartments are hypointense, is used to detect prior biopsy-related residual hemorrhage that may obscure suspicious lesions. T2-weighted imaging defines organ architecture, including the peripheral (PZ) and transition zones (TZ), as well as the central gland (CG), urethra, seminal vesicles, and capsule. Lesions suspicious for PCa appear darker in the PZ compared to normal tissue; by contrast in the TZ lesions will be hypointense and more heterogeneous [3].

DWI is a measure of the ability of water to diffuse freely within the organ. PCa lesions do not adhere to typical prostate architecture, with closer arrangement of cells and denser stroma. Thus the apparent diffusion coefficient (ADC) map, which is a display of ADC values for each voxel of an image, is lower for PCa lesions than for normal prostate parenchyma. “High *b*-value” images, which use *b*-values of ≥1400 s/mm$^2$, can also be used to attempt to improve the detection of clinically significant PCa via identifying significant restriction of movement and thus lesions will appear bright/hyperintense [3]. The amount of diffusion restriction has been associated with PCa grade and reflects the biological aggressiveness of the lesion [3].

The final sequence is DCE. This is obtained through the venous injection of gadolinium-based contrast, with scanning taking place before, during, and after administration. T1 sequences are used to detect the speed with which contrast arrives at the lesion, reflecting hypervascularity. Focal early hyperenhancement and early washout of the lesion implies malignancy, yet caution must be undertaken as benign conditions (BPH, prostatitis) may also produce similar findings. DCE has the most utility in the setting of recurrent PCa after definitive surgical, ablative, or radiotherapy [3].

mpMRI imaging is sensitive for the detection of clinically actionable, aggressive, PCa. Although each parameter has its own sensitivity and specificity, a meta-analysis of combined mpMRI has a sensitivity of 0.74 (95% confidence interval (CI) 0.66–0.81), and a specificity of 0.88 (95% CI 0.82–0.92) [6]. Correlation with pathology has shown a positive predictive value of 98–100% in detecting PCa [7]. Furthermore, mpMRI-TRUS FBx has been shown to be less sensitive for detecting low-risk lesions, a potential advantage that may be exploited to avoid overdiagnosis of clinically indolent disease [8].

Once the MRI is completed, postprocessing of images is performed to delineate the borders of the prostate, suspicious lesions, assign suspicion scores to each lesion. Suspicion scores reflect the likelihood that clinically significant cancer is present. Although multiple scoring systems have been developed (Likert, NIH scoring system), a consensus has arrived via the Prostate Image Reporting and Data Systems version 2.0 (PI-RADS 2.0) to standardize image interpretation and reporting [3]. Lesions are scored from 1 to 5 based on the number and severity of imaging findings (Figure 130.2). Increasing scores have been demonstrated to be associated with increasing detection of clinically significant PCa [9]. Due to the respective cancer diagnostic yield, recent recommendations advise lesions scored 1 or 2 do not need biopsy, while 4 or 5 do require biopsy. A suspicion score of 3 may require biopsy based on clinical findings [10]. The score assignment is different based on the anatomic area (PZ vs. TZ). Scores for the various parameters are based on lesion size, hypo/hyperintensity (based on location and parameter), heterogeneity, and morphology (Figure 130.2).

## Magnetic resonance–transrectal ultrasound fusion-guided biopsy

Two major FBx techniques exist: cognitive fusion and mpMRI-TRUS FBx. “In-gantry” MRI biopsy is a targeted biopsy method that was initially employed; the patient is sedated and scanned within the MRI apparatus during sampling; thus this method is time consuming, costly, and requires special equipment. Because of this it is not feasible for broad use. Cognitive fusion is where the surgeon interprets the MRI and attempts to mentally target, on ultrasound, a lesion identified on MRI. Although the literature is not in full agreement, cognitive fusion is heavily operator dependent and requires extensive knowledge of prostate anatomy and image interpretation [11]. We focus this chapter on the mpMRI-TRUS FBx method. This method and its delivery platforms have two distinct advantages: (i) targeted biopsy based on imaging; (ii) tracking of biopsy needle trajectories for repeat biopsies and management planning (i.e. surgical/focal therapy planning based on lesion location). These systems semi-automatically merge the real-time TRUS image to the preanalyzed MRI, and allow for targeting of lesions and storage of biopsy needle trajectory.

### Indications for fusion biopsy

There are recently described defined indications for the use of mpMRI and FBx in the management of PCa; however, the use of this novel technology is still an active area of research and its indications are evolving and expanding rapidly. Currently four potential clinical scenarios for using mpMRI-TRUS FBx exist and have been recently described in the National Comprehensive Cancer Network Guidelines:

#### Biopsy-naive patient who has suspicion of PCa

This indication describes using mpMRI in the initial workup of a patient who may have PCa, but has yet to be worked up and diagnosed by a urologist [12]. This is an area of great interest with a limited but growing body of data to support the use of mpMRI-TRUS FBx in the initial biopsy setting. Pokorny et al. published a report in 2014 which found that mpMRI-TRUS FBx, when performed in men with suspicious mpMRI lesions, increased the detection of intermediate/high-risk PCa by 17.7%, while concomitantly reducing the detection of low-risk PCa by 89.4% as compared to standard TRUS biopsy

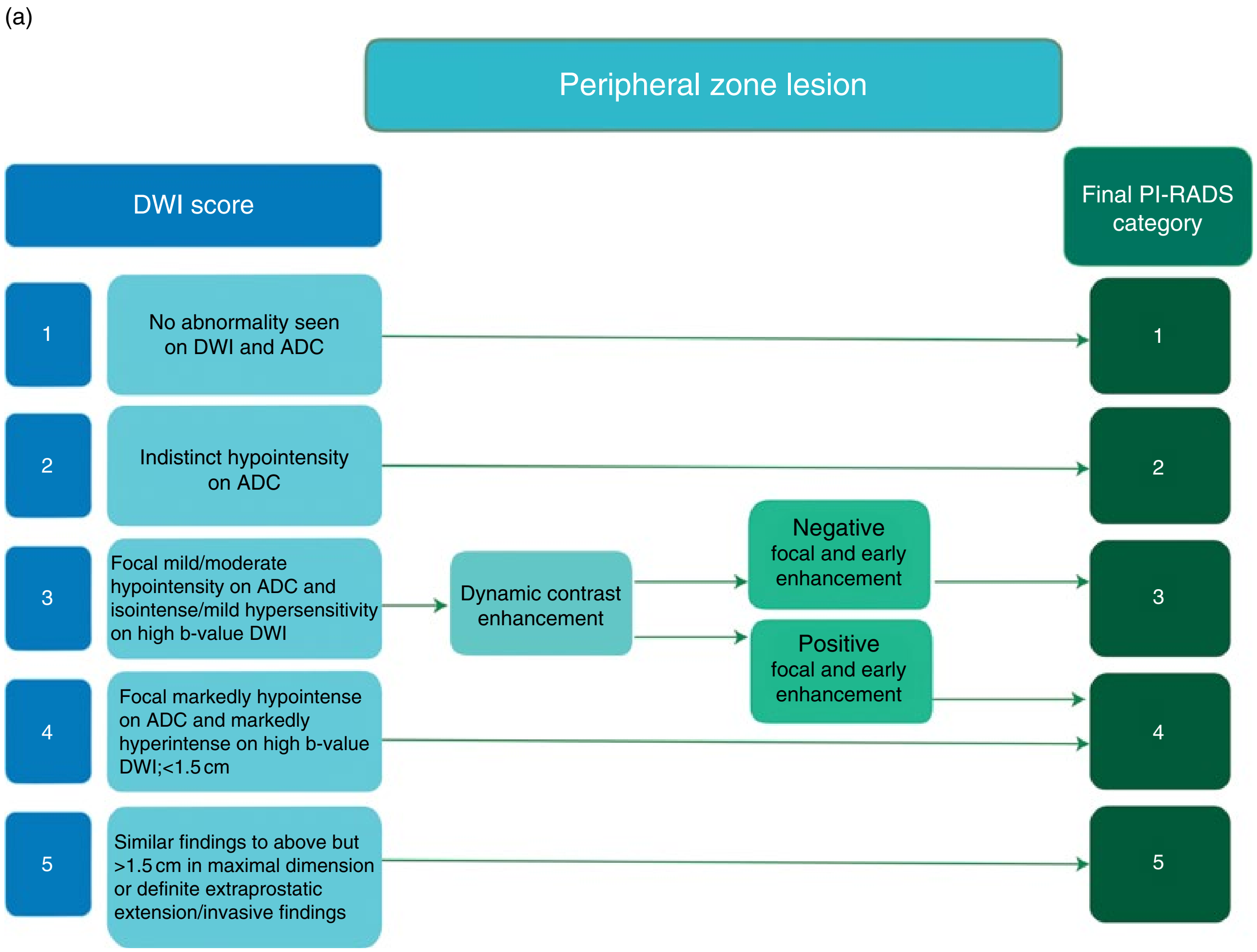
(a)
Peripheral zone lesion
DWI score
Final PI-RADS category
1
No abnormality seen on DWI and ADC
1
2
Indistinct hypointensity on ADC
2
3
Focal mild/moderate hypointensity on ADC and isointense/mild hypersensitivity on high b-value DWI
Dynamic contrast enhancement
Negative focal and early enhancement
Positive focal and early enhancement
3
4
Focal markedly hypointense on ADC and markedly hyperintense on high b-value DWI;<1.5 cm
4
5
Similar findings to above but >1.5 cm in maximal dimension or definite extraprostatic extension/invasive findings
5

**Figure 130.2** Prostate Image Reporting and Data Systems (PI-RADS) version 2.0 scoring system. This system assigns suspicion to prostatic lesions detected on multiparametric MRI for (a) the peripheral zone (PZ) and (b) the transition zone (TZ). DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient; T2W, T2-weighted; BPH, benign prostatic hyperplasia.

(SBx) alone [13]. In contrast, Tonttila et al. published a randomized control trial of 130 men comparing SBx to mpMRI and cognitive FBx, and found that FBx did not improve PCa detection [14]. Using the Artemis (described later) mpMRI-TRUS FBx system Mendhiratta et al. found in a cohort of biopsy naive men that mpMRI-TRUS FBx detected more Gleason Score (GS) ≥7 PCa than SBx ($P = 0.037$), and that most of the PCa found by SBx was low risk [15].

### Continued suspicion of PCa despite a prior negative TRUS biopsy

This indication is for using mpMRI-TRUS FBx to identify areas that may have been missed or undersampled during an initial SBx. A common presentation is a patient who has a rising PSA in light of a totally negative initial TRUS-guided biopsy [10]. Anatomic areas that mpMRI-TRUS FBx has shown utility for PCa detection include the anterior prostate [16], distal apex [17], and subcapsular prostate [18]. Vourganti et al. reported in 2013 that mpMRI-TRUS FBx discovered PCa in 37% of men who had a prior negative SBx, and that 11% had high-grade (≥GS 8) PCa that went undetected on SBx conducted at the time of FBx [19]. To investigate whether repeat standard biopsy is needed at the time of mpMRI-TRUS FBx, Salami et al. found in 2015 that FBx was more likely to identify clinically significant (GS ≥7, or GS 6 with >2 cores positive and/or >50% of any core involved) PCa as compared to standard biopsy ($P < 0.001$), but that SBx may be needed at mpMRI-TRUS FBx to avoid missing the 3.5% of clinically significant PCa that these authors found [20]. Sonn and colleagues published a series in 2014 of 105 men undergoing mpMRI-TRUS FBx for continued suspicion of PCa. They found that mpMRI-TRUS FBx, as compared to SBx, detected 1.4 times as many clinically significant PCa lesions [21].

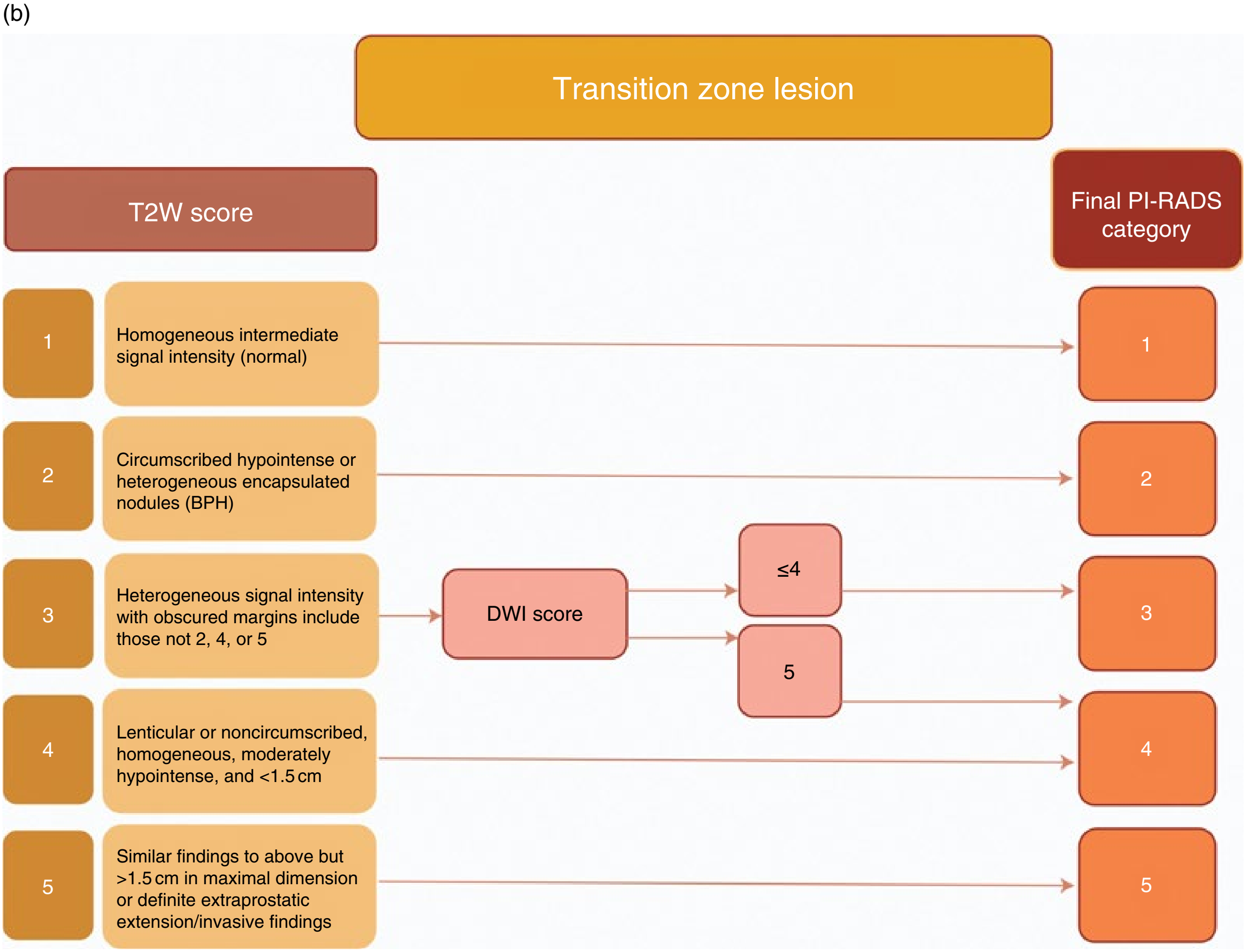
(b)
Transition zone lesion
T2W score
Final PI-RADS category
1
Homogeneous intermediate signal intensity (normal)
2
Circumscribed hypointense or heterogeneous encapsulated nodules (BPH)
3
Heterogeneous signal intensity with obscured margins include those not 2, 4, or 5
4
Lenticular or noncircumscribed, homogeneous, moderately hypointense, and <1.5 cm
5
Similar findings to above but >1.5 cm in maximal dimension or definite extraprostatic extension/invasive findings
DWI score
≤4
5
1
2
3
4
5

**Figure 130.2** (Contiuned)

**Risk stratification in active surveillance**

This indication implies using mpMRI in the active surveillance (AS) setting, whereby patients may be followed with serial PSA, DRE, mpMRI, and biopsy in various combinations and time frames to follow the patient [22, 23]. Specifically, mpMRI-TRUS FBx has utility in patients on AS with rising PSA or concern regarding lesion location (i.e. anterior lesion) and during confirmatory biopsy to establish candidacy by overcoming sampling error. An early report in 2013 by Stamatakis et al. found that imaging factors (lesion number, density, and highest lesion suspicion score) were significantly associated with patients being reclassified as not meeting AS criteria upon confirmatory biopsy [24]. Along this vein, Hu et al. investigated reclassification upon confirmatory re-biopsy using mpMRI-TRUS FBx and found that lesion suspicion score on mpMRI was associated with reclassification ($P = 0.001$), and that men with high-suspicion targets were three times more likely to be reclassified ($P = 0.006$) [25]. To investigate whether serial mpMRI scans have utility in predicting pathologic progression from GS 6 disease, Felker and colleagues studied 49 men over time and found the sensitivity and specificity of mpMRI for predicting progression to be 37% and 90%, respectively [26]. Their data suggest that mpMRI has a low false-positive rate and they concluded that mpMRI added incremental value when combined with clinical factors (core length and PSA density) for predicting progression. A recent report by Ma et al. evaluated the utility of mpMRI-TRUS FBx in AS and concluded that, given the relatively low sensitivity of mpMRI-TRUS FBx alone, a SBx should also be performed in the AS setting [27].

**Biochemical recurrence after definitive therapy**

After definitive therapy, a rise of PSA implies biochemical recurrence (definitions of which vary based on definitive treatment modality); mpMRI has been shown to have utility in identifying the recurrence. Specifically, Ho et al. demonstrated that combining mpMRI characteristics with clinical parameters had value in predicting biochemical recurrence as compared to clinical factors alone [28]. A study by Park and colleagues recently published using PI-RADS v2 scoring on mpMRI to predict biochemical recurrence found that PI-RADS suspicion score was the only parameter (among clinical, imaging, and pathologic parameters) that was an independent predictor of biochemical recurrence on multivariate analysis [29].

## mpMRI-TRUS FBx workflow

As briefly described earlier, the mpMRI-TRUS FBx workflow includes the following steps, carried out in sequence: MRI acquisition and analysis, ultrasound imaging at the time of biopsy, MRI-TRUS image co-registration, and targeted sampling (Figure 130.3).

### Image segmentation

The prostatic border is "segmented" or contoured using imaging software on serial T2-weighted axial slices. Similarly, each lesion may be contoured to provide a rendered lesion volume or a single slice selected to provide a centroid point. Thus, targets are defined as volumes or center points on the corresponding T2-weighted image. The calculated prostate volume (based on segmentation) and targets are superimposed on the T2-weighted images, and then are uploaded to the biopsy workstation.

### TRUS sweep and 3D ultrasound volume construction

At the time of biopsy, a three-dimensional (3D) TRUS volume of the prostate is constructed using stacking two-dimensional slices acquired during a prostate sweep using the TRUS probe. The TRUS prostate model undergoes semi-automatic segmentation by a software algorithm and the performing physician can manually adjust the borders. The 3D TRUS volume is "fused" or co-registered to the MRI images to allow for real-time targeting during FBx (Figure 130.3) [30]. Internal landmarks (cysts, calcifications, etc.) may be used to optimize co-registration. Furthermore, the pressure on the TRUS probe can be altered to ensure parallel deformations noted during MRI image acquisition (generally due to the endorectal coil).

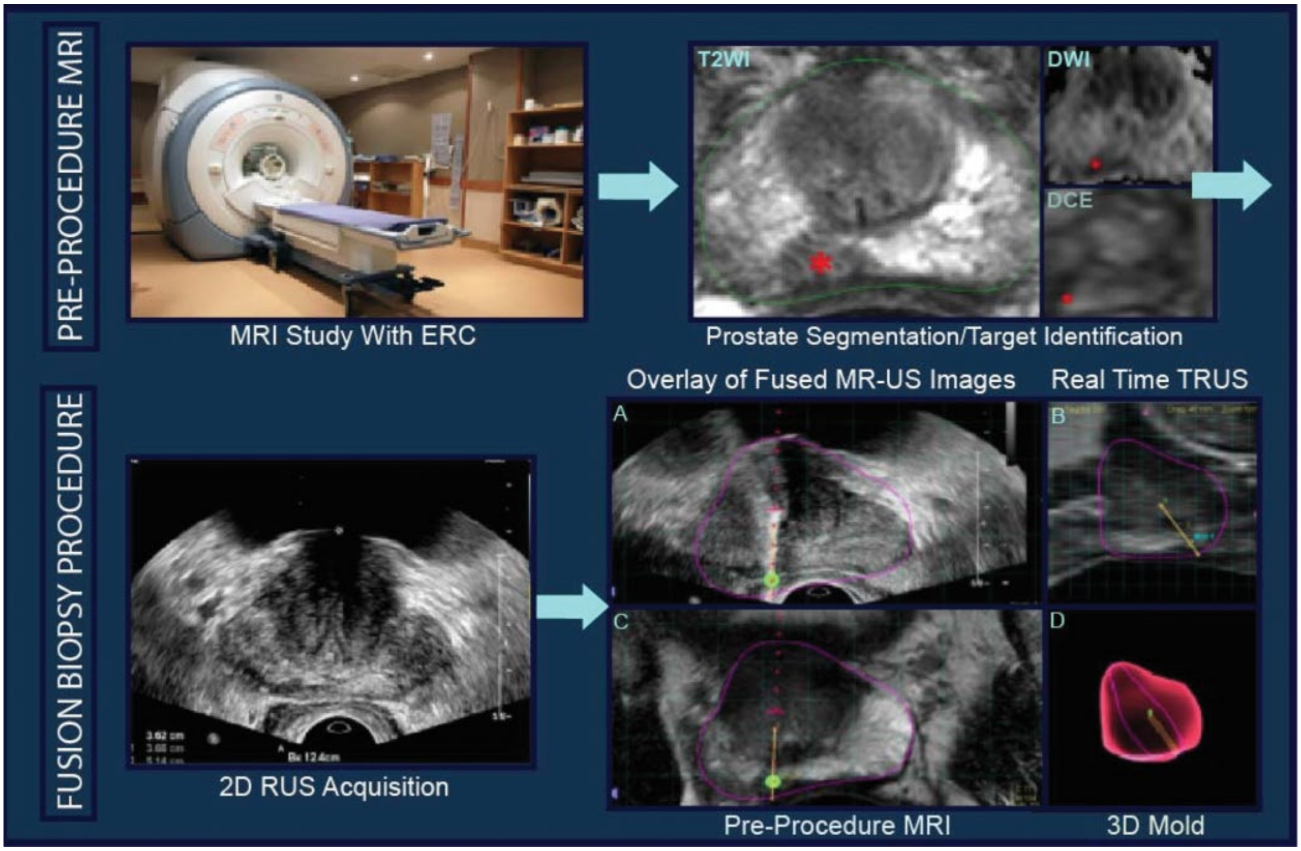

Figure 130.3 Workflow for mpMRI-TRUS FBx. The main steps include MRI acquisition and analysis (segmentation and defining lesions). The transrectal ultrasound (TRUS) sweep is performed at the time of biopsy and the preprocedure MRI images are "fused" to the live TRUS images.

Registration is conducted by computer software driven algorithms. There are two main algorithms for registration: rigid and elastic.

## Image registration and biopsy

With the rigid registration, the unaltered surface edges of the prostate from the MRI and the ultrasound rendered images are used; the two images are aligned via translational or rotational adjustments to allow the algorithm to most accurately merge the images. Rigid registration allows the internal geography of the organ to be preserved in the fused image; the drawback is that the two images and thus targets may not align completely. By contrast, the elastic registration algorithm transforms the 3D MRI volume such that the MRI prostate contours are force-fit to the 3D ultrasound-derived volume. It follows, therefore, that with elastic registration, internal prostate geography may be distorted while the contours are preserved. It is critical with elastic registration that the TRUS sweep and 3D construction is very accurate to avoid misalignment. Increasing the number of transformations potentially allows for error to be introduced at each step; however, platforms that utilized both rigid and elastic registration have demonstrated high degrees of accuracy.

Operators can check the registration via the platform-specific user interface; typical examples are co-display of MRI and TRUS image data with the ability to blend MRI and ultrasound or having the fused images displayed side-by-side. If registration is suboptimal, manual adjustments to the segmentation and registration by the operator can be conducted prior to tissue sampling. Fusion platforms exist that allow for both transrectal and transperineal approaches (see specific commercial systems later). For transrectal biopsy, the patient is placed in the left lateral decubitus position, or in lithotomy for transperineal sampling (Figure 130.4). Antibiotic prophylaxis conforms to the American Urological Association's best practice policy statement on urologic surgery antimicrobial prophylaxis [10].

## Biopsy needle navigation and mapping

For the fusion platforms to function properly, the real-time position of the biopsy probe and needle in 3D space must be monitored so to guide the user to the image defined targets. This will be discussed in-depth here with the specific commercial systems. Regardless, such monitoring is needed to carry out the other major functions of mpMRI-TRUS FBx: navigation and mapping.

Navigation or tracking describes the mpMRI-TRUS FBx system, guiding its user toward the target lesion in real time by determining the probe or needle real-time location in 3D space. The live TRUS images with the overlaid mpMRI information direct the operator to the lesion location for biopsy needle deployment. Once the needle has been deployed and the biopsy tissue obtained, mapping describes the various mpMRI-TRUS FBx system's capabilities to record the location of the biopsy needle using the MRI as the "map" (Figure 130.5). Biopsy core trajectories may be overlaid. This map can be stored

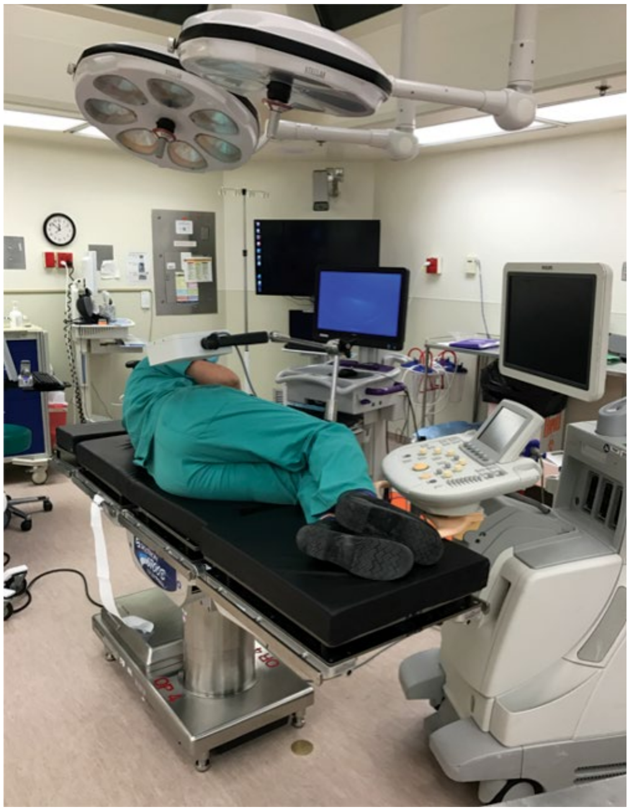

**Figure 130.4** Patient positioning. The patient is typically in in the left lateral decubitus position with the urologist stationed posterior to them.

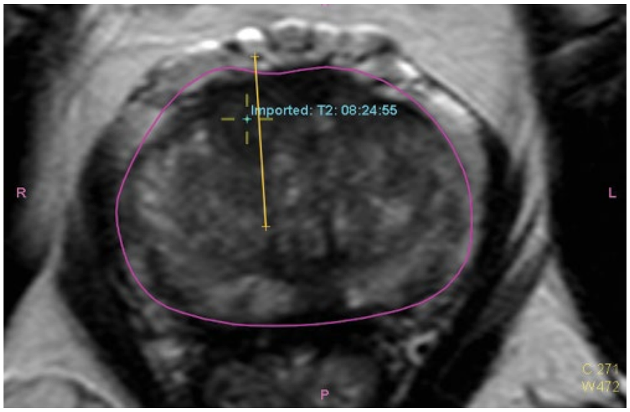

**Figure 130.5** Mapping. This is an example image from the UroNav system of a segmented (purple outline) prostate and the mapped needle trajectory (yellow line) overlaid on the MRI image.

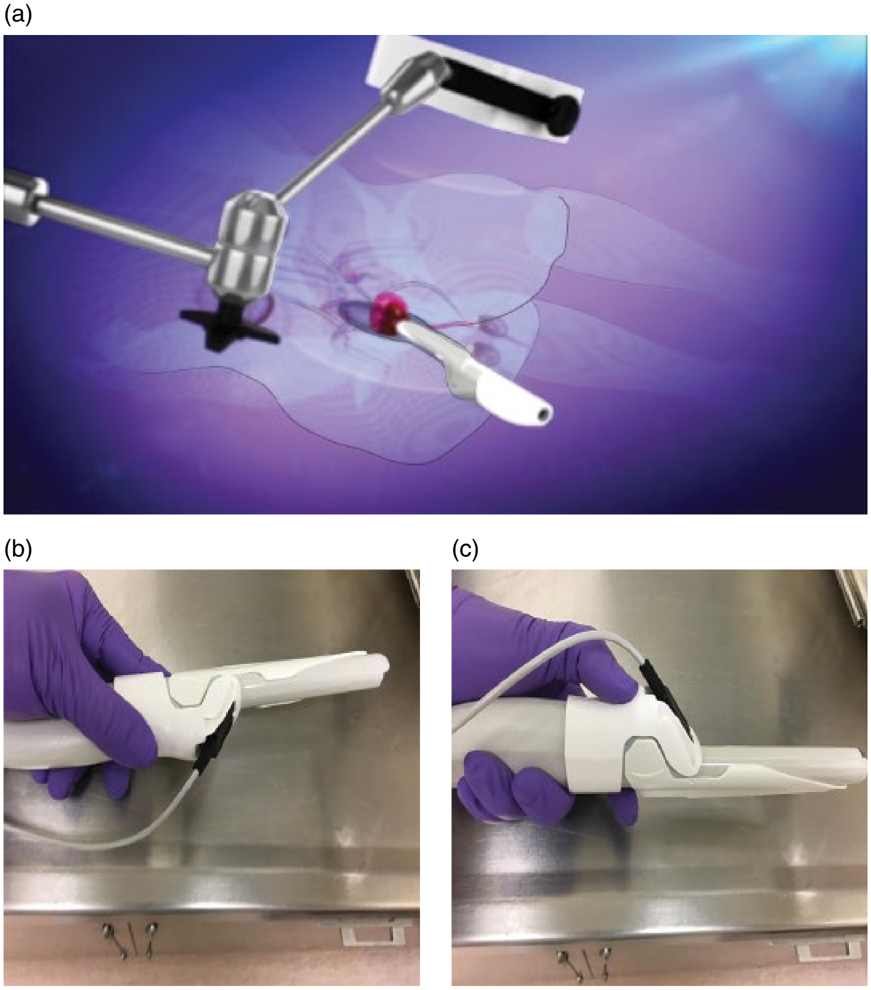

**Figure 130.6** Tracking. (a) Positions of the electromagnetic field generator and the biopsy probe that allow for the tracking function. (b,c) A UroNav biopsy probe with electromagnetic tracker clipped to its custom sheath along with needle guide.

on the system for later use to resample areas of interest such as in AS. If all cores are mapped, a systematic core that is positive may be recalled despite no lesion being visible on MRI [31].

There are three main methods of needle tracking: electromagnetic tracking; position-encoded joint tracking (built within robotic arm of a system); and TRUS-TRUS tracking.

Electromagnetic tracking is performed by affixing a sensor to the TRUS probe which, when positioned in an externally produced magnetic field (typically an electromagnetic field generator that can be positioned above the patients' pelvis at the time of biopsy), can relay the position of the sensor in real time to the FBx platform (Figure 130.6). The signal is then converted by the platform software to a 3D spatial position. This allows the user to approach target lesions in real time using the freehand TRUS probe. A drawback is the potential for human error due to movement at the time of biopsy needle deployment [32]. This kind of tracking is found in the UroNav (In Vivo, Gainesville, FL, USA), Real-Time Virtual Sonography (Hitachi, Tokyo, Japan), and Virtual Navigator (Esaote, Genoa, Italy) platforms.

In contrast to the freehand TRUS-based FBx platforms, other systems utilize robotics to target lesions. Such systems contain self-articulating arms with built-in positional angle-sensing encoders, which control the TRUS probe's movement toward the image-based target (Figure 130.7). This tracking system is called position-encoded joint tracking. These systems continuously measure the sensor to assist the user with obtaining the correct biopsy angle and probe position for tissue sampling as they move the arm toward the target [33]. They do allow the user some probe manipulations: the degrees of freedom are typically forward/reverse and rotational. The benefit is stability and thus decreased mechanical biopsy error, as once positioned the probe will remain in place. The limited ability to review MRI images continuously during the procedure

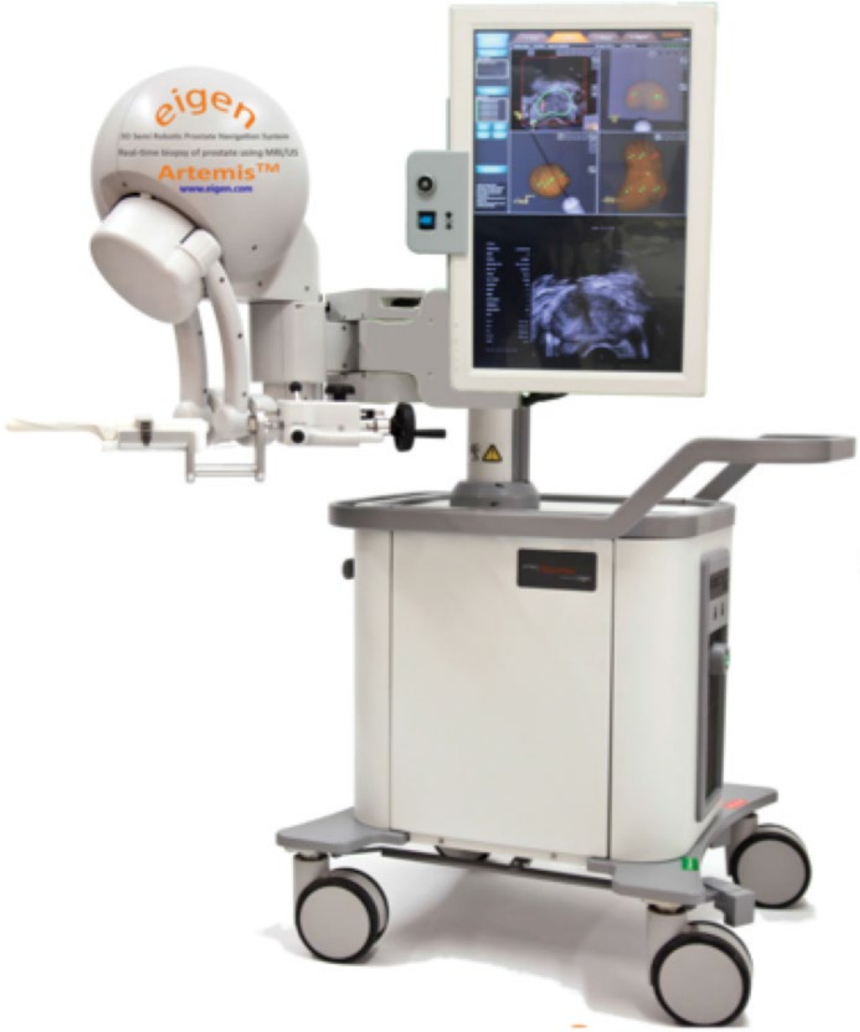
eigen
3D Semi Robotic Prostate Navigation System
Real-time biopsy of prostate using MRI/US
Artemis™
www.eigen.com

**Figure 130.7** Artemis biopsy system. Note the angle-sensing encoders shown on the right.

and the tracking device's bulkier size are drawbacks for this modality [34]. The Artemis (Eigen, Grass Valley, CA, USA), BiopSee (Pi Medical, Athens, Greece), FusionBx System (Focal Healthcare, Toronto, Ontario, Canada), and Biojet (BK Ultrasound, Peabody, MA, USA) platforms utilize this tracking modality.

Lastly, TRUS-TRUS registration and tracking system is found in the Urostation (Koelis, Grenoble, France) platform. After the initial 3D TRUS sweep of the prostate and 3D ultrasound construction, a second TRUS sweep and second 3D TRUS reconstruction and registration is conducted prior to each biopsy needle deployment. Elastic registration of the real-time 3D TRUS volume is co-registered to MRI images allowing for the identification of isoechoic lesions. However, this system does not track the probe in real time. The user must review needle core locations after sampling, which may introduce error if the probe is moved between the prebiopsy scan and core sampling.

## Commercial mpMRI-TRUS FBx systems

The remainder of this chapter will review the various commercial mpMRI-TRUS FBx platforms: their workflow, strengths and weaknesses, and data pertaining to the specific platform. It is important to note that this field is evolving rapidly and that each system was developed in a specific context (i.e. some systems can only conduct rigid or elastic registration). Because of this, the data for each system reflect the context of that system's development and many have evolved since their inception.

Please refer to Figure 130.3 for a general overview of the FBx workflow; under each system we will highlight features of that system's unique workflow.

## UroNav

The UroNav platform was developed through a collaboration of academia and industry (National Institutes of Health and Philips/In Vivo Healthcare) and was approved by the US Food and Drug Administration (FDA) in 2006. This system is adaptable to different ultrasound manufacturers and MRI/imaging systems. It includes both elastic and rigid registration capabilities. UroNav utilizes electromagnetic tracking and freehand TRUS ultrasound methodology. A transperineal platform was recently introduced.

The workflow for this system starts with acquiring mpMRI images, radiological segmentation/lesion marking, and uploading of the MRI to the platform workstation. At the time of biopsy, the electromagnetic field generator is stationed above the patient's pelvis to afford probe tracking. The ultrasound sweep of the prostate is then conducted, allowing the software to construct a 3D ultrasound prostate volume. This 3D TRUS prostate is segmented by the UroNav software (with user adjustments as needed). The user can also adjust the image registration after segmentation. At this point, the user can proceed with the targeted biopsies as the targets are shown as multicolored "bullseyes" on the fused images of the UroNav display. The navigation software assists in guiding users to the target until the tracked needle guide is in-line with the target. Insertion of the needle to the proximal lesion edge ensures that the biopsy will be of the correct trajectory. Biopsies can then be taken in both the axial and sagittal planes [35]. Mapping of needle core trajectories can be stored by the user.

In a landmark paper from 2014, Siddiqui et al. studied 1003 prospectively enrolled men and showed a 30% increase in the detection of high-risk cancers compared to SBx [8]. Furthermore, mpMRI-TRUS FBx detected 17% fewer low-risk cancers. This finding was validated by Rastinehad et al. in a propensity-matched cohort who found a durable, statistically significant difference in PCa detection rate using mpMRI-TRUS FBx as compared to TRUS-guided biopsy alone [36]. One question that arises regarding these systems is their accuracy, a question addressed by Xu and colleagues [37]. They showed that the error of UroNav is 2.4 ± 1.2 mm based on phantom studies.

## Real-Time Virtual Sonography and Virtual Navigator

These general-purpose fusion systems (Real-Time Virtual Sonography, Hitachi, Japan; Virtual Navigator, Genoa, Italy] were originally designed to merge TRUS images to a multitude of different imaging modalities (CT, MRI, etc.). They are similar in workflow to the UroNav method described above: mpMRI images are obtained, segmented, and then registered with real-time TRUS at the time of biopsy. An electromagnetic amplifier is placed above the patient to facilitate needle tracking. Both of these systems use a freehand TRUS probe.

The data for using these platforms in mpMRI-TRUS FBx are more limited. In 2010, using Real-Time Virtual Sonography, Miyagawa et al. found that this platform, used transperineally, in a cohort of 85 men with continued suspicion for PCa, was superior to random TRUS biopsy on a per-core analysis for detecting PCa (32% (67/192) vs. 9% (75/833) cores, $P < 0.01$) [38]. Delongchamps et al. found in 2013 that using Virtual Navigator for mpMRI-TRUS FBx detected a significantly higher amount of PCa relative to systematic biopsy in 131 men who were evaluated for PCa ($P = 0.0065$) [39].

## Artemis

This platform marks the delineation between the freehand TRUS probe systems and the mechanical position encoders. Within the joint of each arm of the Artemis platform are built special angle-sensing encoders (Figure 130.5). Artemis (Eigen, Grass Valley, CA, USA) was approved in 2007 by the FDA. This system is able to function with several different ultrasound and MRI/imaging systems, uses elastic registration, and does not require an electromagnetic field generator.

For Artemis, the workflow begins in a familiar manner with mpMRI acquisition and radiological segmentation. At the time of biopsy, using the robotic mechanical arm, an initial prostate sweep is obtained to form the ultrasound 3D prostate model. As with the freehand systems, software will automatically segment the ultrasound-based model, with manual adjustments made as needed. After registration, Eigen navigation software guides the user-driven biopsy needle to the predefined MRI targets. Mapping functionality can record the location of obtained cores. Given the differences in this system from traditional freehand biopsy, there is a learning curve to effective utilization of the platform. However, once an operator becomes experienced, the system yields highly precise reproducible biopsies that minimize human error.

In 2015, Meng et al. published a series of 601 men that found that mpMRI-TRUS FBx detected more PCa with a GS ≥7 and less PCa of GS 6 than standard biopsy ($P < 0.001$) [40]. Furthermore, they found that mpMRI-TRUS FBx identified greater numbers of PCa with a GS ≥7 as compared to standard biopsy in men with no prior biopsy ($P = 0.012$), a prior negative biopsy ($P = 0.010$), and a prior PCa diagnosis ($P = 0.043$). Filson et al. studied 1042 men prospectively and found a 35% detection rate for clinically significant (GS ≥7) PCa and that 20% of patients with a negative MRI had GS ≥7 [41]. In agreement with prior findings, they found that the combination of mpMRI-TRUS FBx and standard biopsy resulted in increased clinically significant PCa detection. This system has proven its biopsy error rate to be 1.2 ± 1.1 mm [34]. This error rate is smaller than the freehand systems and may be attributable to the unique stability of the mechanical arm.

### Biojet

This system also uses a mechanical arm with angle-sensing encoders for TRUS probe tracking, similar to the Artemis system. Biojet (BK Ultrasound, Peabody, MA, USA; DK technologies, Barum, Germany] is unique in that it is capable of being used either transrectally or transperineally. This system utilizes rigid registration only. The workflow of this system is similar to the Artemis system. In 2015 in a small prospective study of 20 patients performed by Shoji et al. showed that Biojet detected PCa at significant higher levels compared to systematic biopsy (31.8% (14/44) vs. 6.7% (16/240), $P < 0.0001$) [42].

### Biopsee

In contrast to the mechanical articulating arms of Artemis and Biojet, BiopSee (Pi Medical, Athens, Greece) uses a bidirectional stepper that is affixed to the operating room table. This gives the system more precise control of the TRUS probe. Notably, this system is intended for transperineal biopsy. The probe is affixed to the stepper, into which encoders are embedded. These are used to monitor probe position (depth and rotation are the monitored parameters). This system utilizes rigid registration.

Although intended for transperineal biopsy, the workflow for this system is similar to those described earlier. mpMRI imaging is obtained, the prostate segmented, and lesions marked by the radiologist. On the day of biopsy, a sweep of the prostate is conducted to generate a 3D ultrasound model. The 3D TRUS model is rigidly registered to the MRI. From there the fusion biopsy is performed. There is, however, a caveat of a learning curve, not only for using the mounted probe, but also for the transperineal component. This may add time to this mpMRI-TRUS FBx procedure. Kuru et al., in 2013, showed that in 347 men cores obtained through the BiopSee targeting system detected statistically significant more PCa than systematic biopsy (30.0% (386/1281) vs. 8.2% (523/6326), $P = 0.01$) [43].

### Urostation

In contrast to the other commercial systems described, Urostation (Koelis, Grenoble, France) utilizes a novel TRUS-TRUS image registration algorithm for needle tracking. It is a freehand probe system that, since it only utilizes TRUS and mpMRI, does not require additional costly hardware such as field generators or FBx-specific hardware. Of particular note is the fact that the TRUS-TRUS registration is used to retrospectively determine needle position on an mpMRI obtained prior to biopsy.

In terms of workflow, the methodology leading up to biopsy is unchanged from the other platforms. Once the MRI is obtained, segmented, and lesions demarcated, the patient is brought for biopsy. A 3D TRUS prostate model is obtained via a probe sweep. It is at this stage that the workflow diverges from other systems. The initial 3D TRUS model is registered to the MRI elastically. As each biopsy core is obtained, another 3D TRUS model is constructed with the needle deployed into the lesion. This is registered to the initial 3D TRUS model to confirm correct needle placement. This distinct exercise is conducted sequentially for all lesions. In order for the imaging of the deployed biopsy needle to be accurate, the user must hold it in place for 3–5 seconds. In 2012 Rud and colleagues retrospectively investigated the PCa detection rate in 90 men and found it to be 52% (60/115) using Urostation [44]. Expanding on this Mozer et al. included 152 men and found that Urostation detected a significantly higher proportion of men with clinically significant PCa (43/152 vs. 37/152, $P = 0.03$) [45].

## Discussion and conclusion

Currently, the gold standard for pathologic confirmation of PCa remains TRUS biopsy. However, mpMRI-TRUS FBx has served to bridge the gap of inherent limitations in nondirected sampling. Though not without its shortcomings, this technology has seen significant uptake in a short period of time and outcomes from expert centers have been reproducible when implemented thoughtfully [36]. The development of FBx holds the potential to completely shift the paradigm of PCa diagnosis and management. It offers more accurate biopsy of targetable lesions that has been shown to improve the diagnosis of clinically significant PCa while avoiding the detection of indolent disease [46]. For patients who harbor MRI-visible lesions, current practice remains the inclusion of both targeted and systematic biopsy, as even at expert centers MRI can miss up to 20% of clinically significant prostate cancers [20, 41].

This technology has broad applicability across the spectrum of PCa care: diagnosis, AS, staging, surgical planning, and local recurrence after whole-gland or focal therapy. Widespread adoption must, however, be balanced with judicious use as the cost is not nominal. In addition, implementation must be performed responsibly and conscientiously. Achieving an optimal outcome requires a multidisciplinary approach, as the entire process is dependent on seamless interaction between radiologists and urologists. In addition to high-quality imaging, there exists a learning curve to both prostate mpMRI interpretation and FBx that must be overcome for accurate, reproducible, and reliable results.

Introduction of this technology into the broader urologic community is another area that needs further evaluation. Cost-effectiveness in a variety of settings is a concern given the requirement for imaging and additional hardware costs for biopsy. Early cost modeling has demonstrated mpMRI-TRUS FBx does not add additional cost to the current standard of care workup [47]. As the majority of information from imaging is gleaned from T2-weighted images and DWI, there is support for biparametric MRI as a potential intermediary step after PSA screening but prior to biopsy [12]. The potential of using a "screening MRI" (forgoing the time and cost of using contrast) is one way in which the urology community is trying to adapt to decrease cost, and broaden mpMRI-TRUS FBx use. One must also keep in mind the learning curve for a new skillset and the need for support and integration of our colleagues in other specialties when incorporating this novel technology into an existing practice. Overall, mpMRI-TRUS FBx is a novel technique that allows the urologist for the first time to visualize and target-specific lesions within the prostate while still using real-time ultrasound imaging at the time of biopsy. As the urology community continues to advance our knowledge of this platform's utility, the ability to provide targeted, precision care for our patients will also improve. Because of this, better patient selection and risk stratification will translate to superior oncologic outcomes.

See accompanying Video 130.1 .

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# 131

# Focal Therapy of Prostate Cancer

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## Introduction

The global incidence of prostate cancer is estimated at 30.6 per 100 000 per year and is the second most incident cancer among men [1]. In the United States, it is the most common solid organ malignancy among men and the third leading cause of death [2]. Much controversy has arisen regarding prostate cancer overdiagnosis and overtreatment that are thought to have exposed many men to the side-effects of traditional radical treatments. Although these treatments have been oncologically effective they often result in collateral damage to the surrounding cavernosal nerves, urinary sphincter and other adjacent organs [3]. Tools for early detection of prostate cancer such as multiparametric magnetic resonance imaging (mpMRI) and MRI-fusion targeted biopsies, as well as recognition of Gleason grade 4 and 5 cancers as the subset of cancers which are biologically lethal, have led to an interest in gland-sparing targeted therapies with less morbidity [4].

## Historical perspective

The idea of prostate focal therapy was borne out of the successful paradigm shift from the Halsted mastectomy to local excision for breast cancer. Early attempts in prostate gland-sparing treatments involved subtotal ablations, whereby the sparing of one, or possibly both, neurovascular bundles was attempted [5]. Later, the term “male lumpectomy” was coined to describe hemi-ablation of the prostate as the first form of focal therapy [6, 7]. Today, advances in technology have allowed surgeons to better visualize the prostate and localize cancer, and has made possible true image-guided focal destruction of the offending cancer with a margin of normal tissue.

## Concepts in focal therapy

At an early stage of prostate cancer, malignant foci may be localized to a few discrete areas of the prostate. If these could be eradicated without harming the remainder of the prostate gland, collateral damage to the cavernosal nerves, urinary sphincter or rectal wall could be minimized depending on the area(s) where the cancer is located.

## Index lesion

A developing concept in focal therapy is based on the finding that the natural history of prostate cancer is typically driven by a primary lesion, rather than secondary lesions [8]. Despite heterogeneity within primary lesions, the majority of metastatic prostate cancer has also been found to originate from a single precursor cell [9]. Karavitakis et al. analyzed 100 consecutive whole-mount radical prostatectomy specimens, finding that although tumors were often multifocal (78%) and bilateral (86%), the 100 index tumors identified invariably defined pathological features of the cancer and of 170 satellite tumors, 87% were low grade, and 99.4% less than 0.5 ml [10]. With the concept of the index lesion, if the dangerous foci in the prostate could be eradicated, oncological control of the cancer could be achieved while maintaining quality of life.

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## The complementary roles of focal therapy and active surveillance

The last decade has seen many advances in the biological understanding of prostate cancer. Two of the largest active surveillance cohorts reached 10–15 years of follow-up, showing an extremely low metastasis rate among men with D'Amico low-risk prostate cancer [11, 12]. In one of the cohorts with an extended inclusion criterion with some men having Gleason 3 + 4 cancer, it was found that these men with intermediate-risk cancer formed the majority of those in whom cancer progressed [13]. In the randomized Prostate Intervention Versus Observation Trial (PIVOT), although overall survival benefit was not seen, there was a survival benefit in the intermediate-risk subgroup with prostatectomy rather than observation [14]. Indeed, Gleason grade 4 cancers appear to have many more hallmarks of cancer compared to Gleason grade 3, and likely represent the relevant therapeutic target [15].

These findings have led to interest in a complementary strategy whereby intermediate- or high-grade cancer foci are eradicated with focal therapy, while the remainder of the gland with low-grade cancer remains on active surveillance [16]. During surveillance, if any higher grade cancers are detected they could potentially be treated focally again, with the aim of achieving long-term oncological control and effectively transforming prostate cancer into a chronic disease, commensurate with its long natural history.

To these ends, a successful focal strategy depends on a multidisciplinary team of prostate cancer specialists working on the following tenets:

- Accurate determination of disease extent/location through advanced imaging and biopsy
- Ascertaining that the patient will benefit from treatment and be compliant to follow-up
- Complete ablation of the index lesion(s)
- Posttreatment monitoring utilizing advanced imaging and biopsy with a view to future retreatments or conversion to whole-gland treatment, if necessary.

## Patient selection

Patient selection is the cornerstone of a successful focal therapy strategy. The approach is workable only if the extent of clinically significant cancer can be accurately ascertained. Once determined, the clinician will have to decide whether the cancer can be accurately targeted for complete eradication, using the guidance and available ablative technologies.

### Biopsy

The majority of biopsy-based patient selection studies were predicated on the use of hemi-gland ablations as the prototype form of focal therapy whereby it was important to determine whether cancer was unilateral or bilateral. At that time, many surgeons felt that focal therapy should be applied only in men with low-risk prostate cancer. Though this situation is less likely today, the data remain instructive on the ability of biopsy to map cancer. Barzell and Melamed first showed in a series of 80 patients that using an extensive transperineal mapping biopsy (TMB) as the gold standard, staging transrectal ultrasound-guided (TRUS) biopsies had a false negative rate as high as 47% and sensitivity and negative predictive value as low as 54% and 49% respectively in determining suitability for hemi-ablative cryotherapy [17]. In a slightly larger cohort of 110 men with unilateral cancer on TRUS biopsy, Onik and Barzell demonstrated that more than half were disqualified after undergoing TMB [18]. In a population of 538 men who had all undergone radical prostatectomy, Polascik et al. showed that biopsy unilaterality was the strongest predictor of pathological unilaterality with a sensitivity of 88.4%, specificity 34%, and positive and negative predictive values of 28% and 91%, respectively [19].

TRUS biopsy has served urologists well in the diagnosis of prostate cancer. However, in determining the true grade and extent of cancer, it is untargeted, suffers from inconsistency due to its random nature and may systematically miss anterior cancers due to preferential posterior zone sampling [20]. Nonetheless, Tsivian et al. showed that increasing the number of biopsy cores (sextent vs. extended) at TRUS biopsy was associated with a significant improvement in specificity (from 37.1% to 53.9%) and negative predictive value (from 91.8% to 95.8%) [21]. Moreover, if an increased burden is detected on TRUS biopsy (2 or less vs. more than 2 positive cores), Truesdale et al. found a greater likelihood of experiencing pathological persistence of cancer or biochemical recurrence after focal treatment [22]. Although a direct comparison was not available, Abdollah et al. showed that at 24-core TRUS biopsy, in predicting unilateral disease, specificity remained at 49.4% and positive and negative predictive values 22.6% and 98.9%, respectively, demonstrating the limitations in enhancing test performance by increasing the number of biopsy cores transrectally [23].

Using a combination of clinical parameters, Fu et al. attempted to identify a set of variables to predict unilateral cancer in a cohort of 1495 men, finding that only prostate specific antigen (PSA) ≤4 ng/ml and unilateral cancer on biopsy were significant factors [24].

On the other hand, Gallina et al. were unable to develop a model in a cohort of 321 men, finding only that the number of positive cores were significant with an area under the curve (AUC) of 0.52 [25]. The majority of the studies mentioned here had the objective of predicting low-risk cancer. With recognition that Gleason ≥7 cancers are the ones likely to drive progression, metastasis and mortality, contemporary interest resides in identifying these higher grade cancers rather than low-grade ones.

## Multiparametric MRI

Advances in MRI have re-ignited interest in focal therapy due to the possibility of image-based cancer mapping. mpMRI typically comprises T2, diffusion-weighted imaging (DWI) and dynamic contrast enhanced (DCE) imaging that preferentially detects higher grade prostate cancers and larger cancer foci [26, 27]. DWI relies on the relative ease of movement of water molecules. This is restricted in areas of increased cell density and may be directly related to the presence of histological high-grade cancer [28].

As an imaging modality, mpMRI has less bias toward any particular region of the prostate compared to TRUS biopsy and can be useful in the detection of anterior cancers. In a cystoprostatectomy series of 345 patients free from screening-related selection bias, Nevoux et al. identified 104 incidental prostate cancers, of which 33% were anteriorly located beyond the reach of an ordinary biopsy needle [29]. Among radical prostatectomy specimens, an incidence rate for anterior cancers of 15–21% has been reported [30, 31]. If detected at an early stage, anterior cancers could be treated with focal or zonal ablation, sparing the cavernosal nerves bilaterally and improving quality of life of men undergoing prostate cancer treatment [32].

Accurate staging is a critical component of identifying the ideal focal therapy candidate, especially with an emphasis on treating men with higher grade cancer. Using various inclusion criteria, contemporary mpMRI series report an accuracy of 62–74%, sensitivity of 35–63%, specificity of 73–91%, positive predictive value of 36–85%, and negative predictive value of 57–92% in the detection of extracapsular extension [33–37]. Gupta et al. evaluated 158 men who had undergone radical prostatectomy and found that mpMRI staging outperformed the Partin tables in predicting pathological extracapsular extension (AUC 0.88 vs. 0.70) [38].

However, mpMRI does have its limitations and should not be viewed as a panacea for patient selection. It remains important for urologists to "correlate clinically." mpMRI is subject to technical variability with differential performance between machines of different field strengths. For example, a magnetic field strength of 3 T improves spatial resolution and image acquisition times compared to that of a 1.5 T scanner by virtue of a better signal-to-noise ratio [39]. On the other hand, the signal from a 1.5 T scanner may be augmented by an endorectal coil (ERC) due to its proximity to the prostate [40]. Furthermore, a significant learning curve exists and an accurate interpretation is highly dependent on reader experience both in identifying cancer and detecting extracapsular extension [41, 42]. Standards in mpMRI interpretation with regards to cancer identification have recently been jointly promulgated by the European Society of Urology and Radiology (ESUR) and the American College of Radiology (ACR), culminating in the Prostate Imaging Reporting and Data System (PI-RADS) scoring system, which aims to alleviate inter-reader variability [43].

Jeong et al. reported on 574 men who underwent 12-core TRUS biopsy, 1.5 T mpMRI without ERC, and subsequent prostatectomy, finding that MRI contributed only marginally in predicting unilateral cancer [44]. On the other hand, Tran et al. reported that mpMRI read using PI-RADS, in combination with TMB, offered a negative predictive value as high as 91% in identifying hemi-prostates with clinically significant prostate cancer [45].

## Targeted/fusion biopsy

Visualization of the prostate using mpMRI allows urologists to perform targeted sampling of suspicious areas of the prostate to plan for focal therapy. MRI-TRUS fusion biopsy can be performed using visual estimation targeting (VET), otherwise known as cognitive/mental fusion, whereby the biopsy is performed using ultrasound guidance and the proceduralist estimates the position of the suspicious lesion. The alternative method is to use software fusion whereby the MRI image is fused to the ultrasound image using a variety of software algorithms and presents as an overlay on the ultrasound image for the proceduralist to target. In expert hands, VET can be as good as software fusion [46]. On the other hand, software fusion has a learning curve as well because the overlay of the MRI image onto the ultrasound image is often imperfect and the user has to adjust accordingly to achieve an accurate biopsy [47]. Ultimately, patients can only be identified accurately for focal therapy by an experienced multidisciplinary team of radiologists and urologists. Such a team who will mount the learning curve together is a critical component of a focal therapy program.

### Contemporary patient selection criteria

The majority of early studies in focal therapy included a majority of low-risk cancer patients. Similarly, many contemporary phase I/II trials regarding new techniques necessarily include patients who have low-volume, low- to intermediate-risk cancer. The ideal focal therapy candidate has been the subject of several expert consensus meetings. In general, there has been a shift in focus from eradicating all cancer to that only of clinically significant cancer. The findings of the consensus meetings are summarized in Table 131.1.

## Ablation patterns and current technologies

### Types of ablation

Many different ablation patterns have been termed focal therapy, leading to significant heterogeneity within the focal therapy literature. Some of these techniques, such as “hockey-stick”-type ablations, would be more appropriately classified under the umbrella term of partial prostate ablation (Figure 131.1). In an international consensus meeting on definitions in focal therapy, Postema et al. reported that focal therapy should include treatment of a lesion, quadrant ablation, and hemi-ablations [52]. Some authors would further argue that treatment of a lesion can be further classified into image-targeted lesion ablation versus non-image-targeted, whereby the lesion is treated based on biopsy information.

### Cryotherapy

Prostate cryotherapy has been the modality of choice for focal therapy in the United States [53]. It is usually performed using a transperineal approach, generally under ultrasound guidance though there are limited reports of in-bore MRI cryotherapy. Third-generation cryotherapy probes allow for an active freeze and thaw, and through variable ice length adjustment, allow conformation of the iceball to the desired shape of the planned ablation zone. With its extremely high acoustic impedance, ice reflects up to 99% of ultrasound signals and produces a characteristic ultrasound appearance within the tissue [54]. This facilitates live visualization of the edge of the iceball at 0 °C, allowing the operator to control the extent of cryoablation using ultrasound guidance. Urethral warming devices protect the urethral mucosa from necrosis during cryotherapy [55, 56]. The use of a warmer is now considered standard of care and reduces the rates of urethral slough, incontinence and urinary retention [57]. Thermosensors are placed immediately prior to the procedure to ensure that a lethal temperature of −20 to −40 °C is achieved in the part of the gland to be ablated, while a safe temperature is maintained in Denonvilliers’ fascia and the urethral sphincter [58]. The ability to deliver lethal ice into the desired ablation zone, use of ultrasound and temperature monitoring, and urethral warming to protect collateral structures makes cryotherapy an excellent modality for focal therapy. In addition, it is suited to focal treatment of anterior zone cancers with its transperineal approach [32].

### High-intensity focused ultrasound

High-intensity focused ultrasound (HIFU) was not widely available in the United States until recently due to regulatory restrictions and much of the experience has been European. Transrectal HIFU represents a truly noninvasive therapeutic modality and is well suited to hemi-ablations and posterior zone focal therapy. However, due to energy dissipation and gradual edema over the intervening prostate tissue, the anterior gland may be more difficult to treat [59–61]. The goal of HIFU is to achieve a target temperature of at least 55 °C for 5 seconds within the ablation zone [62, 63]. MR thermometry is an emerging technique that allows for monitoring to ensure lethal temperatures in the ablation zone and safe temperatures in the urethra and sphincter [64]. However, this would necessitate the procedure to be performed in-bore in the MRI suite and its efficacy remains unproven.

### Transurethral ultrasound ablation

One interesting new development that has arisen due to miniaturization of HIFU probes is transurethral HIFU (transurethral ultrasound ablation (TULSA)) [65]. Via a transurethral approach, HIFU could potentially be much more efficiently applied to the anterior prostate. However, clinical experience with this technology is currently lacking.

### Laser

Laser offers the possibility of truly focal ablation. The ablation zone is guided by the laser fiber and tissue destruction occurs only within a fixed distance from the fiber tip. This allows for accurate and predictable tissue destruction zones that would be theoretically safe within close proximity to vital structures [66]. The disadvantage is that ablation of larger lesions or anatomical zones/regions may be cumbersome with longer procedure times. The laser fiber can be placed transperineally or transrectally via a delivery trocar.

**Table 131.1** Summary of consensus meetings on patient selection 2010–2016.

| | | De la Rosette 2010 [48] | Ahmed 2012 [49] | Donaldson 2015 [50] | Tay 2016 [51] |
|---|---|---|---|---|---|
| Goal | | Eradication of all cancer | Eradication of all cancer | Eradication of clinically significant cancer | Eradication of clinically significant cancer |
| Cancer determination | Overall | TMB | TMB and mpMRI | TMB or systematic + mpMRI | mpMRI + systematic biopsy |
| | mpMRI | Can be recommended at state-of-art centers | Recommended | No clear recommendation | Recommended as far as possible |
| | Biopsy of suspicious lesion | – | To be studied | Recommended | Recommended, MRI-TRUS fusion biopsy |
| | Biopsy of nonsuspicious area | – | TMB | Recommended | Recommended, at least 12-core TRUS biopsy |
| Disease factors | Risk group | Low to moderate risk | – | Intermediate | Intermediate |
| | Maximum grade | – | – | – | 4 + 3 |
| | Maximum size | T2a clinically or T2b radiologically | – | No agreement | Up to 1.5 ml or 3 ml if not crossing midline; up to 20% of prostate volume or 25% if crossing midline |
| | Residual disease permissible | None | None | 3 + 3 up to core length 5 mm | 3 + 3 up to core length 1 mm |
| Patient factors | Age/life expectancy | At least 10 years life expectancy | NA | Not a primary determinant; best suited to life expectancy >10 years and not <5 years | According to major guidelines. No upper or lower limit whereby focal is contraindicated |
| | Sexual function | Effect unknown, counselling recommended | NA | NA | Important, but not the only indication for choosing focal therapy |

TMB, transperineal mapping biopsy; mpMRI, multiparametric magnetic resonance imaging; TRUS, transrectal ultrasound-guided.

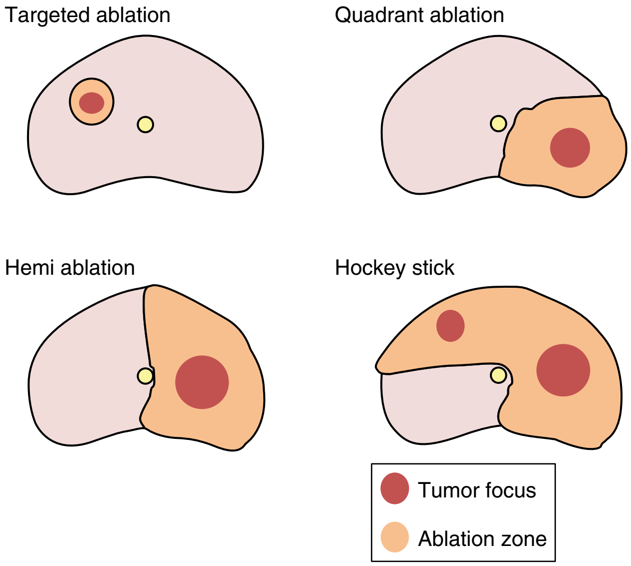

**Figure 131.1** Patterns of ablation.

### Irreversible electroporation

Irreversible electroporation (IRE) is a nonthermal ablative technique that uses short pulses of direct current electricity to produce irreversible pores in the cell membrane, leading to cell death [67]. IRE is lethal only to cells, preserving connective tissue architecture that theoretically could act as scaffolding for new cells to grow. In a 16-patient ablate and resect study, Van den Bos et al. reported that the majority of the men did have fibrinoid necrosis in the unilateral neurovascular bundle and denudation of the prostatic urethra [68]. In this study, the interval between ablation and resection was only one month, and whether the remaining connective tissue does allow regrowth and later functional recovery is unknown.

### Vascular-targeted photodynamic therapy

In vascular-targeted photodynamic (VTP) therapy, low-power near-infrared laser light destroys targeted tissues that have been photosensitized with an intravascular agent preferentially taken up by tumor cells [69]. This results in production of reactive oxygen species in the target zone causing irreversible damage to cell membranes and small arterioles leading to tumor necrosis [70]. Development of the photosensitizer has undergone several iterations with WST9 (TOOKAD®) being used in early trials and the latest being WST11 (TOOKAD Soluble) [71].

### Brachytherapy

Although brachytherapy has been used widely in whole-gland treatment, there has been little published in way of using it for focal therapy apart from simulation studies showing an adequate dose delivery using a focal planning approach [72, 73]. The theoretical benefit with brachytherapy is that the radiation dose decreases rapidly within several millimeters of the radiation source. This allows for a highly conformal approach to radiation delivery. Using seed or low-dose rate (LDR) brachytherapy, urinary toxicity rates seem to be low, and dependent on pretreatment symptoms and urethral dose [74]. On the other hand, high-dose rate (HDR) brachytherapy is associated with a urethral stricture rate as high as 8.2% within the first 2 years of treatment [75]. The majority of these occur at the level of the prostatic apex or bulbous urethra.

### Other modalities

Technical advances in external beam radiation have made it possible to deliver a highly focused dose within the prostate, sparing vital structures [76]. Dosimetric feasibility has been demonstrated in the use of stereotactic body radiotherapy for focal therapy though there has not been any clinical trial [77]. Various nanoparticles used to guide photothermal therapies are still in very early phase [78].

## Choosing the best modality

There is currently no clear benefit of one modality over another in terms of efficacy in tissue destruction. However, the size of the ablation zone and anatomical approach does have implications to successful delivery of ablative energy. For example, the laser tip produces a small ablation zone that is ideal for an image-guided focal ablation of a small lesion, but would take too long if a larger ablation zone is planned (e.g. quadrant or hemi-ablation). Transperineal approaches such as cryotherapy or IRE allow for better access to the anterior gland for anterior focal therapy whereas transrectal HIFU is well-suited to focal destruction of posterior zone cancers [32]. Ultimately, as urologists become conversant with these techniques, an à la carte approach may be adopted, where the modality/delivery combination is adapted to the patient/lesion [59].

## Post focal therapy follow-up

As we move away from whole-gland treatments, traditional markers of therapeutic success are becoming less relevant. After curative radical prostatectomy, PSA is expected to be undetectable and after radiation therapy, a significant rise is needed to define biochemical

Table 131.2 Contemporary focal therapy series and their outcomes.

| Author | N | Pre-diagnostic workup | Declared inclusion criteria | Final demographic | Ablation plan | Follow-up protocol | Median follow-up (mo) | Oncological outcome | Sexual function outcomes | Complications |
|---|---|---|---|---|---|---|---|---|---|---|
| **Cryotherapy** | | | | | | | | | | |
| Onik 2008 [81] | 48 | TRUS biopsy (restaging TMB after 2001) | Unilateral cancer | Low risk 23 (48%)<br>Int. risk 18 (38%)<br>High risk 7 (14%) | Hemi-ablation | 3 monthly PSA for 2 yr then 6 monthly<br>Routine biopsy at 12 mo | 54 | 92% 1 year-BPFS; 85% absolute BPFS (ASTRO); 8.3% (outfield) positive biopsy | 90% of those previously potent retained ability to penetrate | NR |
| Trusdale 2010 [22] | 77 | TRUS biopsy | Unilateral cancer | Low risk 44 (57%)<br>Int. risk 31 (40.3%)<br>High risk 2 (2.6%) | Hemi-ablation | 3, 6 monthly serum PSA and 6 monthly after.<br>12-core TRUS if BCR (Phoenix)/positive DRE | 24 | 72.7% BPFS (Phoenix); 3.9% (infield) and 10.4% (outfield) positive biopsy | 1.9 point decrease in IIEF at 12 mo | NR |
| Bahn 2012 [82] | 73 | TRUS biopsy | Unilateral, Gleason 7 or less | Low risk 24 (33%)<br>Int. risk 49 (67%) | Hemi-ablation | 3–6 monthly PSA<br>6–12 monthly TRUS then yearly | 44.4 | 1.4% (infield) and 15.1% (outfield) positive biopsy | 74% had ability to penetrate at 1 year and 86% in 2.4 yr | Rectal injury 0% |
| Ward 2012 [83] | 1160[a] | NR | NR | Low risk 541 (47%)<br>Int. risk 473 (41%)<br>High risk 143 (12%) | NR | NR | 21.1 | 2-yr BPFS 75.7% | 59% had ability to penetrate at 1 yr | Retention 1.2%<br>Rectourethral fistula 0.1% |
| Hale 2013 [84] | 26 | Staging TMB | Low–intermediate risk | Low risk 23 (88.5%)<br>Int. risk 3 (11.5%) | Hemi-ablation | 3 monthly PSA for 2 yr then 6 monthly<br>Triggered TRUS bx if PSA/DRE abnormal | 19.1 | 88% BPFS (using nadir + 0.5); 7.7% biopsy positive | 73% needed assistance<br>No impotence reported | 4% (1 retention needing TURP), 1 UTI 4%<br>Rash 4% (1) |
| Barqawi 2014 [85] | 62 | TMB | 40–85 yr<br>cT1-T2b<br>Gleason 3 + 4 or less<br>Less than 50% positive core<br>After TTMB, <20% total prostate, index lesion <5 ml, 4 or less zones involved | All low risk | Targeted sectoral ablation | PSA at 3, 6, 12, 18, 24 mo<br>12 monthly mandatory 12-core TRUS biopsy | 28 | 71% BPFS (any post-op increase); 19.4% positive biopsy | No change in IIEF at 24 months | NR |
| Durand 2014 [86] | 48 | 12-core staging TRUS biopsy + mpMRI | PSA <10<br>Positive cores <33%<br>% core <50<br>Unilateral<br>Gleason 6 or less | All low risk | Hemi-ablation | 3 monthly for 1st year then 6 monthly PSA<br>12-core TRUS mandatory at 12 months | 13.2 | 98% BPFS (Phoenix); 12.5% (infield) and 14.6% (outfield) positive biopsy | Mild reduction in IIEF at 3 mo then back to baseline at 6 mo | Retention 15%<br>Rectourethral fistula 2%<br>Cavernous corpus necrosis 2%<br>Urethral stenosis 2% |

(*Continued*)

**Table 131.2** (Continued)

| Author | *N* | Pre-diagnostic workup | Declared inclusion criteria | Final demographic | Ablation plan | Follow-up protocol | Median follow-up (mo) | Oncological outcome | Sexual function outcomes | Complications |
|---|---|---|---|---|---|---|---|---|---|---|
| Lian 2015 [87] | 41 | Minimum 12 core biopsy | Unilateral cancer<br>PSA <20<br>1–2 cores<br><50% involvement<br>Gleason 6–7<br>cT2b or less | Low risk 23 (56%)<br>Int. risk 18 (44%) | Hemi-ablation | 3 monthly for 1st year then 6 monthly PSA 12-core TRUS biopsy at 6–12 mo then yearly/triggered | 63 | 95% BPFS (Phoenix); 4.9% (infield) and 12.2% (outfield) positive biopsy | 76.9% of those previously potent retained ability to penetrate | Retention 3.4% |
| **High-intensity focused ultrasound** | | | | | | | | | | |
| El Fegoun 2011 [88] | 12 | NR | PSA </=10 ng/ml, </=3 positive biopsies with only 1 lobe involved, clinical stage </=T2a, Gleason score </=7 (3 + 4), | Low risk 10 (83%)<br>Int. risk 2 (17%) | Hemi-ablation | 3 and 6 monthly PSA then 6 monthly.<br>6 monthly clinical assessments for 5 yr then annually. 6-core mandatory biopsy at 1 yr or if PSA rising | 127 | 90% recurrence free at 5 yr and 38% at 10 yr; 41.7% positive biopsy | NA[b] | Retention (8.3%) |
| Ahmed 2015 [89] | 56 | mpMRI + TRUS biopsy or TMB | PI-RADS 4/5 with concordant biopsy findings<br>Gleason ≤4 + 3<br>PSA ≤20<br>Stage ≤ t3a | Low risk 7 (12.5%)<br>Int. risk 47 (83.9%)<br>High risk 2 (3.6%) | Focal ablation | Clinical review and PSA at 1, 3, 6, 9, 12 mo Targeted biopsy of treated area at 6 mo<br>Contrast-MRI at 2 wk and mpMRI at 6 mo | 12 | 34.6% (infield, 11.5% clinically significant) and 7.7% (outfield) positive biopsy | Erections sufficient for penetration decreased from 71.4% at baseline to 58.9% at 12 mo | 16.1% transient dysuria<br>64.3% transient hematuria<br>42.9% passage of debris<br>17.9% UTI<br>7.2% required endoscopic procedures |
| Van Velthoven 2016 [90] | 50 | mpMRI + targeted biopsy | Concordant biopsy with mpMRI<br>Stage ≤ T2<br>PSA < 15<br>Prostate volume <40 ml<br>Life expectancy ≥5 yr | Low risk 24 (48%)<br>Int. risk 26 (52%) | Hemi-ablation | Clinical review and PSA at 1, 3 and 6 mo then 6 monthly.<br>TRUS biopsy if PSA recurrence (Phoenix) | 39.5 | 72% (Phoenix) and 64% (Stuttgart) BPFS; 6% (infield) and 10% (outfield) positive biopsy | 70% of those previously potent retained ability to penetrate | Retention 8%, UTI 6%, LUTS 18%, stricture 4% |
| Feijoo 2016 [91] | 71 | TRUS biopsy (20 core) + mpMRI | Unilateral disease<br>Stage T1cge ra<br>positive biopsies <33%<br>Gleason score ≤3 + 4<br>PSA <15<br>Life expectancy >10 yr | Gleason 3 + 3 – 58 (86.6%)<br>Gleason 3 + 4 – 9 (13.4%) | Hemi-ablation | Clinical review and PSA at 3, 6 and 12 mo then 6 monthly.<br>Mandatory 12-core TRUS biopsy at 12 mo | 12 | 15.5% (infield) and 9.9% (outfield) positive biopsy | 50% of those preoperatively potent retained IIEF >21 | Retention 8.5% (2 required TURP), UTI 8.5% |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Vascular-targeted photodynamic therapy** | | | | | | | | | | |
| Azzouzi 2015[c] [71] | 117[d] | mpMRI+ TMB | PSA <10 ng/ml<br>Gleason pattern 4 allowed at low volume (<3 cores, ≤3 mm max cancer core length) | Gleason 3 + 3 – 116 (99.1%) | Hemi-ablation (67) and subtotal ablation (50) | PSA at 1, 3 and 6 mo. Day 7 and 6-mo mpMRI. 6-mo mandatory 12-core biopsy | – | 19.4% positive biopsy for hemi-ablation (31.6% overall) | Mild reduction in IIEF | Urethral stenosis 1<br>Orchitis 1<br>Dysuria 1<br>Hematuria 1<br>Prostatitis 1<br>Pelvic pain 1 |
| **Laser therapy** | | | | | | | | | | |
| Eggener 2016[c] [92] | | | cT1c-T2a<br>PSA <15 ng/ml<br>PSAD <0.15<br>Gleason score ≤ 7 in ≤25% of cores<br>mpMRI max 2 lesions, max diameter 15 mm, max volume 2 ml | Gleason 3 + 3 – 23 (85%)<br>Gleason 3 + 4 – 3 (11%)<br>Gleason 4 + 3 – 1 (4%) | Focal ablation with 5 mm margin | Clinical assessment and PSA at 1, 3, and 12 mo<br>3-mo mpMRI with targeted biopsy of infield area<br>12-mo mpMRI and 12-core TRUS biopsy | – | 4% infield positive biopsy at 3 mo<br>11% infield and 30% outfield positive biopsy at 12 mo | No change in IIEF at 12 mo | Hematuria 15%<br>Ecchymosis 11%<br>Retention 8% |

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[a] This was a Cryo On-Line Data (COLD) registry series.

[b] Majority of men were not interested in sexual function in this study.

[c] Phase I/II trials.

[d] This was a combined analysis of three Phase II trials.

BCR, biochemical recurrence; BPFS, biochemical progression-free survival; DRE, digital rectal examination; IIEF, international index for erectile function; Int. – intermediate; mpMRI, multiparametric magnetic resonance imaging; NR, not reported; NA, not applicable; PSA, prostate specific antigen; TRUS, transrectal ultrasound; TMB, transperineal mapping biopsy.

recurrence. After focal therapy, however, PSA depends on the amount of residual prostate epithelia that may continue to grow, rendering it less informative. Similarly, clinical examination of the prostate may be affected by posttreatment scarring.

In a 2015 Joint International Consultation on Urological Diseases (ICUD)/Society Internationale de Urologie (SIU) project on image-guided focal therapy, success is defined within the treated or infield area as the eradication of the tumor focus in the short term, and the absence of clinically significant cancer in the intermediate to long term [79]. This consultation also stressed the importance of monitoring the untreated or outfield area for the development of clinically significant cancer, that in the short term, likely represents selection failure, and in the intermediate to long term may represent *de novo* cancer.

A combined strategy of mpMRI and targeted biopsy offer the best available means to monitor the treated and untreated areas. The 2015 ICUD-SIU consultation recommends an mpMRI with mandatory targeted biopsy of 4–6 cores in the treated area at 3–6 months, then mpMRI at 1–2 and 5 years with targeted biopsy as needed. A systematic biopsy is also recommended at 1–2 and 5 years to provide further histological evaluation of the untreated zone for potential outfield recurrence. It should be noted that as yet, there is limited experience with mpMRI in the postfocal treatment arena, and it is unknown how posttreatment changes interact with mpMRI performance. In one whole-gland HIFU series, the sensitivity and specificity of DCE-MRI were reported to be 73–87% and 73–82%, respectively [80]. As radiological experience in postfocal therapy prostates accrues, it will be instructive to learn especially from the treatment failures.

## Contemporary focal therapy series and their outcomes

As mentioned in the beginning of this chapter, a successful focal therapy strategy is the result of a strong multidisciplinary collaboration, with a focus on patient selection, disease determination, accurate delivery of the energy modality, and meticulous follow-up. Focal therapy outcomes must be interpreted in this context. As such, contemporary outcomes of focal therapy series are presented in Table 131.2.

## Conclusions

Focal therapy is an exciting concept that has potential to extend active surveillance and improve quality of life. The cornerstone of success is effective patient selection and careful and meticulous follow-up. However, until long-term outcomes are available, this approach remains under investigation, and urologists should not hesitate to "convert" a patient to whole-gland treatment if the necessity arises.

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# 132

# Focal Laser Ablation for Carcinoma of Prostate

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## Introduction

Focal laser ablation (FLA), or laser interstitial thermal therapy (LITT), refers to localized destruction of prostate tissue by heat from a fiber-coupled infrared laser [1]. Recent advances in the detection of clinically significant prostate cancer (PCa) using magnetic resonance imaging (MRI) now allow for focal treatment of PCa and real-time monitoring of temperature and treatment effects [2, 3]. In contrast to high-intensity focused ultrasound (HIFU), which employs temperatures high enough to cause immediate vaporization, FLA uses temperatures only high enough to cause coagulative necrosis, while avoiding cavitation, vaporization, or carbonization [4]. In contrast to whole-organ treatment, FLA provides localized cancer control with a reduction in treatment-related adverse events frequently seen with surgery or radiation. In recent years, several pilot studies have demonstrated safety and feasibility of FLA using MRI or MRI/ultrasound fusion technology for direct image guidance of the laser fiber [5–8]. However, long-term clinical data regarding oncologic efficacy and patient outcome are currently lacking.

## Principle of focal laser ablation

The use of lasers for local treatment of solid tumors was first proposed in 1983 by Bown [9]. He demonstrated focal tissue necrosis by inserting a 400 μm laser fiber into a metastatic skin lesion [9]. Building on previous work with laser treatment for benign prostatic hyperplasia (BPH), Johnson et al. established feasibility of FLA in a canine model [10]. Prostatectomy specimens demonstrated a confined area of acute coagulative necrosis surrounding each laser fiber pathway [10]. Amin et al. first described the clinical application of FLA for PCa in a patient with local recurrence following radiation therapy [11]. Biopsy of the treatment zone at three months confirmed presence of coagulative necrosis, but revealed cancer cells in the adjacent prostate tissue [11]. Lindner et al. described the first clinical trial of FLA in 12 men with low-risk PCa [5]. All subjects were successfully treated with minimal morbidity following treatment [5]. Further details of this study are discussed later in the chapter.

FLA for PCa involves image guidance to target the region of interest, sufficient thermal tissue effect to destroy the tumor, minimal injury to adjacent tissue, and accurate surveillance of the prostate after treatment [1, 12]. FLA is based on a photothermal effect in prostate tissue [12]. FLA employs temperatures resulting in coagulation necrosis; even brief exposure to temperatures in excess of 45°C causes cell death via coagulation necrosis [13]. Thermal activity results from the absorption of radiant energy by tissue receptive chromophores that rapidly induce coagulation necrosis [12]. Resultant increased temperatures produce protein denaturation and *in vivo* tissue destruction [1]. Optical and thermal properties of the tissue are dictated by its structure, water content, and blood circulation [14]. Prostate tissue is suitable for FLA due to its optical absorption rate without excess vascularity, which allows localized ablation of tumor [14].

## Technology of focal laser ablation

The ultimate goal of FLA systems is to achieve a local tissue temperature rise to 60–85°C to induce coagulation necrosis. Temperature increases occur due to absorption of photons, causing deactivation of target molecules, and

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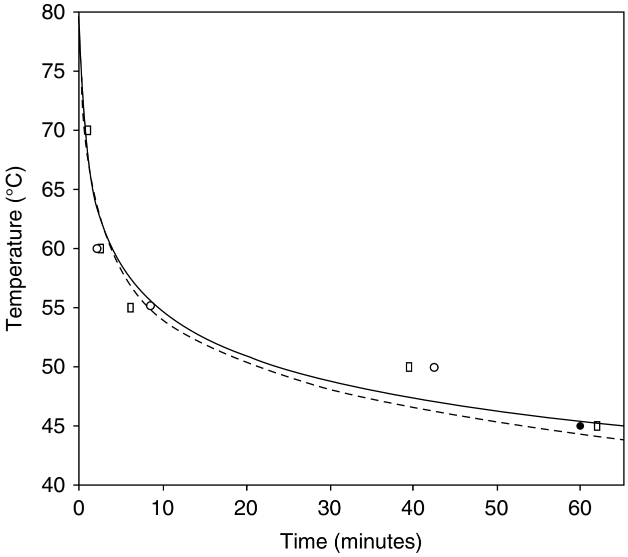

**Figure 132.1** Temperature–time plot for 90% normalized destruction of human benign prostatic hyperplasia (BPH). Open circles represent dye data and open squares histology data. An Arrhenius plot of viability dye and histology results based on 90% normalized destruction of the stromal cells. The *in vivo* data from Larson et al. [18] for the destruction of BPH at 45°C for 1 hour is also plotted for reference (filled circle). *Source:* P Bhowmick et al. In vitro assessment of the efficacy of thermal therapy in human bening prostatic hyperplasia. *Int J Hyperthermia* 2004;20(4): 421–439. Reproduced with permission of Taylor and Francis, Ltd.

ultimately tissue destruction [15]. Energy is delivered using diode lasers that are coupled to laser fibers, thinly spun glass (400–800 µm) with total internal reflection. A diffuser is affixed on the end of the fiber to spread laser energy in a cylindrical, spherical, or conical pattern. Laser parameters that can modify the rate and extent of damage include wavelength, wattage, time, coolant, and tip geometry.

Wavelength choice is important to maximize absorption of laser energy by water and hemoglobin, while maximizing depth of penetration, thus most systems are in the near-infrared range (810 nm, 850 nm, 980 nm) [5, 8, 16]. This tradeoff is also present with the choice of wattage, with lower powers (5–7 W) having slower temperature rises, and higher powers (~30 W) having quick rises, but needing active cooling to prevent fiber destruction. Active cooling can be achieved using a fluid or gas, with existing systems relying on saline or $CO_2$ to actively cool the laser fiber. This active cooling is implemented in existing systems with a dual-lumen, enclosed catheter. Figure 132.1 displays a temperature–time plot of tissue destruction in patients with BPH [17, 18].

FLA is monitored by either MRI or thermal probes, to primarily ensure that sensitive structures (urethra, rectal wall, peri-prostatic nerves) remain below 42°C. MR thermometry measures the proton resonance frequency shift on serial images and yields a relative estimate of temperature in two dimensions, accurate to within a degree [19]. However, this phase shift is sensitive to motion, and artifacts can occur, due to respiration, peristalsis, and at tissue boundaries [20]. The clinical implication of these artifacts is that MR thermometry requires frequent calibration during treatment, and temperature readings outside the prostate may not be valid [6]. Efforts to improve the accuracy and robustness of MR thermometry are ongoing [21]. Conversely, thermal probes provide excellent accuracy but are limited to point measurements [22].

Tissue damage is estimated in real time with the use of the Arrhenius damage model:

$$\Omega(t) = A\int_{0}^{\tau} e^{-\frac{E_a}{RT(t)}}\,dt$$

which gives a rate process for irreversible damage (Ω) as a function of temperature ($T$) [23]. Tissue-specific constants are experimentally derived and vary considerably in the literature. These constants, and the specific point at which irreversible damage occurs, vary with zonal anatomy and prior heating [17]. Contrast-enhanced MRI or ultrasound is then used to confirm the area of damage [5, 8]. Figure 132.2 shows an example of an MRI with Arrhenius-based damage-estimation zone overlay [24].

Future efforts will focus on improved understanding of tissue-specific parameters, influence of cooling sources within the prostate, and large clinical studies to address the variability in prostate tissue response to laser energy.

## Treatment of prostate cancer

### Indications

As with other focal therapies, at this time FLA may be considered for men with clinical stage T2b or less and Gleason score 3 + 4 = 7 or less. Most commonly, FLA is directed at a localized, MR-visible lesion that is suspicious for PCa and confirmed by targeted prostate biopsy cores. Prostate specific antigen (PSA) 20 ng/ml or less and prostate volume 100 ml or less is preferred. Life expectancy in potential FLA candidates should exceed 10 years. Use of FLA following prior treatment for PCa, such as radiation or cryotherapy, has not been reported.

### Temperature monitoring

One of the major advantages of FLA is its compatibility with MRI, allowing for real-time monitoring of temperature changes during FLA treatment [21, 25]. Temperature monitoring, using MR thermometry or thermal probes,

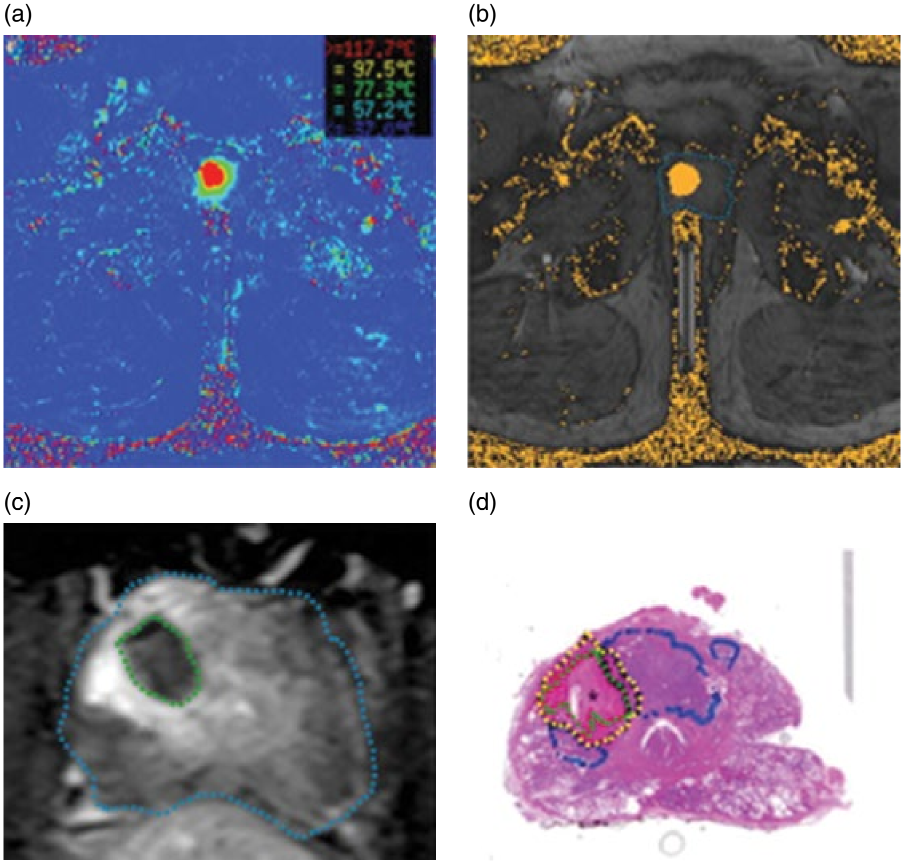

**Figure 132.2** Images of a 67-year-old male with a Gleason score 3 + 4 = 7 in his right transition zone. (a) Real-time MRI–temperature map acquired during focal laser ablation. (b) Anatomical MRI of the prostate (delineated in blue) with the Arrhenius-based damage-estimation zone as orange overlay. (c) Postablation axial T1-weighted contrast-enhanced image. The prostate is delineated in blue and the nonenhancing necrotic tissue in green. (d) Whole-mount H&E stain of the prostate. The necrotic tissue is delineated in green, the perinecrotic tissue in yellow, and vital tumor in blue. *Source:* Bomers JGR, Cornel EB, Fütterer JJ et al. MRI-guided focal laser ablation for prostate cancer followed by radical prostatectomy: correlation of treatment effects with imaging. *World J Urol* 2016;35(5):703–711. Reproduced with permission of Springer Nature Publishers.

is required for precise determination of the extent of thermal damage in prostate tissues and adjacent structures caused by laser energy [26].

MR thermometry measurements acquired during FLA have previously been used to predict cell death in animal models [27, 28]. Validation of these models has been performed using rigid co-registration between thermometry images and postablation MRI or histology, thus enabling comparison of actual areas of cell death against a simulated temperature map [26–28]. Raz et al. used MR thermometry to monitor thermal tissue damage during FLA in two patients [29]. Thermometry scan was repeated every 6 seconds and laser ablation was ceased when temperatures exceeded 45°C [29].

Another method of measuring intraprostatic temperatures is the use of direct thermal probes placed interstitially. Lindner et al. first used fluoroptic temperature probes for real-time monitoring of intraprostatic temperatures during FLA treatment in 12 patients [5]. Further results from this trial are discussed later in the chapter. In a recent Phase I study, MR-compatible fluoroptic temperature probes were inserted into the prostate using ultrasound guidance, allowing real-time safety monitoring independent of MR thermometry during FLA [6]. In the study, thermal probes were placed at various intraprostatic locations to directly monitor temperatures near the rectal wall, prostatic capsule and urethra [6]. Figure 132.3 illustrates intraprostatic placement of thermal probes during FLA treatment [6].

## MRI-guided focal laser ablation (in-bore)

Several preclinical studies performed in phantom, canine, and cadaveric prostates have demonstrated the feasibility of MRI-guided FLA [30–33]. To date, FLA has generally been performed by an interventional radiologist within an MRI tube (in-bore), allowing for direct image guidance and MRI thermometry for temperature

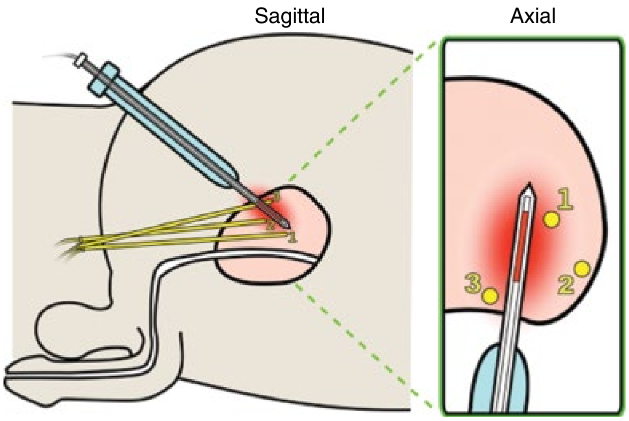

**Figure 132.3** Diagram showing intraprostatic placement of laser fiber (red) and three thermal probes (yellow) during MRI-guided focal laser ablation. Patient is in the prone position within the MRI tube. Thermal probes are used in conjunction with MRI thermometry for independent measurement of temperatures at the margin of treatment zone (1, 2) and near rectal wall (3) as seen on axial inset.

monitoring within the prostate [6]. Raz et al. reported safety and feasibility of in-bore FLA for treatment of low-risk PCa in two patients [29]. No serious adverse events were observed at one month following treatment [29]. Oto et al. demonstrated safety and technical feasibility of MRI-guided FLA in nine men with low-risk PCa [8]. In their study, procedure time ranged from 2.5 to 4 hours and mean laser ablation time was 4.3 minutes with a maximum power of 11.5 W applied during ablation [8]. There were no serious adverse events observed at six-month follow-up [8]. In Table 132.1, a summary of the currently available FLA trials is shown.

In a Phase I trial, Natarajan et al. investigated safety and feasibility of in-bore FLA in eight patients with intermediate-risk PCa [6]. Laser insertion was transrectal and thermal probe insertion was transperineal as in brachytherapy. Both MR thermometry and direct thermal probe recordings were made simultaneously, to assess the accuracy of MR thermometry for monitoring intraprostatic temperatures during treatment [6]. Readings from the probes demonstrated that the thermal effect of FLA was confined to the intended ablation zone with no evidence of heating of adjacent critical structures [6]. There were no serious adverse events observed during six months of follow-up [6]. Total procedure time averaged 292 minutes and actual time in the MRI scanner averaged 223 minutes, intervals similar to those reported in the literature [6, 8].

### Procedure

MRI-guided FLA has been performed to date by an interventional radiologist working within an MRI scanner. Pretreatment high-field 3 T multiparametric MRI, with or without endorectal coil, is performed prior to treatment to establish target lesions, resulting in more accurate laser fiber placement [34]. Targeting of MR-visible regions of interest during FLA treatment is performed using either a transperineal or transrectal approach [34]. In-bore FLA has most often been performed using conscious sedation.

Prior to each procedure, laser fiber locations and desired treatment margins are planned using custom software [6]. Sizeable treatment margins are necessary for complete tumor ablation due to underestimation of prostate tumor volume with current MRI technology [35, 36]. In a recent study comparing preoperative MRI to radical prostatectomy specimens to evaluate MRI accuracy in identifying tumor features, Priester et al. demonstrated that tumor extent may be underestimated by more than 1 cm in most cases [35]. However, future studies are required to define the appropriate treatment margins needed for ablation of the entire tumor.

In-bore FLA is most commonly performed with patients in the prone position on a sliding gantry of the MRI. Once positioned, preliminary images are obtained to identify the region of interest and calculate trajectory angles [34]. An MR-compatible needle guide is then used to insert laser fibers into the prostate. Multiple laser applications, up to 15 W generally, are employed per laser fiber insertion for complete lesion ablation [6]. During treatment, intraprostatic temperatures are continuously monitored using MR thermometry, allowing the detection of any areas that are undertreated or resistant to thermal ablation [34]. FLA is ceased immediately if temperatures exceed monitor thresholds. Irreversible cell death occurs at temperatures greater than 42°C [14]. However, temperatures should not exceed 90°C within the prostate or 40°C near the urethra or rectal wall.

Patients are routinely discharged home within a few hours of treatment with oral analgesics and antibiotics. Prior to discharge, patients should demonstrate spontaneous voiding. Transient urinary retention from prostatic swelling has been an occasional complication. Follow-up clinic visits include PSA, and after 6–12 months, prostate biopsy and MRI. Patients undergoing any form of partial gland ablation are followed as if enrolled in an active surveillance protocol [37].

## MRI/ultrasound fusion-guided focal laser ablation

FLA has generally been performed in an MRI scanner using conscious sedation. With recent advances in MRI/ultrasound fusion technology, localization of tumors using FLA may be performed using MRI/ultrasound fusion guidance. A potential advantage of MRI/ultrasound fusion guidance compared to in-bore FLA is a

**Table 132.1** Treatment and monitoring parameters in studies of focal laser ablation.

| Study | Anesthesia | Real-time imaging | Approach | Laser source | Laser power (W) | Temperature monitoring |
|---|---|---|---|---|---|---|
| Lindner et al. [5] | General | Ultrasound | Transrectal | Indigo diode laser | Unknown | Thermal probes |
| Raz et al. [29] | General | MRI | Transperineal | Visualase diode laser | Unknown | MRI thermometry |
| Oto et al. [8] | Conscious sedation | MRI | Transperineal | Visualase diode laser | 11.5 W | MRI thermometry |
| Lepor et al. [7] | Local | MRI | Transrectal | Visualase diode laser | Unknown | MRI thermometry |
| Natarajan et al. [6] | Conscious sedation | MRI | Transrectal | Visualase diode laser | 11–14 W | MRI thermometry, thermal probes |
| Eggener et al. [44] | Conscious sedation | MRI | Transperineal | Visualase diode laser | 6–15 W | MRI thermometry |

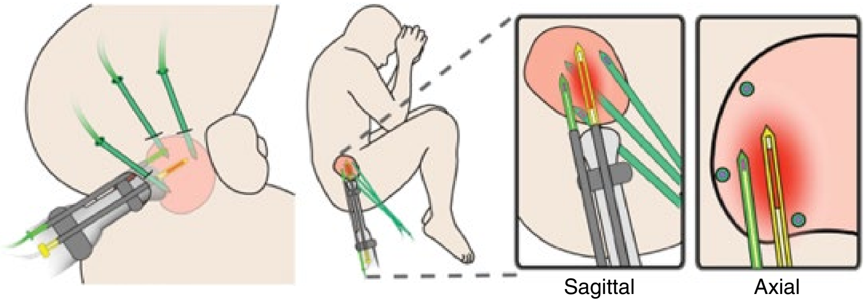

**Figure 132.4** Diagram showing intraprostatic placement of laser fiber (red/yellow) and three thermal probes (green) during MRI/ultrasound fusion-guided focal laser ablation. Laser fiber is inserted transrectally and thermal probes transperineally. Thermal probes provided continuous monitoring of intraprostatic temperature throughout the procedure. Appropriate positioning of the laser fiber within the prostate is constantly verified using real-time ultrasound.

reduction in procedure time by performing the treatment in a clinic setting under local anesthesia without need for real-time MRI visualization. Furthermore, fusion software is able to track biopsy site locations, thus permitting accurate return to the same location within the prostate for FLA treatment and follow-up biopsy [38, 39]. Several fusion devices have been approved by the US Food and Drug Administration (FDA) for commercial use (e.g. Artemis, Eigen, Grass Valley, CA, USA; UroNav, Invivo, Gainesville, FL, USA) [38].

Lindner et al. first demonstrated feasibility of FLA using MRI/ultrasound fusion guidance in 12 patients with low-risk PCa [5]. In their study, an early prototypic fusion device was used to guide the laser fiber to the MRI/ultrasound fused region of interest [5]. FLA was successfully performed in all patients and they observed no perioperative complications and minimal postoperative morbidity [5].

In a recent Phase I trial in 10 men with intermediate-risk PCa (NCT02357121), we investigated the safety and feasibility of FLA using MRI/ultrasound guidance in an outpatient clinic setting under minimal sedation. Total procedure time averaged 95 minutes (range 64–112). All patients were discharged home 1–2 hours following treatment. There were no serious adverse events observed at six months. Figure 132.4 displays an example of MRI/ultrasound fusion-guided FLA.

### Procedure

During MRI/ultrasound fusion-guided FLA treatment, the treating physician images the prostate using ultrasound. While visualizing the prostate on real-time ultrasound, the MRI of that prostate is fused with ultrasound using a fusion device [38]. The fusion results in creation of a patient-specific three-dimensional (3D) prostate model, and on the prostate model, the targeting and ablation of the tumor occurs.

Appropriate positioning of the laser fiber within the prostate is monitored using real-time ultrasound and continuous monitoring of intraprostatic temperatures is performed using thermal probes. The fixed arm of the fusion device provides a fixed platform for insertion and stabilization of the laser fiber during treatment. A motion compensation function in the biopsy tracking software is used to correct discordance from the 3D model due to patient or prostatic movement during treatment. Similar to in-bore FLA, application of laser energy is suspended immediately if temperatures exceed monitor thresholds.

## Effects on prostate tissue

FLA induces a focal area of coagulation necrosis and fibrosis in prostate tissue following treatment [40]. In a study evaluating the effects of FLA on prostate tissue, Lindner et al. demonstrated homogenous coagulation necrosis in the whole-mount prostatectomy specimens of four men with PCa following FLA treatment [41]. Furthermore, these authors observed a localized ablation zone with no evidence of viable cells in treated regions within the prostate [41]. In another study of five men with PCa, Bomers et al. investigated the treatment effects of FLA on prostate tissue prior to radical prostatectomy [24]. Whole-mount prostatectomy specimens revealed a confined area of homogeneous necrosis surrounded by a necrotic area of 1–5 mm thickness with neovascularization and an increased mitotic index [24].

Recent work by our group, in a patient who underwent radical prostatectomy 15 months following FLA, demonstrates the localized treatment effects of FLA [42]. We observed absence of cancer in the treatment zone, but residual cancer in the adjacent prostate tissue [42]. Histology of the treated area revealed a confined, localized area of benign prostatic glands with chronic inflammation, stromal fibrosis, giant cell reaction, and hemosiderin-laden macrophages consistent with thermal effect (Figure 132.5) [42].

## Patient-reported outcomes

Radical prostatectomy and radiation therapy are potentially accompanied by adverse after-effects that impact quality of life [43]. An important reason for selection of focal

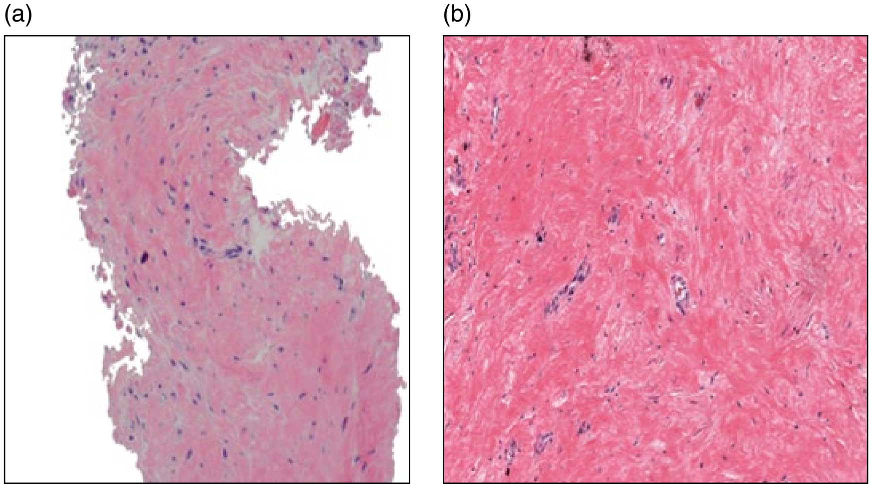

**Figure 132.5** (a) Histology of treatment zone after focal laser ablation treatment showing benign glands with chronic inflammation, stromal fibrosis, giant cell reaction and hemosiderin-laden macrophages consistent with thermal effect. (b) Higher magnification.

therapy is to reduce the chance of treatment-related morbidity. Several FLA trials have employed validated questionnaires to evaluate the effects of FLA on patient quality of life, including urinary and sexual function following treatment [5, 6, 8]. Using the International Prostate Symptom Score (IPSS) and International Index of Erectile Function 5 (IIEF-5) questionnaires, Natarajan et al. observed no significant changes in urinary or sexual function at six months in all men treated with FLA [6]. No urinary incontinence, erectile dysfunction, or change in ejaculation was reported by any patient [6]. Hematuria was the most common adverse event after treatment and resolved without intervention in all cases [6]. Results of FLA studies are shown in Table 132.2.

Lindner et al. reported no significant changes in IIEF-5 or IPSS scores following MRI/ultrasound fusion-guided FLA treatment in 12 men with PCa [5]. In their study, perineal discomfort was the most common adverse event reported (25% of patients) [5]. In a recent Phase II trial investigating in-bore FLA in 27 men with low- to intermediate-risk PCa, Eggener et al. reported hematuria in 4 subjects (15%), perineal ecchymosis in 3 (11%), and acute urinary retention in 2 (8%) after treatment [44]. Similarly, Oto et al. observed no significant changes in urinary of sexual function at six months following FLA treatment [8]. They reported no symptoms indicative of rectal wall toxicity in any patient during follow-up clinic visits [8]. Thus, FLA appears to be relatively safe, especially in comparison to surgery or radiation therapy.

## Effect of focal laser ablation on serum PSA levels

Recent studies demonstrate a varied effect of FLA on PSA after treatment [6–8]. In a study investigating the effects of in-bore FLA treatment for PCa in 25 men, Lepor et al. reported a mean PSA decrease of 2.3 ng/ml between baseline and three months follow-up [7]. Natarajan et al. observed a significant decrease in median PSA from 8 to 3.3 ng/ml six months after FLA treatment [6]. Furthermore, there was a significant decrease in PSA density and increase in percent-free PSA observed [6]. However, Oto et al. observed no significant change in mean PSA from baseline to six months after FLA treatment [8]. The role of serum PSA levels in follow-up of men undergoing FLA is an important topic for further study.

## MRI changes

The extent of tissue necrosis due to FLA is visible on posttreatment MRI. Qualitative and quantitative prostate MRI features before and after FLA treatment have been described [25, 40]. In one recent study, in which whole-mount prostatectomy slices were co-registered with prostate MRI before and after treatment, Litjens et al. observed several changes in MRI features that might function as quantitative tissue biomarkers for treatment response [40]. These authors also found that residual disease and ablated tissue could not be completely differentiated by postablation MRI alone [40].

In a study of four men with PCa, Lindner et al. observed a correlation between volumes of thermal damage that were visible on MRI and those determined via staining of whole-mount radical prostatectomy specimens after FLA treatment [41]. Oto et al. demonstrated a hypovascular defect on dynamic contrast-enhanced MRI immediately after FLA treatment in eight patients [8]. In another study of eight men with PCa, Natarajan et al. observed a well-defined, underperfused region on DCE MRI in each patient immediately after FLA. There were no consistent changes in T2- or diffusion-weighted

**Table 132.2** Clinical results of focal laser ablation studies.

| Study | No. of patients (*n*) | Baseline PSA | Primary Gleason score | Posttreatment PSA | Change in urinary function | Change in sexual function | Serious adverse events | Oncologic efficacy |
|---|---|---|---|---|---|---|---|---|
| Lindner et al. [5] | 12 | Mean 5.7 | 6 | Not reported | None (IPSS) | None (IIEF-5) | None | TRUS-guided biopsy at 3–6 mo = no PCa in ablation zone in 8 men, no PCa in or outside ablation zone in 6 men |
| Raz et al. [29] | 2 | Median 3.8 | 6 | Not reported | Not reported | Not reported | None | Not reported |
| Oto et al. [8] | 9 | Mean 5.5 | 6 | Mean 5.7 (1 mo),<br>4.7 (3 mo),<br>5.5 (6 mo) | None (IPSS) | None (SHIM) | None | MRI-guided biopsy at 6 mo = no PCa in ablation zone in 7 men, residual PCa in 2 men |
| Lepor et al. [7] | 25 | Mean 5.3 | 7 | Mean 2.9 (3 mo) | None (IPSS) | None (SHIM) | None | MRI-guided biopsy at 3 mo = 26 of 28 sites biopsied with no PCa |
| Natarajan et al. [6] | 8 | Median 7.5 | 7 | Median 3.3 (6 mo) | None (IPSS) | None (IIEF-5) | None | MRI/US fusion biopsy at 6 mo = no PCa in ablation zone in 5 men, residual PCa outside ablation zone in 6 men |
| Eggener et al. [44] | 27 | Mean 4.4 | 6 | 3.4 mean (12 mo) | None (IPSS) | SHIM lower at 1 mo ($P = 0.03$) and 3 mo ($P = 0.05$), no significant change at 12 mo ($P = 0.38$) | None | MRI-guided biopsy at 3 mo = no PCa in ablation zone in 26 men, TRUS-guided biopsy at 12 mo = residual CaP in 10 men |

IPSS, International Prostate Symptom Score; IIEF-5, International Index of Erectile Function; SHIM, Sexual Health Inventory for Men; US, ultrasound; TRUS, transrectal ultrasound.

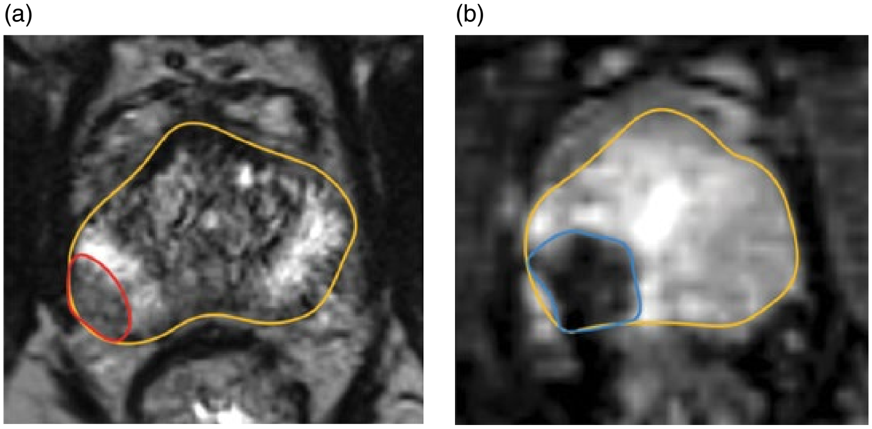

**Figure 132.6** (a) Multiparametric axial T2-weighted MRI of prostate (yellow line) before FLA treatment showing the MR-visible region of interest (red line). (b) Dynamic contrast-enhanced MRI of prostate (yellow line) showing the hypovascular defect immediately after treatment.

imaging, and median prostate volume decreased [6]. Figure 132.6 displays the MRI of a patient before and after FLA treatment [6].

## Oncologic efficacy

Eggener et al. observed no cancer in 26 of 27 men (96%) three months after in-bore FLA [44]. At 12 months, three men (11%) had cancer in the treatment zone and eight (30%) had cancer identified outside the treatment zone on repeat biopsy [44]. Most residual cancer identified was clinically insignificant [44].

At six-month targeted biopsy, Natarajan et al. identified no residual cancer in the ablation zone in five of eight men (63%), and no cancer outside the treatment zone in two of eight men (25%) after in-bore FLA [6]. Lindner et al. demonstrated that 50% of patients had no evidence of cancer on biopsy six months after FLA treatment [5]. In their study, 67% of patients had no cancer identified in the treated area [5]. Lepor et al. reported that 26 of 28 sites biopsied three months after FLA treatment had no evidence of residual PCa [7].

## Focal laser ablation after radical prostatectomy

Local recurrence of PCa after whole-organ treatment with radical prostatectomy occurs in 25–30% of cases [45]. Experience using FLA to treat post-prostatectomy local recurrence is limited to a single reported case [46]. In that report, Woodrum et al. used MRI guidance to detect PCa recurrence, then inserted a laser fiber via a trans-perineal approach [46]. MRI effectively allowed identification of the recurrent tumor and ablation with the laser fiber [46]. DCE MRI after the procedure had no definitive abnormal enhancement [46]. No posttreatment biopsy was performed [46].

## Conclusion

Laser ablation is a promising treatment alternative for localized, organ-confined prostate cancer, further enhanced by its ease of integration with high-resolution 3 T multiparametric MRI. Several recent studies have demonstrated safety and technical feasibility of FLA using direct MRI guidance or MRI/ultrasound fusion guidance. However, long-term clinical data regarding its effect on patient quality of life and oncologic efficacy are sparse. Further research is necessary to establish FLA as a viable alternative to whole-organ treatment. Future clinical studies will aid in defining treatment margins and identifying appropriate candidates for FLA treatment.

See accompanying video 132.1.

## Acknowledgments

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# 133

# Image-guided Prostate Brachytherapy

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## Introduction

Prostate cancer remains the most common cancer in men; for 2018, an estimated 164 690 cases will be diagnosed (19% of all cancers), with 29 430 deaths (9% of all cancers in men) [1]. Only 10% of prostate cancer diagnoses in the prostate specific antigen (PSA) testing era are high-risk prostate cancers, which justifies approaches that focus treatment on the prostate itself and minimize impact on quality of life.

According to the National Comprehensive Cancer Network (NCCN) guidelines [2], reasonable approaches to the management of non-metastatic prostate cancer include surgical approaches and radiation approaches (external beam radiation therapy (EBRT), brachytherapy, or a combination of both), potentially supplemented by androgen-deprivation therapy. EBRT using relatively few sessions of highly focused, high-dose-per-session radiation therapy (hypofractionation, generally referred to as stereotactic body radiation therapy (SBRT) or stereotactic ablative radiosurgery (SABR)) [3, 4] is becoming more widely accepted as well, but is practiced primarily in experienced centers. Brachytherapy is an approach that allows permanent (low dose rate, or LDR) or temporary (high dose rate, or HDR) delivery of radioactive isotopes within the prostate, which deliver localized therapeutic dose though decay of radioactive isotopes and emission of radiation. Other treatment modalities, including cryotherapy [5] and radiofrequency ablation (RFA) [6] appear to be effective in select cases, but are not yet considered standard of care.

In this chapter we review the history, techniques, and outcomes of brachytherapy approaches in the management of prostate cancer.

## History of prostate brachytherapy

Prostate brachytherapy is one of the oldest radiation therapy techniques, first described by Pasteu and Degrais in 1913 [7] and brought into regular use by Young, the pioneer of the radical perineal prostatectomy [8, 9]. Interstitial techniques were originally performed with digital guidance alone using transperineal radium needles as reported by Barringer, a urologist practicing at the New York Memorial Hospital in his 1924 publication, detailing cases starting as early as 1915 [10]. This needle-based approach was later supplanted by less expensive gold-encapsulated seed treatments [11]. Due to poor visualization of the target, these techniques yielded poor oncologic outcomes, and were not widely adopted. Subsequently, an open surgical retropubic approach was utilized by Whitmore and colleagues at Memorial Sloan Kettering Cancer Center starting in 1970, which also included a bilateral pelvic lymphadenectomy [12, 13]. Local control was still poor with this technique (only 44% at 10 years in node-negative patients), which was felt to be due to suboptimal seed distribution within the prostate gland. In addition, the procedure required a laparotomy, and soon lost favor compared to modern prostatectomy and EBRT approaches.

Image-guided (ultrasound-based) transperineal prostate brachytherapy was introduced by Holm et al. in 1983 [14] and subsequent developments in multiplanar transrectal ultrasound (TRUS) allowed for safe and effective transperineal placement of radioactive sources [15–17]. Subsequently, multiple techniques have been developed incorporating imaging both before (preplanning) and during (intraoperative) LDR brachytherapy implantation procedures to deliver optimal therapy, and robust long-term

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

outcomes and toxicity data have been generated through prospective trials and large institutional experiences. In addition, new techniques for temporary HDR brachytherapy have been developed, after Yoshioka et al. [18] reported the favorable results of HDR brachytherapy as monotherapy for various risk groups of localized prostate cancer in 2000. Guidelines for LDR and HDR prostate brachytherapy have been established by the American Brachytherapy Society (ABS) [19, 20] and its role in the management of prostate cancer is further delineated in the NCCN guidelines [2]. Technical standards for prostate brachytherapy are also well established, with formal roles for the physician and medical physicist and reporting guidelines set by the American Association of Physicists in Medicine (AAPM) [21]. Dosimetric parameters and reporting for permanent prostate brachytherapy are also carefully defined in the AAPM Task Group reports 43 and 137 [22, 23].

## Patient selection for prostate brachytherapy

In terms of radiation-based treatment approaches in the management of prostate cancer, brachytherapy is appealing in that it is the most conformal treatment available for the prostate, focusing the vast majority of radiation exposure on the target organ while limiting dose to the rest of the body more than any other radiation technique, including advanced charged-particle therapy. In addition, the treatment can be delivered in a single session with certain approaches. Prostate brachytherapy is generally an outpatient procedure and the patient may resume 100% of physical activity within 24 hours after implantation and treatment delivery is complete.

Appropriate patient selection is crucial in the application of prostate brachytherapy. Guidelines have been set forth by the American Urological Association (AUA) [24] and the ABS [19, 20]. According to the ABS, there are several absolute contraindications to TRUS-guided permanent prostate brachytherapy, including inability to tolerate spinal or general anesthesia; the presence of distant metastases (identified clinically or on metabolic or cross-sectional imaging); large defects from a prior transurethral resection of the prostate (TURP) that would preclude effective seed placement; life expectancy of less than 10 years; or the presence of the ataxia telangiectasia (AT) mutation, which would predispose to excessive toxicity from radiation.

Other considerations include a high International Prostate Symptom Score (IPSS) [25] of >20 (although it was noted that most prospective studies have used a cutoff score of 15 or 18), history of prior radiation therapy to the pelvis, large median lobes (e.g. Figure 133.1), prostate volume >60 ml at the time of implant, or inflammatory bowel disease [26–29]. For patients with enlarged prostates that would present a technical challenge to implant (due to pubic arch interference, for example, as shown in Figure 133.2), cytoreduction with androgen-deprivation

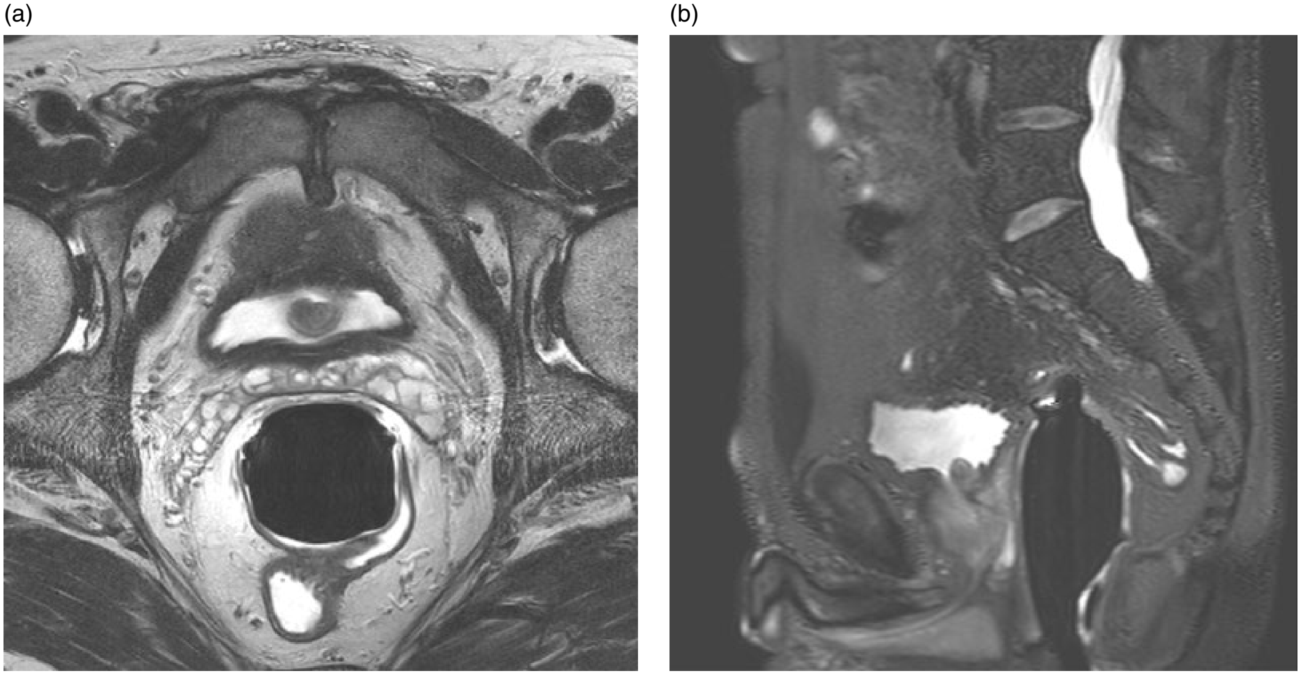

Figure 133.1 Median lobe enlargement. (a) Axial and (b) sagittal views, MRI T2-weighted fast spin echo sequences.

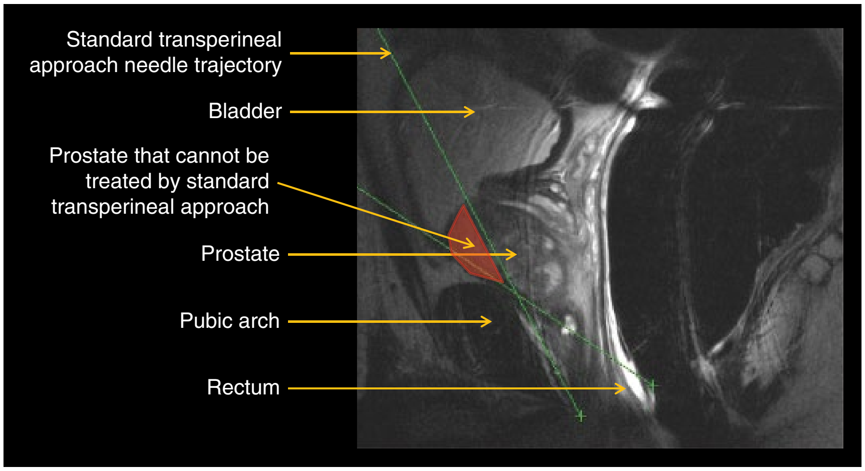
Standard transperineal approach needle trajectory
Bladder
Prostate that cannot be treated by standard transperineal approach
Prostate
Pubic arch
Rectum

**Figure 133.2** Pubic arch interference in transperineal prostate brachytherapy.

therapy (ADT) is an option, with average reduction in prostate volume of approximately 30% after 3–4 months [30, 31]. Both bicalutamide and luteinizing hormone-releasing hormone analogs (LHRHa) can provide effective ADT-based cytoreduction; in a study by Petit et al. [32] median cytoreduction was 26% for bicalutamide and 32% for LHRHa methods, with greater sexual function-related toxicity in the LHRHa group.

Prostate brachytherapy is ideal for the management of prostate cancer confined to the prostate gland, similar to radical prostatectomy. The risk of extraprostatic disease should be considered when selecting treatment. ABS recommendations based on NCCN risk group suggests that prostate brachytherapy alone without supplemental EBRT or ADT is appropriate for low-risk prostate cancer, as well as intermediate-risk prostate cancer; of note, for those patients with high- to intermediate-risk disease, supplemental EBRT and/or ADT should be considered [33]. Brachytherapy alone (monotherapy) is not recommend for patients with high-risk prostate cancer, and supplemental EBRT and ADT are favored [20]. The recommendations are mirrored in NCCN guidelines for the management of prostate cancer [2].

According to the ABS guidelines, there is no absolute lower or upper age limit for prostate brachytherapy, and studies have not shown a significant difference in outcome for patients treated at a younger age (<60 years) compared to patients treated over 60 years of age [34]. A common issue raised when deciding between radiation and surgery-based approaches in the management of prostate cancer is the risk of a secondary cancer from exposure to radiation therapy, particularly bladder and rectal cancers [35–37]. However, when examining the risk of secondary cancers by treatment modality, it has been noted that brachytherapy does not carry the same association with secondary cancers as EBRT, likely due to its highly conformal nature with minimal exposure to normal tissue [36, 38–40]. The possibility of an increased risk of secondary cancers, especially if brachytherapy is combined with EBRT, should still be discussed with each patient.

Brachytherapy (both LDR and HDR) may be used as salvage therapy in the setting of a localized prostate recurrence [2].

## Technical issues in prostate brachytherapy

### Approach, visualization, and access for prostate brachytherapy

Brachytherapy implantation is generally performed according to the method described by Holm et al. [14, 15] via a transperineal approach with real-time ultrasound visualization of the prostate. The TRUS probe is generally mounted on a stepper unit attached to a stabilizer arm, which supports the probe and template grid and facilitates a calibrated caudal/cephalad motion (Figure 133.3). Accurate placement of the needles is achieved with this

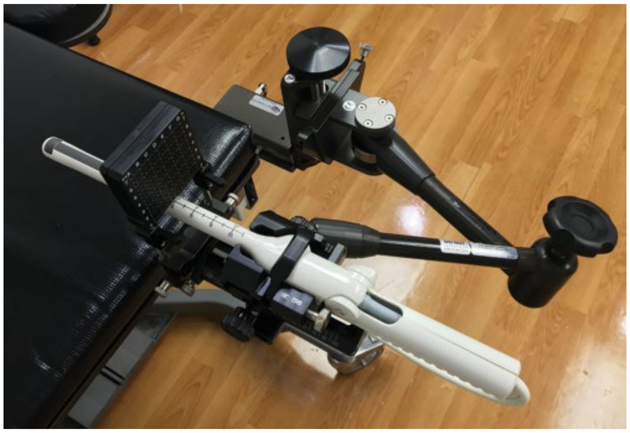

**Figure 133.3** Transrectal ultrasound probe mounted on stepper/stabilizer unit for brachytherapy procedures.

technique, which allows real-time adjustment of implanted needles relative to the target organ (Figure 133.4). Once needle placement is confirmed, the radioactive isotopes may be delivered through them into the substance of the prostate gland, either permanently (LDR approaches using $^{125}$I, $^{103}$Pd, $^{131}$Cs, see Figure 133.5) or temporarily (HDR approaches generally using $^{192}$Ir afterloader) (Figure 133.6).

## Low dose rate permanent prostate brachytherapy

### Source selection for low dose rate prostate brachytherapy

Perhaps the most common isotope used for permanent prostate brachytherapy is iodine-125 ($^{125}$I) first introduced in 1965, which is often sold in the form of silver iodide deposited on a silver rod, sealed in a titanium shell.

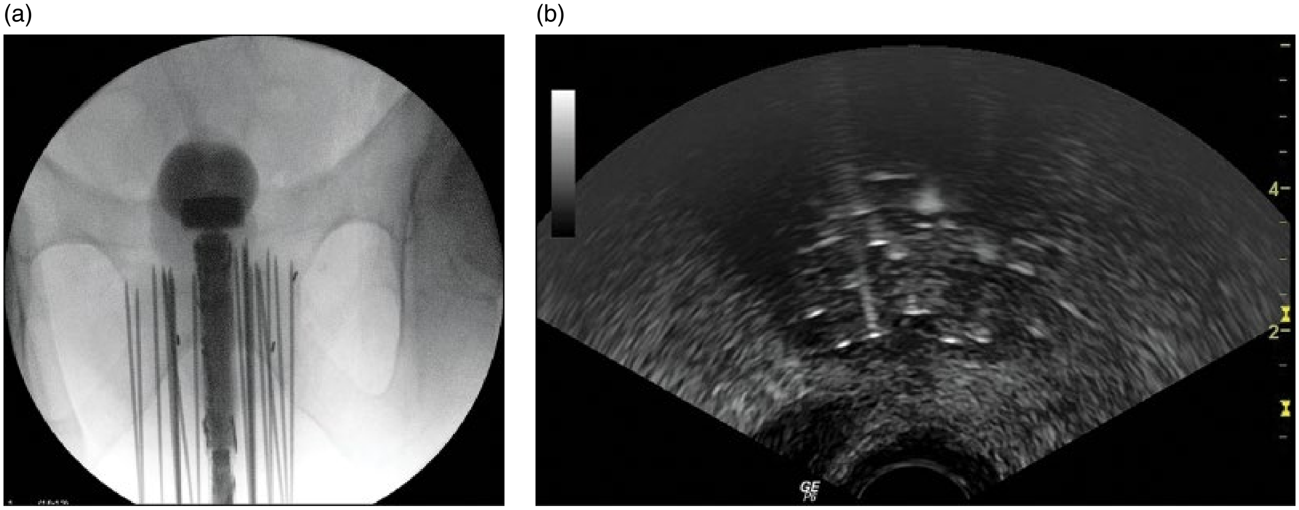

**Figure 133.4** Implanted needles in the prostate gland visualized on (a) fluoroscopic and (b) ultrasound imaging.

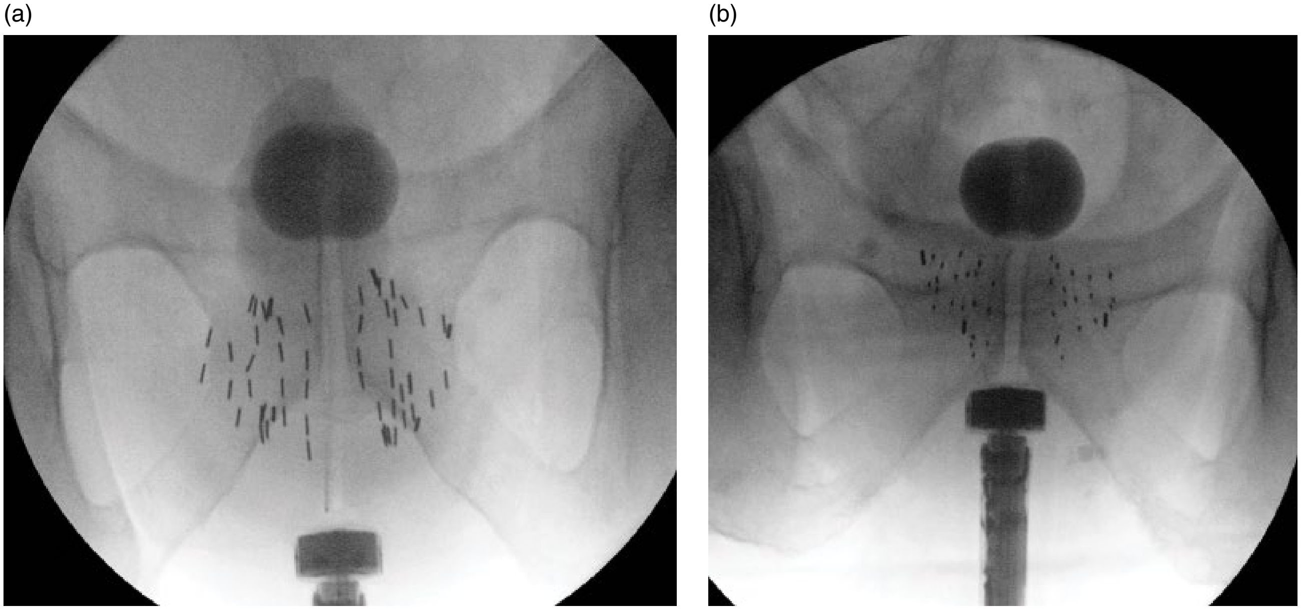

**Figure 133.5** Postprocedure fluoroscopic images of implanted seeds: (a) $^{125}$I implant; (b) $^{103}$Pd implant.

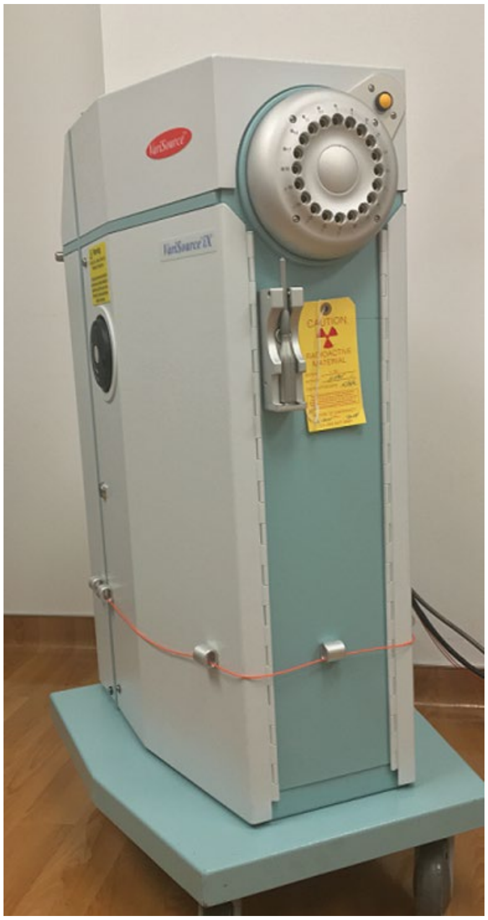

Figure 133.6 Typical afterloader used in high dose rate brachytherapy procedures (Varian Varisource IX afterloader, Varian Inc.).

$^{125}$I emits photons from electron capture decay (half-life ($T_{½}$) of 59.4 days) with energies ranging from 27.4 to 35.5 keV, as well as lower energies resulting from interaction with the seed materials (average energy 27.4 keV). Palladium-103 ($^{103}$Pd) was introduced in 1986. $^{103}$Pd decays in the same manner as $^{125}$I but with a shorter half-life ($T_{½}$ of 17 days), emitting photons with energies of 20.1 and 23 keV. Cesium-131 ($^{131}$Cs) was introduced in 2004 for permanent prostate brachytherapy. $^{131}$Cs has the shortest half-life of the standard commercially available radionuclides ($T_{½}$ of 9.7 days) with photon energies ranging from 29.5 to 34.4 keV (average energy 30.4 keV), similar to $^{125}$I. This allows dose delivery over a shorter overall time interval, thus limiting the period during which patients must follow radiation safety precautions [19, 21].

It has been hypothesized that a more rapid rate of dose delivery would result in a greater activity against high-grade tumors due to their faster doubling time [41], but this has not been borne out in multiple studies. In a prospective randomized trial comparing $^{125}$I versus $^{103}$Pd implants by Wallner et al. [42] there was no difference in 3-year actuarial biochemical control rates for patients with low-risk prostate cancer. In a more recent study by Kollmeier et al. that included patients with low-, intermediate-, and high-risk localized prostate cancer [43], no differences were noted in long-term genitourinary or gastrointestinal toxicity or 5-year biochemical relapse-free survival for patients treated with $^{125}$I versus $^{103}$Pd implants. The "strength" of the source, measured by its activity, may play a role; in a randomized trial by Narayana et al. [44] higher strength $^{125}$I implants were found to have improved dosimetric coverage at a lower overall seed cost, with shorter operating room times; the study was not designed to assess long-term toxicity or clinical outcome.

### Pre- and intraoperative planning and treatment delivery for LDR brachytherapy

As optimal dosimetry requires placement of seeds in a distribution that provides optimal coverage of the prostate gland while reducing dose to critical nearby structures (urethra, bladder/bladder neck, and rectum), careful planning is required to determine appropriate seed placement. This can be done in advance of the actual operative procedure (preplanning) or on the same day of the procedure (intraoperative planning) [45]. In general, patients undergo a gentle bowel preparation prior to the day of their planning procedure with Fleet's enemas or laxatives; patients undergoing both planning and treatment on the same day following an intraoperative protocol require a more thorough bowel preparation such as HalfLytely. Percutaneous brachytherapy treatment planning is performed by placing the patient in extended lithotomy position, and introducing the TRUS probe into the rectum (Figure 133.3). The prostate and surrounding organ anatomy is surveyed to identify possible issues during treatment, such as pubic arch interference (see, for example, Figure 133.2), which would interfere with anterior needle placement; this can also be assessed in part by prior cross-sectional (CT or MRI) imaging [46]. The "volume study" used to generate the plan is constructed by acquiring consecutive axial ultrasound images at 5 mm intervals from the base of the prostate to the apex, with a superimposed and calibrated template on each image. Longitudinal images are also acquired to ensure that no axial slices were missed and to verify the base to apex length measurement [21] (Figure 133.7).

The preplanning approach generally calls for linked or stranded seeds to be placed based on an implant plan generated from the TRUS-based "volume study" acquired prior to the actual procedure date, although a preplan can also be used to generate a manual/individually placed seed distribution. One advantage of techniques using

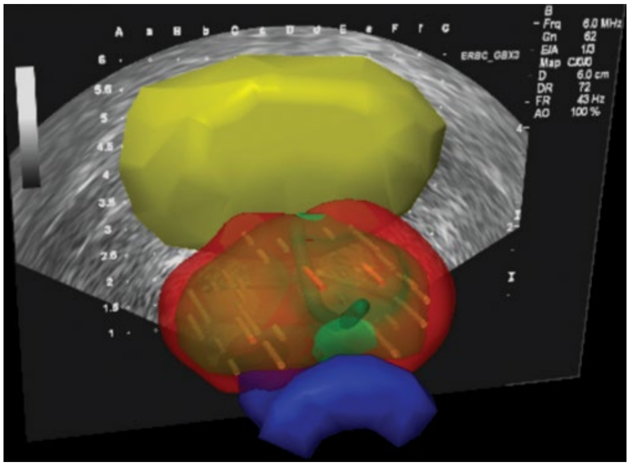

**Figure 133.7** Three-dimensional reconstruction of prostate volume study. Bladder depicted in yellow, prostate in light green, urethra in dark green, and rectum in blue. The prostate is encompassed by a dose cloud in red generated by the implanted seeds.

stranded seeds is that the seeds are much less likely to migrate from their planned positions within and around the prostate; this has been evaluated in a prospective trial by Reed et al. [47] in which they compared two groups of patients; one group used seeds held in a #1 Vicryl strand, and the other used loose seeds. They did not identify a significant dosimetric difference between the two approaches, although there was significantly more seed loss in the loose seed cohort. It is unclear if this seed loss is clinically significant. Saibishkumar et al. also studied the clinical impact of the stranded versus loose seed approach [48] and found that the use of stranded seeds increased unfavorable dosimetric parameters for the rectum and urethra, and resulted in a trend towards increased acute toxicity rate.

Intraoperative planning, in comparison, is performed at the time of the implant, and accounts for patient anatomy in the anesthetized state; this process can be done both prior to needle placement [49] or after the needles are placed [45]. While many variations exist for this form of treatment, plans performed prior to needle placement generally utilize preloaded seeds and spacers or stranded seeds, whereas plans generated after needle placement utilize an applicator (such as the Mick Applicator shown in Figure 133.8, Mick Radio-Nuclear Instruments Inc., now an Eckert & Zigler BEBIG Company, Mount Vernon, NY, USA) that allows individual, manual seed placement according to the plan under direct real-time ultrasound visualization. Both techniques have been evaluated against preplanned seed placement. Shah et al. compared preplanned brachytherapy against intraoperative, pre-needle plans and found that the intraoperative plans provided superior dosimetric and biochemical control outcomes [49]. Zelefsky et al. compared preplanned brachytherapy against intraoperative 3D optimized plans following needle placement and found that the intraoperative technique improved both target coverage as well as reducing dose to the urethra and rectal wall [45]. Investigators have also incorporated a “dynamic-adaptive” planning approach that takes into account the contribution of each manually placed seed as the procedure is performed, allowing for intraoperative modification of treatment to reduce the risk of a suboptimal plan [50].

### LDR prostate brachytherapy implant quality assessment

Clinical outcomes following brachytherapy administration have been shown to be strongly related to the quality of the implant. This assessment of quality is performed following implant administration in the setting of LDR brachytherapy with 3D imaging of the prostate

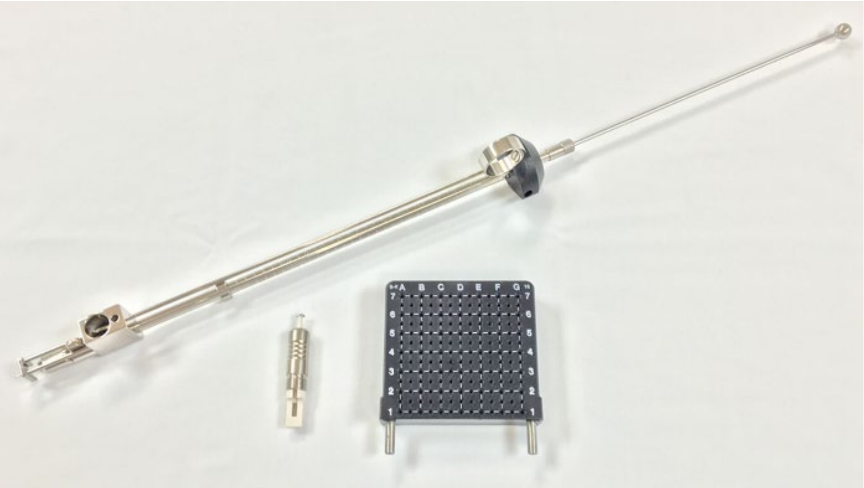

**Figure 133.8** Mick applicator, seed cartridges, and needle placement template grid.

performed at a set time point after treatment; generally 30 days of $^{125}$I implants, although earlier assessments may also be performed (especially for $^{103}$Pd and $^{131}$Cs, with their more rapid decay). Multicenter pooled studies have been performed to evaluate the prognostic impact of post-implant dosimetry on ultimate outcome. In a report by Stone et al. [51], data from 3928 permanent brachytherapy implants at six institutions was analyzed, and doses of ≥140 Gy were correlated with improved biochemical control. The dose to the prostate is assessed in terms of the minimum dose delivered to 90% of the prostate volume ($D_{90}$) as measured on CT imaging [52]. Another multi-institutional analysis of patients with T1–T2 prostate cancer treated with permanent seed implantation corroborated this conclusion, showing that $D_{90} < 130$ Gy was associated with increased risk of biochemical recurrence [53]. Other target dosimetric parameters often assessed include the prostate volume receiving 100% of the prescribed dose ($V_{100}$) and the prostate volume receiving 150% of the prescribed dose ($V_{150}$) [22, 23].

## High dose rate temporary prostate brachytherapy

Although permanent interstitial brachytherapy with radioactive seeds has been a standard treatment for localized prostate cancer for decades, HDR brachytherapy, using a temporary source introduced using a remote afterloader, is a much more recent advance (see Figure 133.5). HDR brachytherapy is defined as the delivery of radiation at a dose rate of >12 Gy per hour [20]. The technique for HDR temporary prostate brachytherapy is similar to that of LDR brachytherapy performed with intraoperative planning; needle implantation is performed with an anesthetized patient in extended lithotomy position under TRUS guidance. Treatment needles can be placed directly, or "pathfinder" needles may be placed and then replaced with flexible plastic guide catheters. The treatment needles or guide catheters are held in place with a template locked and sutured to the perineum. In some institutions, they may be held in place by a rigid foam or dental sealant. Flexible cystoscopy is generally performed to ensure that the treatment needles/catheters are not inserted into the urethra or through the bladder wall. Imaging is then acquired for treatment planning (ultrasound, CT, or MRI), and a computer-optimized treatment plan is generated (Figure 133.9). The remote afterloader is then attached to the needles or catheters and treatment is delivered; the implant can then be removed or left in place if additional fractions are planned [54].

HDR brachytherapy may offer many advantages over LDR brachytherapy, including increased likelihood of tumor control due to the high biological effectiveness of high-dose fractions (assuming a low α/β ratio for prostate cancer), data suggesting reduced rates of acute and late toxicity relative to permanent seed implantation [55], improved conformality of dose to the prostate (potentially superior to SABR/SBRT [56]), and no permanent radiation sources within the prostate (reducing radiation safety concerns from dose delivery to the patient's family and associates) [57].

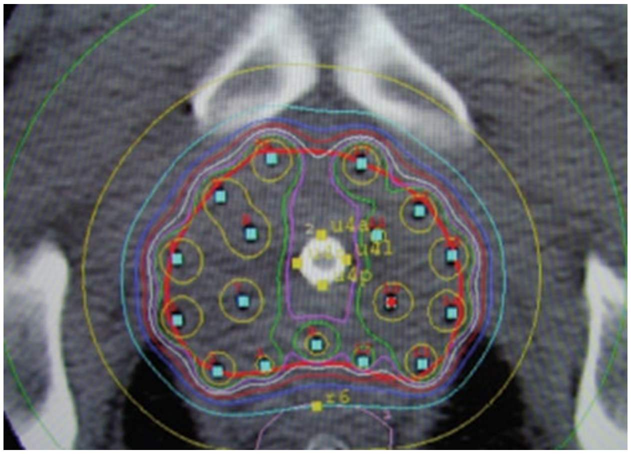

**Figure 133.9** High dose rate prostate implant plan; 17 needles placed. Foley catheter in place in center.

Both the ABS [20] and the American College of Radiology (ACR) have provided guidelines (appropriateness criteria) for the use of HDR brachytherapy in the management of prostate cancer [58]. In terms of patient selection, the ABS recommendations are similar to those for LDR brachytherapy, although an additional absolute contraindication was added for preexisting rectal fistula.

## Salvage brachytherapy

Brachytherapy is a reasonable option as salvage treatment for locally recurrent prostate cancer initially treated with EBRT. Because brachytherapy delivers highly conformal therapy, bladder, and in particular urethral and rectal doses can be stringently minimized while high doses can be given to tumor-bearing prostate tissue, making brachytherapy an excellent treatment option for patients who have failed EBRT. Both LDR and HDR techniques have been reported for the salvage of local radiation failures.

Burri et al. [59] reported the results of salvage LDR brachytherapy in 37 patients with a median follow-up of 86 months. A median dose of 140 Gy was administered. The 5-year and 10-year biochemical relapse-free survival was found to be 65% and 54%, respectively.

Grade 3–4 toxicity was noted in 11% of patients, including one patient who developed a rectal fistula. A Phase II study of salvage LDR brachytherapy has completed accrual. HDR brachytherapy has also been used successfully in the salvage setting. In a Phase II trial from Memorial Sloan Kettering Cancer Center, 42 patients who had local recurrence underwent whole-gland HDR brachytherapy, receiving 800 cGy × 4 in one insertion over two days. The actuarial biochemical relapse-free survival probability was found to be 70% at 5 years. Rectal toxicity was minor, and patients demonstrated worse urinary symptoms after salvage HDR, with 20% probability of developing a grade 2 event [60].

## Combination therapy (use of both brachytherapy and EBRT)

The limited penetration of therapeutic dose beyond the prostate capsule by low-energy photon brachytherapy sources may be limiting in patients with risk for significant extraprostatic disease extension. Conversely, for these high-risk patients, EBRT alone has been associated with a significant failure rate, which is reduced by the addition of long-term ADT [61–63] and radiotherapy dose escalation [64–66]. Even with contemporary dose-escalated EBRT, a meta-analysis suggests that plateau of benefit has not yet been reached [67], and the requirement for long-term ADT persists, as demonstrated by the DART 01/05 trial [68]. Supplementation of brachytherapy with EBRT, or "combination therapy," is argued to retain the unique intraprostatic dose escalation of brachytherapy while improving extraprostatic coverage. The dose of supplemental EBRT, sequencing of treatment, and choice of LDR or HDR is largely set by institutional preferences in the absence of strong comparative data.

For EBRT dose, while one randomized trial from a high-volume group found no difference between 44 Gy EBRT + 90 Gy $^{103}$Pd boost versus 20 Gy EBRT + 115 Gy $^{103}$Pd boost [69], few high-grade or locally advanced patients were included, and the excellent biochemical control of 93% at 10 years is a testament both to a likely more favorable risk population than is the primary beneficiary of combination therapy and that group's expertise. In general, many still use 40–50 Gy of supplemental EBRT dose.

With regard to sequencing of the implant, those who use brachytherapy first before EBRT, such as the authors of this review, cite the potential benefits of (i) minimizing pre-implant urinary symptoms/swelling to reduce risk of acute urinary obstruction and (ii) allowing supplemental EBRT to address deficiencies in the implant dosimetry. For LDR implants in this sequence, $^{103}$Pd is favored for its shorter half-life in order to minimize overlap in dose delivery with EBRT, initiated four weeks after the implant. Other institutions, such as UCSF, and contemporary NRG/Radiation Therapy Oncology Group (RTOG) protocols (i.e. RTOG 0924) prescribe brachytherapy boosts about four weeks after completion of EBRT. A Phase II randomized feasibility study of HDR brachytherapy before or after EBRT for combination therapy in high-risk prostate cancer patients is ongoing in the United Kingdom [70], in an attempt to address this question.

The choice of LDR or HDR for the brachytherapy similarly remains subject to institutional preference, as well as tradeoffs in their relative strengths as discussed elsewhere in this review. The ACS-ABR 2015 practice parameter on permanent LDR implant notes typical $^{103}$Pd dose of 80–110 Gy and $^{125}$I dose of 100–110 Gy when given in conjunction with EBRT, with the recommendation to consider the resultant biologically effective dose (BED) as delineated by investigators at Mt. Sinai [71, 72]. Constraints on organs at risk are largely institution dependent but should consider urethra and rectal dose most prominently and according to an institutional standard. The literature on HDR EBRT regimens is even more varied, with institutional preference again dominating choice but perhaps an overall trend towards fewer fractions to take advantage of the theorized low $\alpha/\beta$ ratio rationale for hypofractionation, as reviewed by Morton and Hoskin [73] and noted in the 2012 ABS practice parameter statement on HDR brachytherapy [20]. Common approaches include 7 Gy × 3, 10.5 Gy × 2, 15 Gy × 1, and constraints vary strongly according to regimen published.

## Prostate brachytherapy dose selection and organ-at-risk constraints

When developing a prostate brachytherapy treatment plan, multiple considerations are involved, both in terms of appropriate coverage of the target organ (the prostate), and how best to protect proximal structures (organs at risk, or OARs) such as the urethra, bladder, and rectum. Guidelines have been provided by the ABS based on review of the available literature, clinical trials, and the experience of designated committees for both LDR and HDR brachytherapy [19, 20]. The NCCN also provides some guidance with respect to appropriate dose prescriptions and utilization [2].

In terms of LDR prostate brachytherapy, ABS recommends prescribed doses for LDR monotherapy of 140–160 Gy for $^{125}$I and 110–125 Gy for $^{103}$Pd implants. When administering combination therapy with EBRT (41.4–50.4 Gy given in 1.8 Gy per fraction), these doses are reduced to 108–110 Gy for $^{125}$I and 90–100 Gy for $^{103}$Pd implants [19]. According to NCCN guidelines, the recommended prescribed doses for LDR monotherapy are 145 Gy for $^{125}$I and 125 Gy for $^{103}$Pd implants. When administering combination therapy with EBRT (generally 40–50 Gy given at 1.8–2 Gy per fraction), these doses are reduced to 110 Gy for $^{125}$I and 90–100 Gy for $^{103}$Pd implants [2]. According to ABS recommendations, OAR constraints are provided for the urethra and rectum; for the urethra, the goal is to keep the percent volume of the urethra receiving 150% of the prescription dose ($UV_{150}$) to <5% (effectively a point maximum given the small volume of the urethra), and the percent volume of the urethra receiving 125% of the prescription dose ($UV_{125}$) to <30%; for the rectum, the goal is to keep the volume of rectal wall receiving 100% of the prescription dose ($RV_{100}$) to <1 cm$^3$ on the preplan and <1 cm$^3$ on post-implant dosimetry.

For HDR prostate brachytherapy, given the flexibility of dose administration, a wide range of dose and fractionation regimens are possible, with monotherapy treatment delivered in 1–6 fractions (from single-fraction doses as high as 24 Gy in a single fraction to six fraction treatments of 6.5–7.25 Gy per fraction), and boost treatments (with external beam doses of 41.4–50.4 Gy given in 1.8 Gy per fraction) ranging from 15 Gy in one fraction to four fractions of 6 Gy per fraction. According to NCCN guidelines, HDR brachytherapy can be performed as monotherapy or in combination with EBRT; for monotherapy, two fractions of 13.5 Gy each is proposed, and when combined with EBRT (again, generally 40–50 Gy given at 1.8–2 Gy per fraction), two fractions of 9.5–11.5 Gy per fraction, three fractions of 5.5–7.5 Gy per fraction, or four fractions of 4–6 Gy per fraction are appropriate [2]. According to ABS recommendations, OAR constraints for urethra, rectum, and bladder are deferred to those used at experienced centers; the maximum urethral dose is generally kept to less than 110–130% of the prescription dose, and the dose to 1–2 cm$^3$ of the bladder and rectum are kept to less than 70–80% of the prescription dose [20].

Although these constraints are useful in planning appropriate treatment for prostate cancer with brachytherapy, continuous evaluation of the impact of dose to organ substructures is ongoing, as a dose measurement to the urethra as a whole may not be as relevant as the dose to an organ subunit. Due to the preponderance of genitourinary toxicities in prostate brachytherapy, areas of particular interest are the bladder neck and the bladder trigone; a study by Hathout et al. [74] investigated the impact of dose to the bladder neck, defined as the region 5 mm around the catheter-defined urethra between the catheter balloon and the prostatic urethra, and identified that patients receiving >50% of the prescription dose to 2 cm$^3$ of the bladder neck were at higher risk of developing ≥ grade 2 acute and late genitourinary toxicity.

## Results of prostate brachytherapy treatment

### LDR prostate brachytherapy outcomes

Prostate brachytherapy has mature longitudinal outcome data and has been shown to be a highly effective therapy. Attempts to compare prostate brachytherapy as monotherapy to radical prostatectomy in a prospective randomized trial was attempted in the Alliance for Clinical Trials in Oncology (ACOSOG Z0070) (Surgical Prostatectomy Versus Interstitial Radiation Intervention Trial (SPIRIT)) trial, but it was closed early due to non-accrual, having enrolled only 56 of a planned 1980 patients [75, 76]. Comparison studies using biochemical (PSA) surrogates suggest that prostate brachytherapy is at least equivalent to radical prostatectomy and possibly superior to EBRT. There is no clear role at this time for the addition of ADT to LDR prostate brachytherapy when used as monotherapy for the treatment of low- or intermediate-risk prostate cancer.

Potters et al. [77] reported on their experience with prostate brachytherapy in 1449 patients with Gleason 6–7 prostate cancer, showing an overall 12-year biochemical freedom from recurrence (BFR) using the ASTRO-Kattan definition of 78%; for low-risk patients, 12-year BFR was 89%. Grimm et al. [78] reported a PSA progression-free survival at 10 years of 87% for low-risk patients (PSA <10, Gleason score ≤6, cT1–T2b). Multi-institutional outcomes were reported by Zelefsky et al. [53] with pooled data from 11 institutions for 2693 patients with non-metastatic T1–T2 prostate cancer (including patients with Gleason scores up to 10, no PSA limit) treated with brachytherapy monotherapy. The 8-year biochemical relapse-free survival according to the ASTRO definition was 82%, 79%, and 48%, respectively, for low-, intermediate-, and high-risk patients. Notably, they found that for all patients with quality implants (where the dose to at least 90% of the prostate, or $D_{90}$, was ≥130 Gy), the 8-year biochemical relapse-free survival was 93%, compared to 76% for those with poor-quality implants. For patients ≤60 years of age with clinically localized low- or intermediate-risk prostate cancer, Kollmeier et al. [79] reported 8-year biochemical relapse-free survival outcomes of 97% for low-risk patients and 94% for intermediate-risk patients; of those potent prior to treatment, erectile function was preserved in >50% of patients and the majority (66%) did not require erectile dysfunction medication.

In a prospective Phase II trial conducted by Lawton et al. (RTOG Study 98-05) [80] designed in part to test the portability of ultrasound-guided prostate brachytherapy to the community setting (rather than specialized centers only), 101 patients from 27 institutions were treated with $^{125}$I permanent interstitial brachytherapy. Patients had T1b–T2a disease, and most (88%) had Gleason 6(3 + 3) disease with a median PSA of 5.9 ng/ml. With a median follow-up of 8.1 years, there were no prostate cancer-specific deaths, and the cumulative incidence of biochemical failure was only 8%. Incidence of grade 3 toxicity was 3.2% (all genitourinary), and there were no higher grade toxicities. This compared favorably to surgical series such as the Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) trial reported by Bill-Axelson et al. [81], where ADT intervention was performed in over 20% of patients at 8 years, and in a large cohort of 1055 patients with cT1–3a NxM0 cancer treated with radical prostatectomy reported by Kattan et al. [82] biochemical failure at 8 years was approximately 30%.

## HDR prostate brachytherapy outcomes

HDR prostate brachytherapy does not have as long a track record as LDR prostate brachytherapy, but has been heavily investigated with prospective trials. Yoshioka et al. [18] first reported the favorable results of HDR brachytherapy as monotherapy for patients with localized prostate cancer in 2000 (including all T-stages). With a median follow-up of 5.4 years, the 5-year biochemical relapse-free rate was 83%.

Subsequently, five prospective Phase I/II trials of HDR monotherapy with promising results have been published [55, 57, 83–85]. Martinez et al. [83] treated 41 patients with Gleason 6–7 disease with PSA ≤10 and T-stage ≤ cT2a, with 38 Gy in four fractions, which was well tolerated. Corner et al. [84] reported on 100 patients with locally advanced prostate cancer (T-stage ≤ T3b, PSA <40, N0/M0), who received escalating doses from 34 Gy in four fractions to 31.5 Gy in three fractions; no biochemical recurrences were observed, albeit with median follow-up of no more than 30 months. Ghilezan et al. [86] reported on 94 patients with T-stage ≤ cT2b, Gleason 6–7 prostate cancer with PSA ≤12, who received 24–27 Gy in two fractions. Treatment was well tolerated with no > grade 2 genitourinary or gastrointestinal toxicities. Zamboglou et al. [87] reported on 718 patients with localized prostate cancer (low-, intermediate-, and high-risk patients were eligible) treated with 34.5–38 Gy in 3–4 fractions. Eight-year biochemical control for the entire cohort was 90%; at 5 years, biochemical control was 95%, 93%, and 93%, respectively, for low-, intermediate-, and high-risk patients. Hauswald et al. [88] reported long-term outcomes for 448 patients with low- and intermediate-risk prostate cancer treated with 42–43.5 Gy in six fractions. At 10 years, biochemical progression-free survival was 98.9% and 95.2% for low- and intermediate-risk patients, respectively.

More recently, Prada et al. [89] reported the first single-fraction HDR monotherapy data, in which 40 patients with favorable clinically localized prostate cancer were treated with a single fraction of 19 Gy. To reduce the risk of rectal toxicity, a transperineal injection of hyaluronic acid into perirectal fat to increase the distance between the prostate and rectum was performed prior to treatment [90]. The 32-month actuarial biochemical control was 100% and 88%, respectively, for low- and intermediate-risk groups with no ≥ grade 2 gastrointestinal or genitourinary toxicity. HDR prostate brachytherapy has proven to be a highly effective and well-tolerated treatment modality across the prostate cancer spectrum, and increased utilization is expected. There is no clear role at this time for the addition of ADT to HDR prostate brachytherapy when used as monotherapy for the treatment of low- or intermediate-risk prostate cancer.

## Combination brachytherapy and EBRT outcomes and patient selection

Patient selection for combination therapy follows the same technical considerations for monotherapy; however, what level of disease risk requires combination therapy remains debated. Although there is consensus on adding supplemental EBRT to brachytherapy for high-risk disease, it is less clear when combination therapy is beneficial in intermediate-risk patients, compared to either EBRT alone or brachytherapy alone. The randomized Phase III trial RTOG 0232 in intermediate-risk patients comparing combination EBRT/brachytherapy versus brachytherapy alone is closed and its pending report upon maturation of follow-up will offer critical data. In the interim, given the good prognosis of "favorable" intermediate-risk patients [33], the benefit of combination therapy in intermediate-risk patients is likely most appreciable in those with multiple risk features. In this context, while an early study by Blasko et al. [91] found no benefit to combination therapy versus brachytherapy alone (5-year biochemical relapse 15% vs. 16%), it is quite possible that its retrospective design contains residual confounders from initial treatment selection that obscure true differences in a subgroup of patients.

In a similar vein, two older studies randomized intermediate/high-risk patients to EBRT with or without brachytherapy and found reduced biochemical relapse, but these used definitive EBRT doses (55–66 Gy) now considered subtherapeutic. Since that time, select primarily single-institution retrospective studies have demonstrated improved relapse-free survival or positive biopsy reduction with combination EBRT and brachytherapy [92, 93], even translating into reduction of distant metastasis risk in a series from Memorial Sloan Kettering Cancer Center of intermediate-risk patients [94] and in a multi-institution comparison of Gleason 9–10 patients undergoing combination therapy versus EBRT versus prostatectomy [95]. Perhaps the most convincing argument in favor of the benefit of combination brachytherapy and EBRT for treatment of prostate cancer has come from the abstract presentation of the ASCENDE-RT Phase III trial, which randomized 276 high-risk (69%) and 122 intermediate-risk (31%) patients to EBRT alone (78 Gy total) versus EBRT (46 Gy) and LDR brachytherapy boost (115 Gy $^{125}$I) following a year of ADT [96]. With median follow-up of 6.5 years, there was a significant reduction in biochemical relapse (7 years 71% vs. 86%), at the cost of increased acute and late urinary toxicities. As it remains the case that no prospective randomized study in prostate cancer has yet demonstrated a metastasis risk reduction or survival benefit to dose escalation of radiotherapy, many are eagerly awaiting the long-term data of this study required for evaluation of such clinical endpoints.

## Toxicity and quality of life

Due to the close proximity of critical structures such as the urethra, bladder, and rectum, some toxicity from brachytherapy is unavoidable. Although high-grade toxicity is low, even grade 2 toxicity may significantly affect patient quality of life, and informed consent of the risks and benefits of treatment must be obtained from the patient. A prospective quality-of-life (QOL) study for patients undergoing radical prostatectomy, brachytherapy, or EBRT for prostate cancer was reported by Sanda et al. in 2008 [97]. Patients receiving brachytherapy had better performance in the sexual domain than surgery or EBRT, but were noted to have worse performance in urinary domains (irritation, obstruction) than other treatment modalities. A prospective cohort study of 704 patients with low- and intermediate-risk prostate cancer treated with radical prostatectomy, EBRT, or brachytherapy was reported by Ferrer et al. in 2013 [98]. In their study they also showed that prostate brachytherapy had increased irritative/obstructive complaints relative to EBRT and surgery, but had the least impact on sexual function and bowel complaints. The relative benefit of brachytherapy compared to other treatment modalities in terms or retained sexual function continues to be borne out in recent studies [99].

Keyes et al. [100] reported on a group of 2011 patients with NCCN low- and low- to intermediate-risk prostate cancer treated with $^{125}$I LDR brachytherapy, with a minimum follow-up of 25 months (median 54.5 months), who had been followed with prospective assessment of treatment quality and genitourinary toxicity. Late RTOG grade 0, 1, 2, 3, and 4 toxicity was seen in 70%, 21%, 6.4%, 2.3%, and 0.08% of patients, respectively. QOL assessments were also performed on the RTOG 98-05 study reported by Feigenberg et al. [101] demonstrating an overall very good heath-related QOL following prostate brachytherapy, with transient increases in urinary incontinence to 14% at six months, decreasing to 1% at 1 year, and decrease in ability to achieve erection from 73% at baseline to 57% at 1 year.

## Comparative effectiveness and value

In 2008, the Institute for Clinical and Economic Review (ICER) released their final appraisal of prostate brachytherapy versus intensity-modulated EBRT or proton beam therapy [102]. Based on an analysis of 166 studies, they found that prostate brachytherapy carried the lowest lifetime cost (US$29 575 for brachytherapy, US$41 591 for intensity-modulated EBRT, and US$72 789 for proton beam therapy), although there was relatively little difference in quality-adjusted life years (QALYs) (13.9 for brachytherapy, 13.81 for intensity-modulated EBRT, and 13.7 for proton beam therapy).

This benefit may be maintained against nonradiation treatment modalities as well. Hayes et al. [103] conducted a cost-effectiveness analysis for observation versus initial treatment in patients with low-risk prostate cancer using Medicare scales; treatments included brachytherapy, intensity-modulated EBRT, and radical prostatectomy. Although they found observation to be more cost-effective than initial treatment, for patients who did proceed to treatment, prostate brachytherapy was the most effective and least expensive initial therapy. The base-case average lifetime costs for patients aged 65 were US$24 520 for watchful waiting, US$35 374 for prostate brachytherapy, US$38 180 for radical prostatectomy, US$39 894 for active surveillance, and US$48 699 for intensity-modulated EBRT. A French multicenter study was conducted by Buron et al., comparing prostate brachytherapy to prostatectomy [104]; this study used the validated EORTC Quality of Life Questionnaire (QLQ) as well as comparative cost analysis. They found that the two treatments were similar in cost at 2 years (8019 euros for brachytherapy vs. 8715 euros for prostatectomy), and that QOL measures were acutely worse in prostatectomy, but slightly better long term. A nationwide charge comparison in the United States of the costs associated with the treatment of early-stage prostate cancer has shown that brachytherapy administered as monotherapy is associated with the lowest costs compared with radical prostatectomy alone, EBRT alone, and any combination of treatment modalities [105, 106]. In particular, significant cost benefits have been noted in comparison to the use of intensity-modulated EBRT [107].

## Conclusions

In this chapter, we have discussed the history, technical aspects, outcomes, and cost-effectiveness of LDR and HDR brachytherapy approaches in the management of prostate cancer. Prostate brachytherapy has been shown to be an effective treatment for localized prostate cancer, with high-quality long-term outcomes data. Given the relatively favorable prognosis of men with prostate cancer and the wide range of treatment modalities available to treat them, careful patient selection and frank discussion of the relative risks and benefits of available therapy is critical. For patients who choose radiation-based management of their prostate cancer and meet eligibility criteria, brachytherapy should be the primary treatment modality offered given the significant cost-effectiveness advantage over external beam approaches.

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## 134

# Image-guided External Beam Radiotherapy

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## Introduction

External beam radiotherapy (EBRT) has been revolutionized by incorporating modern imaging technologies to precisely deliver radiation. In combination with advanced radiation planning techniques such as intensity-modulated radiation therapy (IMRT) and arc therapy, image-guided radiation therapy (IGRT) allows for high radiation doses to be delivered to the tumor while sparing adjacent normal tissues. Recent advances in the delivery of radiation therapy include harnessing the advances in diagnostic imaging modalities and incorporating them into the planning and delivery of treatment. Examples include computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). In addition, modern computer technology has made it easier to incorporate an increasing number of customized beams and tumor-tracking technologies during radiotherapy delivery, which allows the radiation dose to be further concentrated in the area of interest. The advent of these high-quality imaging techniques coupled with the use of computerized treatment delivery systems have enhanced the accuracy of delivering radiation dose to a target to within millimeters and are the hallmarks of IMRT, stereotactic body radiotherapy (SBRT), and stereotactic radiosurgery (SRS).

Decades ago, traditional radiation treatments used wide margins to accommodate potential movement or other spatial uncertainties during a treatment course. Doses often had to be limited due to the exposure of radiosensitive nearby structures. With more precise image-guided treatments, the dose to a target structure can be increased while reducing the dose to a neighboring critical structure. Certain areas, such as the brain, are particularly amenable to these types of treatments because movement is minimal or can be easily controlled. Many other parts of the body are prone to movement with loss of subcentimeter accuracy with, for example, casual breathing. This respiratory motion is increasingly being accounted for in modern radiotherapy treatments. In addition, tumors can change, either shrinking or actually growing during the treatment course. These movements and changes result in reduced accuracy and either underdosing the target or overdosing nearby critical structures. Treatments can be replanned multiple times during a treatment course for a target that changes in size; this is a promising new technology referred to as image adaptive radiation therapy (IART). For targets that maintain the same size but are more prone to movement, various methods may be used to compensate for that movement.

IGRT is particularly useful for treatment of prostate cancer, where the target size is relatively stable but is prone to movement. IGRT allows for dose escalation, which has been shown to improve the outcome of radiation for localized prostate cancer. Despite higher doses, the increased accuracy allows for tighter margins to be used, resulting in low morbidity. This chapter details the use of IGRT for the treatment of prostate cancer.

## Prostate cancer

### Epidemiology

Prostate cancer is the most common cancer in males. In 2015, 220 800 cases were expected in the United States, with 27 540 expected deaths. Approximately 90% of cases are diagnosed in the locoregional stages, for which the 5-year relative survival approaches 100%. The recent decreases in annual incidence reflects, in part, the decreased rates of detection resulting from reduction in

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the widespread use of prostate specific antigen (PSA) screening that peaked in the 1980s and 1990s. Mortality has been declining since 1990 [1].

## Screening

The role of PSA screening in asymptomatic men remains controversial. In 2012 the US Preventative Services Task Force issued a “D” recommendation for PSA screening [2], but several professional organizations, including the American Urological Association (AUA), continue to recommend PSA screening in selected populations [3]. These conflicting recommendations are due to differences in interpretation of the available evidence regarding the risks and benefits of PSA screening. Published randomized trials comparing the mortality outcomes of a screened group versus a nonscreened group demonstrated conflicting results [4, 5], but both studies suggested a high rate of overdetection and treatment. The AUA currently recommends patients between 55 and 69 years old be offered biennial screening in the context of shared decision-making. They recommended no screening for patients under 40 or over 69 years and concluded that there was not sufficient evidence to recommend screening in men aged 40–54 years. The core recommendation in the new AUA guideline is that men aged 55–69 be offered PSA-based screening for prostate cancer through a shared decision-making process that accounts for their values and preferences. The guideline states than men under 40 or over 69 years of age should not be screened, with the caveat that some men in their 70s with excellent life expectancy may benefit. The most significant reversal from the 2009 best practice statement is that the guideline does not recommend routine screening for men aged 40–54. Any consideration of PSA screening should be in the context of an informed discussion of the risks and benefits of prostate cancer screening prior to biopsy and allowing full consideration of the option of active surveillance instead of treatment for certain patients found to have prostate cancer [3].

## Risk stratification

Once the diagnosis of prostate cancer is made, an appropriate staging workup ensues in order to provide additional prognostic information for risk stratification, which may assist in management decisions. The National Comprehensive Cancer Network (NCCN) Version 3.2016 provides recurrence risk stratification among patients with clinically localized disease based on PSA level, Gleason score, clinical stage, and biopsy specifics (Table 134.1). The American Joint Committee on Cancer (AJCC) incorporates PSA and Gleason score into a stage/prognostic group system (Table 134.2), while the TNM

**Table 134.1** Prostate cancer recurrence risk according to the National Comprehensive Cancer Network (NCCN) Practice Guideline in Oncology 3.2016.

| | |
|---|---|
| Very low | T1c |
| | Gleason < 6 |
| | PSA < 10 ng/ml |
| | <3 positive cores |
| | PSA density < 0.15 ng/ml/g |
| | <50% cancer in each core |
| Low | T1–2a |
| | Gleason 2–6 |
| | PSA < 10 ng/ml |
| Intermediate | T2b–T2c or |
| | Gleason 7 or |
| | PSA 10–20 ng/ml |
| High | T3a or |
| | Gleason 8–10 or |
| | PSA > 20 ng/ml |
| Very high | T3b–T4 or |
| | Primary Gleason pattern 5 or |
| | >4 cores with Gleason score 8–10 |

**Table 134.2** Prostate cancer anatomic stage/prognostic group according to the American Joint Committee on Cancer Prostate Cancer.

| Group | T | N | M | PSA | Gleason |
|---|---|---|---|---|---|
| I | T1a–c | N0 | M0 | PSA < 10 | Gleason ≤ 6 |
| | T2a | N0 | M0 | PSA < 10 | Gleason ≤ 6 |
| | T1–2a | N0 | M0 | PSA X | Gleason X |
| IIA | T1a–c | N0 | M0 | PSA < 20 | Gleason 7 |
| | T1a–c | N0 | M0 | PSA ≥ 10– < 20 | Gleason ≤ 6 |
| | T2a | N0 | M0 | PSA < 20 | Gleason ≤ 7 |
| | T2b | N0 | M0 | PSA < 20 | Gleason ≤ 7 |
| | T2b | N0 | M0 | PSA X | Gleason X |
| IIB | T2c | N0 | M0 | PSA Any | Gleason Any |
| | T1–2 | N0 | M0 | PSA ≥ 20 | Gleason Any |
| | T1–2 | N0 | M0 | PSA Any | Gleason ≥ 8 |
| III | T3a–b | N0 | M0 | PSA Any | Gleason Any |
| IV | T4 | N0 | M0 | PSA Any | Gleason Any |
| | T Any | N1 | M0 | PSA Any | Gleason Any |
| | T Any | N Any | M1 | PSA Any | Gleason Any |

system for clinical and pathologic staging remains the same. A CT or pelvic MRI is recommended for patients with T3 and T4 disease and for patients with a nomogram indicated probability of lymph node involvement >10%. A bone scan is recommended for the following patients: T1 disease with PSA >20 ng/ml, T2 disease with a PSA >10 ng/ml, Gleason score 8 or higher, T3 disease, T4 disease, and patient with symptoms consistent with bony metastases.

## External beam radiation therapy for prostate cancer

### Patient selection

Patients with disease localized to the prostate without evidence of lymph node or distant metastasis may be candidates for definitive EBRT. There are relatively few general contraindications to the use of radiation therapy for treatment of definitive disease. These include prior treatment with pelvic radiation therapy and presence of active autoimmune disease, particularly scleroderma and lupus. Inflammatory bowel disease may be considered a relative contraindication for patients undergoing pelvic node irradiation, since treatment may be poorly tolerated [6, 7], but may be safe for patients undergoing treatment to the prostate alone [8]. Patients with low- or very low-risk group disease can be treated with either EBRT or brachytherapy. Patients with intermediate-risk disease can be treated with EBRT ± androgen-deprivation therapy (ADT) and ± brachytherapy or brachytherapy alone. Patients with high- and very high-risk group disease are treated with EBRT ± ADT ± docetaxel chemotherapy and ± brachytherapy.

#### Selecting patients for brachytherapy

When deciding whether or not to use brachytherapy, either alone or in combination with EBRT, it is useful to consider pretreatment urologic symptoms and prostate size. Acute urologic symptoms may also be more severe with brachytherapy, which makes it less ideal for patients with significant symptoms of benign prostatic hypertrophy (BPH) and those with large glands, the general cutoff being 50–60 ml. Urinary symptoms are commonly rated using the AUA International Prostate Symptom Score (IPSS) (Table 134.3), which is the same at the BPH Symptom Score but with a quality-of-life (QOL) question added. The American Brachytherapy Society suggests that patients with IPSS >15–17 are not ideal candidates for brachytherapy [9]. A history of transurethral resection of the prostate (TURP) is a relative

**Table 134.3** International Prostate Symptom Score (IPSS).

| | Not at all | Less than 1 time in 5 | Less than half the time | About half the time | More than half the time | Almost always | |
|---|---|---|---|---|---|---|---|
| Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating? | 0 | 1 | 2 | 4 | 4 | 5 | |
| Over the past month, how often have you had to urinate again < 2 h after you finished urinating? | 0 | 1 | 2 | 4 | 4 | 5 | |
| Over the past month, how often have you found you stopped and started again several times when you urinated? | 0 | 1 | 2 | 4 | 4 | 5 | |
| Over the past month, how often have you had a weak stream? | 0 | 1 | 2 | 4 | 4 | 5 | |
| Over the past month, how often have you had to push or strain to begin urination? | 0 | 1 | 2 | 4 | 4 | 5 | |
| | **None** | **1 time** | **2 times** | **3 times** | **4 times** | **5 or more times** | |
| Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning? | 0 | 1 | 2 | 4 | 4 | 5 | |
| Total symptom score ________________ | | | | | | | |
| | **Delighted** | | | | | | **Terrible** |
| If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that? | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

contraindication to brachytherapy because of the increased risk of urethral toxicity, including incontinence, and poor dosimetry. Other factors that contribute to higher acute toxicity include a greater number of needles used to do the implant and the use of hormonal therapy [10].

### Combination external beam radiation therapy and brachytherapy

There are no high-quality published data to support either using EBRT alone or combination EBRT and brachytherapy in the treatment of intermediate- to high-risk prostate cancer. However, at the time of press, a large prospective, randomized Canadian trial, the ASCENDE-RT trial, has reported in abstract form that combination therapy with EBRT and brachytherapy offers superior biochemical control when compared to EBRT alone in patients with intermediate- and high-risk group prostate cancer when radiotherapy is given with androgen deprivation. In theory, the higher incidence of extracapsular extension and seminal vesicle invasion in intermediate- to high-risk patients is more adequately covered by EBRT than brachytherapy, which is the rationale for avoiding brachytherapy alone in these patients. On the other hand, certain intermediate-risk patients are likely to be candidates for brachytherapy alone. In a retrospective review of 668 brachytherapy patients, there was no statistically significant difference in the 8-year actuarial biochemical relapse-free survival (BRFS) between low- and intermediate-risk patients, 98.4% and 98.2%, respectively [11]. These data suggest that most intermediate-risk patients have a low risk of micrometastatic disease in the pelvis. Even though the risk of extracapsular disease is higher in these patients, these areas may be adequately covered by an implant, since most extracapsular disease is located within 5 mm of the prostate capsule [12]. In another series of combination therapy, where 63.4% of the intermediate-risk patients had 50% or more positive biopsy needle cores, there was an 80% 15-year BRFS [13]. These data suggest excellent long-term control with the combined approach. However, despite high control rates, the additional use of EBRT may be detrimental in terms of higher rates of morbidity. Therefore, additional pathologic factors, such as number or percentage of positive cores, may be helpful to determine whether or not a combination treatment should be used.

### Postprostatectomy external beam radiotherapy

Adjuvant or salvage EBRT is used in the postprostatectomy setting. Adjuvant radiation is given based on pathologic findings at surgery. In general, the indications for postprostatectomy adjuvant radiation therapy include: positive margins, seminal vesicle invasion, extracapsular extension, and detectable PSA. The European Association for Research and Treatment of Cancer (EORTC) 22911 prospective Phase III trial randomizing postprostatectomy patients with capsular penetration, positive margins, and/or seminal vesicle invasion to immediate radiation therapy of 60 Gy versus observation, showed an improvement in biochemical disease-free survival (BDFS) and disease progression, but no overall survival advantage. The 5-year progression-free survival was 74% for patients undergoing radiation therapy versus 52% undergoing observation. The 5-year rate of grade 3 urinary toxicity was 2.6% in the observation arm and 4.2% in the treatment arm ($P = 0.0726$). Similar findings were reported in a multi-institutional randomized clinical trial comparing adjuvant radiation therapy of 60–64 Gy to observation with a median follow-up of 10.5 years. The metastasis-free survival was 64.5% in the treated group versus 56.9% in the observation group ($P = 0.06$) [14]. More provocatively, the SWOG 8794 trial, with similar design, has demonstrated improvements in biochemical control, local control, distant metastases-free survival, and overall survival when immediate adjuvant radiotherapy is delivered for patients with pathologic T3 disease or positive margins [14].

Salvage radiation therapy is given when the patients experience a postsurgery biochemical recurrence. Salvage radiation has been shown to improve biochemical progression and early salvage radiation at low PSA levels is associated with improved BPFS and rates of distant metastases [15]. There are no trials comparing adjuvant and early salvage radiation therapy.

## Results

### Definition of biochemical failure

Results are generally reported by risk group and using BRFS since significant overall survival data may require decades to obtain. The definition of biochemical failure was changed in 2006. The previous definition was the American Society for Therapeutic Radiology and Oncology (ASTRO) definition for biochemical failure, which required three consecutive rises in PSA above the nadir. Because of problems including backdating and the phenomenon of a temporary benign PSA bounce [16], the Phoenix definition of PSA nadir plus 2 ng/ml has been adopted, which offers a better balance between sensitivity and sensitivity [17]. With either definition, the dependence of outcome on dose and risk group is clear.

### Dose escalation

Numerous high-quality prospective Phase III randomized trials demonstrate the importance of dose escalation in prostate cancer. These trials demonstrate that when radiation doses are increased from 64–70 Gy to 74–80 Gy, there is a 10–20% improvement in rates of biochemical control [18–22]. A meta-analysis of randomized controlled trials suggested that high dose was beneficial for all risk groups compared to conventional dose treatments [23]. As these trials mature, more tangible clinical improvements are being noted in addition to biochemical control. The MD Anderson dose escalation trial has demonstrated with dose escalation improves rates of distant metastases and prostate cancer deaths in patients with high-risk disease and PSA >10. These improvements in outcome were offset by an increase in the 10-year incidence of Radiation Therapy Oncology Group (RTOG) grade 3 gastrointestinal toxicity was significantly higher with the 78 Gy dose (26% vs. 13%), partially attributed to outdated 3D planning techniques. Significantly higher grade 2 or greater gastrointestinal toxicity was also seen, but there was no significant difference in genitourinary toxicity [23]. Furthermore, a meta-regression analysis predicted close to 100% biochemical control for doses around 90 Gy, especially for the low-risk group.

### Combination therapy

Randomized data demonstrating the benefit of combination therapy in patients with intermediate- and high-risk disease is maturing and has been presented in abstract form (ASCENDE-RT). Numerous retrospective studies also support combination therapy. Long-term BRFS rates for 223 patients with clinical stage T1–T3 prostate cancer treated from 1987 to 1993 with $^{125}$I or $^{103}$Pd brachytherapy after 45 Gy neoadjuvant EBRT without ADT were reported using different risk models. The results for a subset of intermediate-risk patients were described above. Overall, the 15-year BRFS for the entire treatment group was 74%. By risk group, the 15-year BRFSs were: low risk 85.8%, intermediate risk 80.3%, and high risk 67.8% ($P = 0.002$) [13]. Zelefsky et al. have reported that combination-based treatment approaches improve PSA relapse survival as compared with contemporary dose-escalated radiation alone [24].

### Whole-pelvis radiation therapy for high-risk disease

Whole-pelvis radiation therapy is used for high-risk disease to treat microscopic involvement of the pelvic lymph nodes. The dose to the pelvis ranges from 4500 to 5040 cGy in standard fractionation. A higher dose to the prostate can be given as an external beam cone-down or with brachytherapy. RTOG 94-13 was a four-arm study randomizing patients who are at greater than 15% risk of pelvic node metastasis to whole-pelvis or prostate-only radiation therapy and neoadjuvant or adjuvant ADT. At last analysis, it was not clear that there is an advantage to whole-pelvis radiation over prostate-only radiation [25]. Although a whole-pelvic field has been standard for many trials treating high-risk prostate cancer, two of which are described below, further research will be needed to answer the question definitively. Since treatment to the whole pelvis increases the morbidity of treatment, the answer is of the utmost importance.

### Androgen deprivation for high-risk disease

Neoadjuvant and concurrent ADT is generally recommended. RTOG 85-31 demonstrated a significant improvement in disease progression and absolute survival at 10 years with the addition of ADT to standard EBRT whole-pelvis plus cone-down to total doses of between 65 and 70 Gy [26]. Between 1987 and 1992, 977 patients were randomized to goserelin with radiation therapy or at time of relapse. The 10-year survival rate was 49% in the treatment arm versus 39% in the delayed arm ($P = 0.002$). The 10-year local failure rate was 23% in the treatment arm versus 38% in the delayed arm ($P < 0.0001$). Similarly, a randomized Phase III trial of the EORTC showed a significant disease-free survival (DFS) and overall survival in favor of hormone therapy. Between the years 1987 and 1995, 415 patients were randomized to whole-pelvis radiation therapy of 50 Gy plus a 20 Gy prostate cone-down with or without goserelin and cyproterone acetate. At median follow-up of 65.7 months, there was a significantly improved 5-year DFS of 74% versus 40% with the use of hormonal therapy ($P = 0.0001$).

The 5-year overall survival was 78% in the hormone group versus 53% in the radiation therapy alone group ($P = 0.0002$) [27].

## Toxicity profile

### Anatomic considerations

By virtue of its anatomic location, anterior to the rectum and posteroinferior to the bladder, treatment to the prostate results in mainly acute urinary and rectal side-effects. The urethra, running right through the gland, can hardly be avoided. Neurovascular bundles responsible for erectile function run alongside the right and left posterolateral apical aspects of the gland (Figure 134.1). As a result of their location, these structures receive a relatively high dose of radiation therapy and sustain most

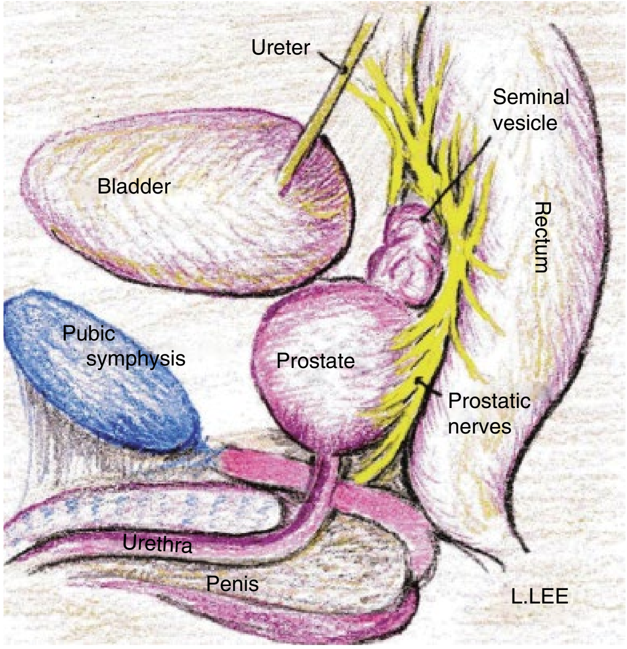


**Figure 134.1** Prostate *in situ*.

of the collateral damage from treatment. Imaging plays a primary role in locating these structures to assist in minimizing the planned dose and also maintaining precision of treatment delivery. The ultimate goal is to improve the therapeutic margin by increasing dose to the prostate, while reducing dose particularly to the bladder and rectum.

## Grading toxic events

The EORTC/RTOG criteria of acute and chronic radiation morbidity are provided for all different clinical systems. Acute morbidities for lower gastrointestinal and genitourinary side-effects, often cited for prostate cancer treatment, are listed in Table 134.4. The criteria for late effects are determined after the 90th day from the commencement of therapy and are listed in Table 134.5 [28]. Common Terminology Criteria for Adverse Events (CTCAE) provide similar information and are also frequently used. Version 4.0, released in May 2009 and updated in September 2009, includes a range of grades for various toxicities. The grading system ranges from 1 to 5: asymptomatic, symptomatic, severely altered function, life-threatening consequences, and death, respectively (Table 134.6). Rectal toxicities include rectal fistula, hemorrhage, mucositis, necrosis, obstruction, pain, perforation, and ulcer. Urinary toxicities include urinary fistula, frequency, incontinence, retention, tract obstruction, tract pain, urgency, cystitis and hematuria. Other adverse events that may apply to prostate cancer treatment include ejaculatory disorder and erectile dysfunction.

### Morbidity data

Current NCCN practice guidelines recommend doses of 75.6–79 Gy for low-risk disease and 78–80 + Gy for intermediate- to high-risk disease. Acute toxicities were reported for 772 patients undergoing IMRT to 81–86.4 Gy

**Table 134.4** Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring criteria.

| Score | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| Lower gastrointestinal | No change | Increased frequency or change in quality of bowel habits not requiring medication/ rectal discomfort not requiring analgesics | Diarrhea requiring parasympatholytic drugs/mucus discharge not necessitating sanitary pads/ rectal or abdominal pain requiring analgesics | Diarrhea requiring parenteral support/ severe mucus or blood discharge necessitating sanitary pads/ abdominal distention (distended bowel loops on radiograph) | Acute or subacute obstruction, fistula or perforation; GI bleeding requiring transfusion; abdominal pain or tenesmus requiring tube decompression or bowel diversion |
| Genitourinary | No change | Frequency of urination or nocturia twice pretreatment Habit/dysuria, urgency not requiring medication | Frequency of urination that is less frequent than every hour Dysuria, urgency, bladder spasm requiring local anesthetic (e.g. phenazopyridine) | Frequency with urgency and nocturia hourly or more frequently/dysuria, pelvic pain or bladder spasm requiring regular frequent narcotic/gross hematuria with/ without clot passage | Hematuria requiring transfusion/acute bladder obstruction not secondary to clot passage, ulceration or necrosis |

**Table 134.5** European Association for Research and Treatment of Cancer (EORTC)/Radiation Therapy Oncology Group (RTOG) criteria of late effects.

| Score | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| Small/large intestine | None | Mild diarrhea; mild cramping; bowel movements 5 times daily; slight rectal discharge or bleeding | Moderate diarrhea and colic; bowel movement >5 times daily; excessive rectal mucus or intermittent bleeding | Obstruction or bleeding requiring surgery | Necrosis/perforation fistula |
| Bladder | None | Slight epithelial atrophy; minor telangiectasia (microscopic hematuria) | Moderate frequency; generalized telangiectasia; intermittent macroscopic hematuria | Severe frequency and dysuria; severe telangiectasia; frequent hematuria; reduction in bladder capacity (<150 ml) | Necrosis/contracted bladder capacity (<100 ml), severe hemorrhagic cystitis |

**Table 134.6** Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 grading system.

| Grade refers to the severity of the adverse event: | |
|---|---|
| Grade 1 | Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated |
| Grade 2 | Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL)[a] |
| Grade 3 | Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL[b] |
| Grade 4 | Life-threatening consequences; urgent intervention indicated |
| Grade 5 | Death related to adverse event |

[a] Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

[b] Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

**Table 134.7** Acute toxicity with intensity-modulated radiation therapy (IMRT) to 81–86.4 Gy ($n = 772$).

| Toxicity grade | Gastrointestinal | Genitourinary |
|---|---|---|
| 0 | 568 (74%) | 258 (33%) |
| 1 | 169 (22%) | 296 (38%) |
| 2 | 35 (4%) | 217 (28%) |
| 3 | 0 | 1 |

**Table 134.8** Late toxicity intensity-modulated radiation therapy (IMRT) to 81–86.4 Gy ($n = 772$).

| Toxicity grade | Gastrointestinal | Genitourinary |
|---|---|---|
| 0 | 688 (89%) | 570 (74%) |
| 1 | 69 (9%) | 121 (16%) |
| 2 | 11 (1.5%) | 76 (9.5%) |
| 3 | 4 (0.5%) | 5 (0.5%) |

between the years 1996 and 2001 (Table 134.7). These doses are at the upper end of the recommended dose spectrum and they resulted in relatively low morbidity. Most patients developed grade 0–1 acute toxicity and there was one grade 3 urinary complication of obstruction. Late toxicity is shown in Table 134.8. With a median follow-up of 24 months, most patients had no residual gastrointestinal symptoms (89%) and many had no urinary symptoms (74%). At a median of nine months, 1.5% had developed grade 2 rectal bleeding and 0.5% grade 3 bleeding requiring transfusion or laser cauterization. At a median of six months, 9.5% had developed grade 2 chronic urethritis requiring medication for symptom control and 0.5% grade 3 urethral stricture requiring dilation. Among the 540 patients who were potent prior to treatment, 52% maintained erectile function at 2 years post treatment [29]. Longer follow-up will be important for documenting chronic toxicity at these doses. For patients treated between 1988 and 2000 to 66–81 Gy using either 3D conformal techniques or IMRT, CTCAE criteria were reported for a median 10-year follow-up. The 10-year actuarial incidence of grade 2 or greater gastrointestinal toxicity was 9% and of genitourinary toxicity was 15%. The use of IMRT reduced the incidence of proctitis from 13% to 5% ($P > 0.001$) [30].

## Quality of life

A prospective study examining acute and late toxicity and QOL up to 18 months after IMRT to 76 Gy showed similar findings to the morbidity data reported above and acceptable QOL. Acute urinary grade 2 and 3 toxicity was 38% and 2%, respectively. Acute bowel grade 2 and 3 toxicity was 13% and 0%, respectively. Temporary detriment in QOL, mainly due to urinary symptoms, reverted back to initial scores by 18 months [31]. A QOL comparison of treatment with 3D conformal therapy to 70 Gy versus IMRT to 76 Gy using fiducial markers to verify position, showed no detriment for the higher dose using IMRT at 1 and 6 months after treatment. There was actually an improvement in pain and urinary symptoms within the first month [32]. These techniques are detailed in the section on Treatment planning.

### Secondary malignancies

Secondary malignancies are a rare but dreaded complication of therapeutic ionizing radiation. A secondary malignancy is characterized by occurrence within the prior radiation portal and usually has a latency of several years or longer, especially for solid tumors. The potential for developing secondary malignancies is generally greater for a younger patient because of the likelihood of longer survival compared to an older patient. Surveillance, Epidemiology, and End Results (SEER) data comparing over 50 000 patients treated with radiotherapy and over 70 000 patients treated with surgery for prostate cancer, showed a small but statistically increased risk of developing tumors of the bladder, rectum, and lung, and also sarcoma. There was an increased relative risk of 15% for patients surviving 5 years or more, and 34% for patient surviving 10 years or more. The absolute risk of developing a secondary malignancy from radiation therapy was 1 in 290 patients, increasing to 1 in 70 for those surviving 10 years or more [33]. These data are consistent with other reports [34–37]. When brachytherapy is examined separately, the risk does not appear to be as for EBRT [35, 37]. Therefore, if otherwise reasonable, brachytherapy may be a better choice for the younger patient.

## Treatment planning

### Simulation details

Treatment planning begins with a simulation. The patient is positioned for the treatment and immobilization devices are used to ensure that the patient's position is reproducible on a daily basis. These may include a thermoplastic mold stretched over the pelvis and secured to the table. Various techniques to identify certain structures, such as a Foley catheter and rectal catheter, or contrast dye may be useful to define the bladder and rectal margins. Comfort measures such as a hand ring or wedge under the knees may be offered. Kilovoltage (kV) X-rays, generally a set of orthogonal films overlain with a grid, are obtained at the time of simulation and serve as the baseline for future setup verification. Tattoos are placed on the skin at the center of the anterior and two lateral fields in order to "triangulate" the isocenter. In the traditional four-field box technique, treatment was from anterior, posterior, right lateral, and left lateral directions (Figure 134.2). Field borders were designated on the films and generally corresponded to bone landmarks (e.g. the inferior border was set at the bottom of the ischial tuberosities). Cerrobend, a lead alloy, was constructed in blocks as

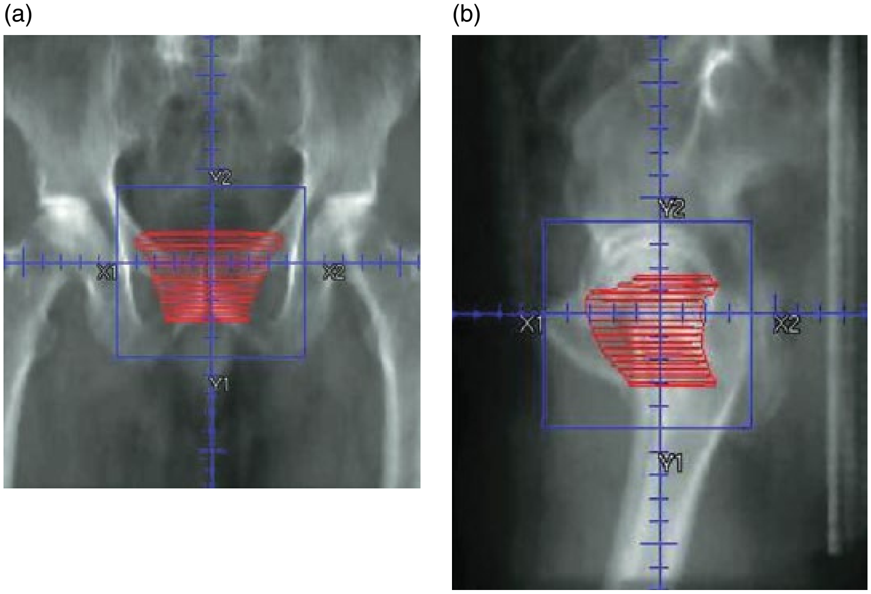


**Figure 134.2** (a, b) Examples of anterior and lateral beam appearance from four-field box technique.

needed (e.g. to shield the posterior rectum based on the configuration of the rectal contrast on the film). Currently, ball bearings are placed on the tattoos and a CT scan of the pelvis is obtained instead of X-ray films. Digitally reconstructed radiographs (DRRs) are generated from the CT information (Figure 134.3).

## Portal imaging

The traditional method of checking a patient's setup during treatment is weekly megavoltage (MV) portal imaging. This involves obtaining a set of orthogonal films, using the skin tattoos to locate the isocenter. These images utilize the MV energy of the treatment itself, which provides films of poor quality, but which are generally suitable for visualizing the bone anatomy. More recently, kV, or diagnostic quality imaging, is now commonly available with modern linear accelerators. When overlain with a grid, these portal images can be compared with the initial set of therapeutic-quality simulation films or DRRs obtained at the beginning of treatment to verify the patient's position (Figure 134.4). Cone-beam CT scans are also available with modern treatment machines, further improving the ability to localize and reproducibly treat the prostate.

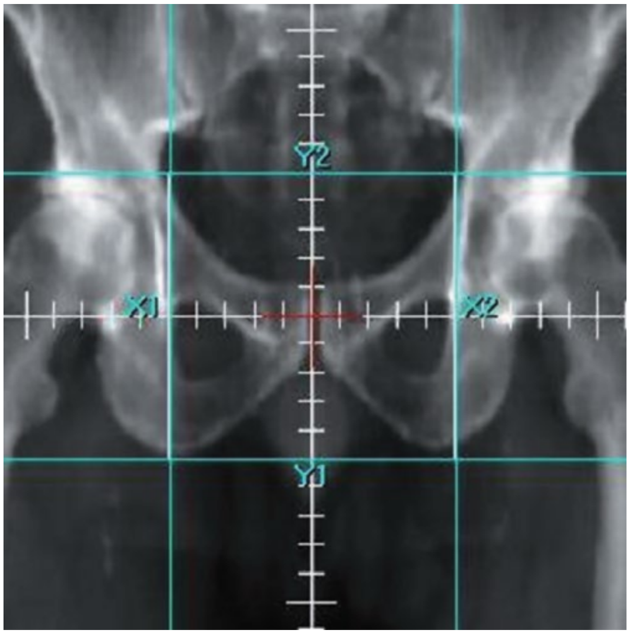


**Figure 134.3** Digitally reconstructed radiograph.

## Target volume delineation

The CT images are reviewed using treatment-planning software, many of which are commercially available. The area of interest is outlined on each slice to generate a target volume. Target volumes generally include a gross tumor volume (GTV), a clinical target volume (CTV) which includes areas at high risk for occult microscopic disease, and a planning target volume (PTV), which includes the CTV with a margin for motion and setup error. For the treatment of prostate cancer, the CTV rather than the GTV is usually outlined. The CTV is generally the prostate gland and some portion of the seminal vesicles (general rules of thumb is proximal third for low-risk disease, proximal two-thirds for intermediate risk, and the whole seminal vesicle for high risk). Recent investigations have demonstrated promising early results for focal or partial gland therapy and for integrated boosts to areas of gross intraprostatic disease, but these approaches are too immature to be considered standard of care. MRI has played an important role in the identification of intraprostatic and extraprostatic disease that should be covered in standard radiation fields. Image fusions with deformable registration technologies are typically integrated into the radiotherapy planning process. The PTV is often represented by a volume that is

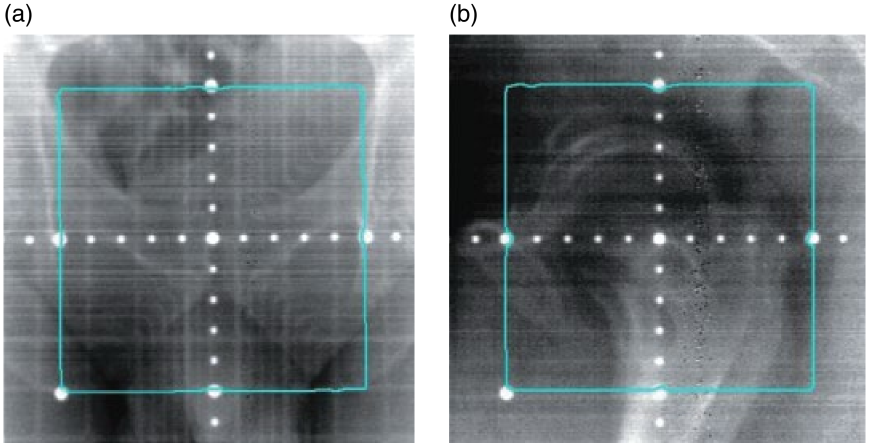


**Figure 134.4** (a, b) Orthogonal portal images for prostate treatment verification.

generated by expanding the prostate volume in all dimensions. Differential margins are often used. With modern IGRT techniques discussed later, it is possible to minimize the PTV margins to the order of 5–7 mm for conventionally fractionated IG-IMRT and even less for SBRT.

### Three-dimensional conformal radiation therapy

Three-dimensional conformal radiation therapy improved upon the traditional four-field box technique but is now generally outdated for modern prostate cancer radiotherapy. CT information obtained at the time of simulation allows an unlimited variety of beams to be chosen to optimize treatment delivery. A typical plan might use five to seven beam angles to target the prostate while avoiding the bladder, rectum, and femoral heads (Figure 134.5). Differential weighting or adjusting the fractional dose per beam fine tunes the coverage of the target volume. Various techniques for beam collimation were employed, including the use of cerrobend blocks, wedges, and multileaf collimators. Examples of two oblique fields of a six-field plan with blocking around PTV is shown in Figure 134.6.

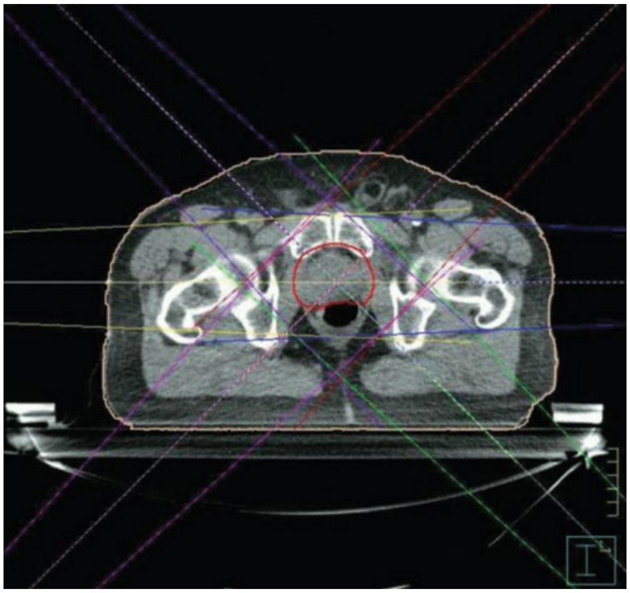
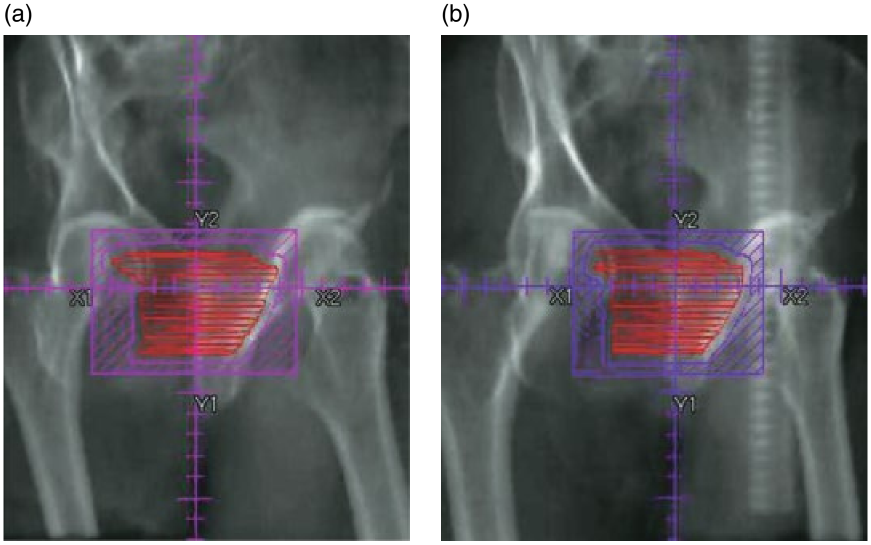


Figure 134.5 Axial slice of six-field 3D conformal plan.

### Rectal dose–volume relationships

Rectal dose–volume relationships have been studied in detail. The percentage of rectal volume receiving 70 Gy ($V_{70}$) predicts for chronic toxicity. In one study the rectal doses of 331 patients undergoing 3D conformal radiation therapy to 75.6 Gy were analyzed. With a median follow-up of 1.6 years, a $V_{70}$ of less than 25%, 25–40%, and greater than 40% resulted in grade 2 or greater toxicity rates of 9%, 18%, and 25% respectively [38]. A similar analysis was done on 163 patients treated with 3D conformal techniques to 74–78 Gy and a median follow-up of 62 months. The 6-year rate of rectal complications of grade 2 or higher was 54% versus 15% for $V_{70}$ of greater than 26.2% versus 26.2% or smaller, respectively [39]. Further analysis showed that even at lower doses, high volume resulted in increased toxicity. There was a 50% or higher incidence of grade 2 toxicity or worse within 2 years if 80% or more of the rectal wall was exposed to 32 Gy [40]. These and other data allowed limits to be set for future treatment planning. These limits are generally achievable with IMRT.

Figure 134.6 (a, b) Examples of two oblique fields of a six-field plan with blocking around planning target volume (PTV) shown in red.



### Intensity-modulated radiation therapy

The advent of IMRT in the mid 1980s revolutionized modern radiotherapy. IMRT expands on the simple wedges used to provide a gradual dose gradient across a field. This technique is coupled with powerful computer planning algorithms and utilizes a series of miniature sliding doors, called mutlileaf collimators (MLCs), which differentially attenuate the radiation beam. Since the MLCs can remain open or closed in innumerable positions, the ability to collimate the radiation beam is vastly improved.

## Treatment delivery

### Setup uncertainty and rectal variability

Traditional methods of orthogonal portal images and skin tattoos lead to margin uncertainties as large as 1–2 cm [41]. Positioning based on bone anatomy is clearly limited in its ability to reproduce organ position. This could be addressed by increasing the margins, but in the area of the prostate, increased margins lead to increased complications [42]. A study of weekly CT scans on six patients showed significant interfraction target position variability. Estimates of PTV margins in the anteroposterior (AP), craniocaudal (CC), and mediolateral (ML) directions to cover the CTV with 95% certainty were: 12.4 mm, 10.3 mm, and 5.6 mm, respectively, for the prostate, and 13.8 mm, 8.6 mm, and 3.9 mm, respectively, for the seminal vesicles [43]. Rectal variability is reproducible and appears to be responsible for most of the variation [44, 45]. For example, the prostate may be located posteriorly if a patient has diarrhea and less rectal filling. On the other hand, the prostate may be located more anteriorly if the patient has proctitis, a full rectal vault, or tends to tense the pelvic muscles during treatment. Therefore, corrections are not universal and ideally should be tailored to the individual.

### Bladder volume

The bladder appears to contribute less to target position variability than the rectum [43]. An empty bladder is more reproducible than a full bladder, but allows a larger volume of bladder to be exposed to the high-dose area. Conformal treatments such as IMRT can reduce bladder volume significantly. Patients can also be treated with a full bladder, but this state tends to be less reproducible with variable bladder volumes from day to day. In addition, the patient may tense the pelvic muscles to postpone urination, which may lead to changes in prostate position [41]. However, if the patient can train himself to have a consistently full bladder for treatment each day, the major advantage is that a significantly smaller volume of bladder will be in the high-dose area.

### Intrafraction error

Intrafraction error, which occurs during a single treatment, dramatically increases the complexity of target motion. Although breathing can result in predictable sinusoidal patterns, motion in the region of the prostate has been described as “slow drift” or “sudden transient” due to acute changes in colonic content [46]. A study of 21 patients was conducted where a CT was done before and after treatments to determine the intrafraction error. Prostate drifts of greater than 5 mm were found in 12% of all fractions, and a margin of 6 mm was determined to compensate for these changes [47]. These unpredictable movements suggest a benefit to localization and tracking the prostate during treatment. IGRT includes various methods to achieve these goals.

## Methods for image-guided radiation therapy

### Placement of fiducials

Fiducial markers are usually made out of metal and vary in size and configuration. Commonly used fiducials are made of gold and can be shaped like pellets or coils. For the prostate, gold fiducials usually measure less than 1 mm in diameter and a few millimeters in length. A textured surface, as with the coils, can reduce migration. Preparation for the procedure includes an enema the night before and on the morning of the procedure. Antibiotics are prescribed prophylactically to prevent infection. For example, ciprofloxacin 500 mg may be taken twice a day for 3 days. When the implantation site is identified on rectal ultrasound, approximately 1–3 ml of lidocaine 1% is injected for local anesthesia. The fiducials are placed into an introducer needle and then placed into the site with a stylet. Toxicity is generally minor, including bleeding such as hematuria, hematospermia, and hematochezia; generally lasting for a day or two. There may be mild rectal discomfort, which is usually improved with acetaminophen. Sepsis is also a possibility, but rare.

### On-board imaging

A logical advance in weekly portal imaging is to use therapeutic-quality X-rays so that the images are closer in quality to the simulation films. A kV X-ray tube mounted opposite an image detector is conveniently added to any existing linear accelerator, and is otherwise known as on-board imaging (OBI). The high resolution allows for better visualization of skeletal anatomy and also of fiducials implanted in soft tissues. An additional benefit of this system is a significantly lower dose of radiation, about 0.01–0.1 cGy/film; MV imaging gives an estimated 4–16 cGy/orthogonal pair [48]. The lower dose given with kV images makes daily imaging for localization more reasonable. In order to make the process of daily filming time efficient, an electronic portal imaging device (EPID) is often used rather than traditional film processing. In addition, a kV fluoroscopy unit can be used to localize fiducials at the start of treatment, and then can provide real-time tracking of the fiducials during treatment [49]. The treatment may be held if the fiducials move out of a predetermined volumetric range, then restarted when the fiducials move back into range. This process is referred to as gating and can be used with other real-time tracking techniques.

## CT-based verification

Since CT-based planning has become the norm for 3D conformal and IMRT planning, using CT for verification is a logical advance. CT provides soft tissue detail and a 3D aspect to verification, a clear improvement upon the traditional 2D orthogonal films. CT-based verification may utilize either kV or MV energies. The pros and cons of these are similar to those for the respective X-ray films. The images can also be obtained using either a helical beam or a large field cone-beam. The helical beam opposite the detector makes multiple rotations around the patient in order to obtain the necessary data to construct the images. The large field cone-beam is opposite a flat panel detector, which can acquire the data in a single rotation [43].

Cone-beam MV CT utilizes the treatment beam itself to provide the images. The system is easy to implement since it only requires an EPID mounted onto an existing machine. The wide field beam is subject to divergence and scatter, which reduces the quality of the images. The dose to the patient is relatively high, approximately 5–15 cGy/scan [50]. Helical MV CT (TomoTherapy, Madison, WI, USA) is a combined CT scanner and linear accelerator that utilizes the continuous motion of the gantry and couch of a diagnostic helical CT scanner to provide both imaging and treatment. It exposes the patient to less radiation, about 1–2 cGy, but it may take longer to acquire the necessary images since multiple rotations around the patient are needed to complete the process. As a result, the images are more likely to show motion artifact due to respiration. Although poor relative to kV images, the image quality of MV CT is sufficient for positioning corrections based on skeletal anatomy. A primary advantage to using MV CT is the reduced artifact from orthopedic hardware [43]. This can be useful for patients with a hip prosthesis. It is particularly useful for visualizing fiducials because of the lack of a star-like artifact that can be present in kV images. Compared to kV imaging, the disadvantages include poorer anatomic image quality and increased dose to the patient.

A kV CT system provides excellent resolution since the CT is of diagnostic quality and is actively under investigation for advances in image adaptive techniques. For example, head and neck tumors have the potential to change rapidly in size during treatment and are often surrounded by multiple soft tissue organs of interest, such as the parotid glands and spinal cord. The CT information used for verification can be used not only to realign the patient, but also to replan the treatment if there are major anatomic differences. The system may be more difficult to implement than MV CT since it requires a CT unit separate from the linear accelerator. Moreover, the patient must remain immobilized in the treatment position for both scans. With a 180° couch rotation, the patient can be moved from the linear accelerator to the mobile CT unit, which then can be moved into position for the scan.

Kilovoltage cone-beam CT can offer several advantages, including superior imaging as well as real-time tracking ability from the fluoroscopic capability. A kV unit is mounted 90° from the gantry of the linear accelerator and opposite an X-ray detector. Submillimeter accuracy has been reported with this system. Since the image registration requires a full rotation over a period of about 1 minute, the system can still be subject to inaccuracies from breathing and other motions. The system is well-suited for intracranial radiosurgery but may require gating techniques for lung tumors.

## Ultrasound verification

The B-mode Acquisition and Targeting System (BATS) is a portable ultrasound localization device. CT data from the simulation are transferred to the system. Ultrasound imaging is performed prior to treatment and matched to the original CT images. If the images differ, the system will then produce the necessary couch shifts in order to realign the patient to match the ultrasound real-time images [51]. Despite the ease of implementation, accuracy may not be as high as with CT verification techniques due to the lower image quality and the potential for the probe itself to move the prostate [52, 53]. Therefore, the technique is more dependent on user skill and interpretation of images. One major disadvantage is the lack of tracking ability.

## Electromagnetic field tracking

A major advantage to electromagnetic field tracking is the lack of additional ionizing radiation. The Calypso 4D Localization System (Calypso Medical Technologies, Seattle, WA, USA) requires the implantation of beacon transponders, which carries the same risks as implantation of fiducials. Although anatomic images are not produced, the corrections are objective and do not require user skill and interpretation.

### Transponder placement

The beacon transponder contains a miniature electrical circuit sealed in a glass capsule, measuring 1.85 mm in diameter and 8 mm in length (Figure 134.7). Like fiducials, transponders are implanted into the left lobe, right lobe, and apex of the prostate gland via 14G introducer needles. Transponders may migrate soon after the procedure. The mean of the standard deviation of intertransponder distance variation measured at 4 days after implantation was 1.3 mm and 0.8 mm at 14 days after implantation [54, 55]. This compares favorably to gold seed markers, for which the mean of the standard deviation of intermarker distance variation measured throughout the course of treatment was 1.0 mm [56]. Like fiducials, beacons may become lost due to implantation into the urethra or into the venous plexus going to the seminal vesicles, but in the majority of cases they are quite stable. Another potential route for loss of a transponder located between the prostate and rectum could be through the rectal wall. In 60 patients, one study reported loss of one beacon via the urethra and one to the venous plexus [55]. The mean standard deviation of the intertransponder distances over a period from 4 days post implant through the last radiation fraction was 0.8 mm. There was no significant difference in the stability of the transponders placed at the base versus the apex [57]. Overall, these data demonstrate significant stability of the geometry of implanted transponders throughout an entire course of EBRT, which is typically 8–9 weeks.

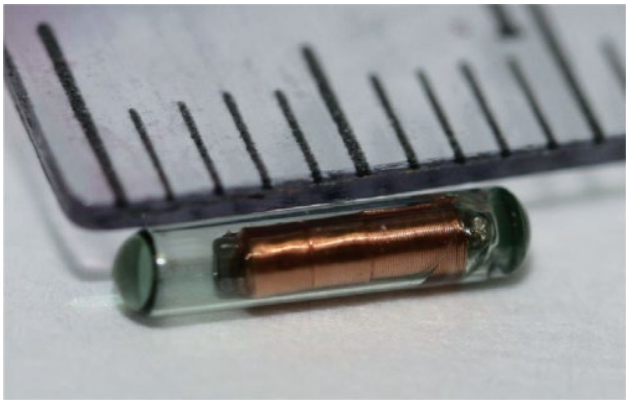


**Figure 134.7** Close up of Calypso (Calypso Medical Technologies, Seattle, WA, USA) beacon transponder next to millimeter ruler demonstrating internal electromagnetic coils.

### Simulation procedure

The patient then returns for simulation about 1–2 weeks later. Patients are supine for the simulation, and CT scan slices of 1–1.5 mm of the pelvis are obtained. Previous work has shown that transponder locations are known to within 0.7 mm using thin-slice CT. Immobilization devices are generally minimal. The treatment-planning CT is done as usual and the isocenter is placed in the middle of the beacons. Then the coordinates of the beacons in reference to the isocenter are entered into the Calypso software.

### Localization

When the patient is ready to be treated, the beacon transponders are located, which includes identifying their positions in 3D space relative to each other. An electromagnetic array, containing source and receiver coils, is placed over the patient. The source coils emit an electromagnetic signal that excites the beacon transponders. The signal is then turned off, and the receiver coils then detect the signal emitted from the transponders. Each transponder has a unique resonant frequency so that each one can be distinguished from the others. A best geometric fit is determined to match the coordinates from the simulation data entered previously into the system. This correction is translated into couch movements, which will move the patient to the corrected position. When a patient is set up with skin tattoos and verified with the Calypso system, most of the corrections are within 1.5 cm, but approximately 10% are greater than 1.5 cm, demonstrating the value of localization. Compared with the kV X-ray localization methods, the accuracy of the Calypso system is less than 1.5 mm.

### Tracking

For tracking, position updates are obtained at 10 Hz frequency and the differences between the actual isocenter and the calculated isocenter are displayed graphically, providing the fourth dimension of time (Figure 134.8). If the movement is outside a set threshold of, for example, 3 mm, then the operator has the option of stopping the treatment until the target is back in alignment, or performing a couch correction if needed. Most of the lateral shifts are within 5 mm but about 8% exceed 1 cm. Large lateral shifts tend to be more common in large patients.

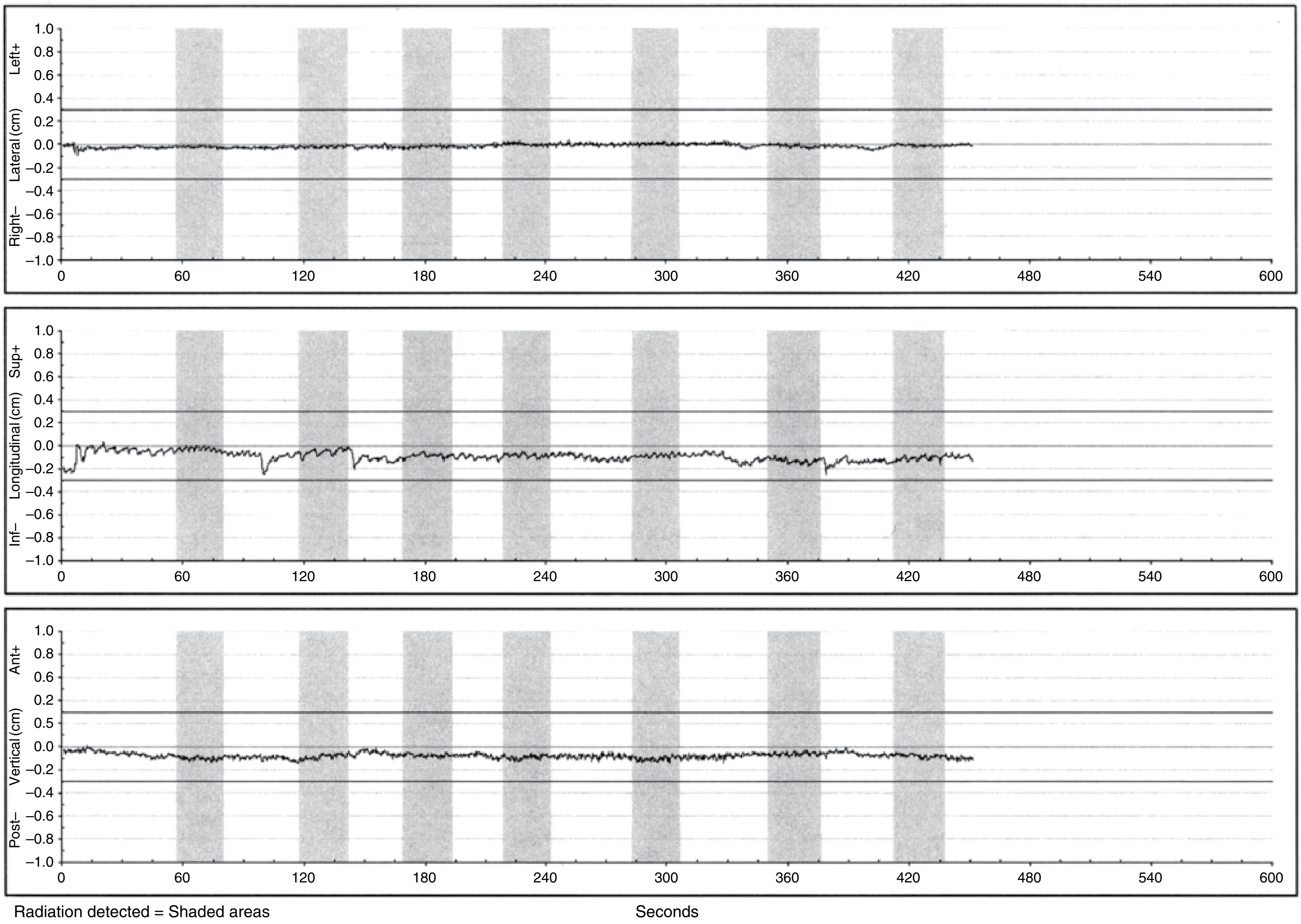


**Figure 134.8** Calypso session report showing patient remaining within set threshold; gray areas represent when the radiation is turned on.

Superoinferior shifts tend to be within 5 mm, suggesting relatively limited movement in these directions. Anteroposterior shifts, depending on rectal contents, are most common and are usually within 1.5 cm. Tracking data show that motion of more than 5 mm for longer than 30 seconds occurs during 15% of the fractions [56]. With the exception of a slow posterior shift associated with relaxation, many of these movements are unpredictable and pose a challenging problem for future improvements and developments.

## Conclusions

IGRT offers a wide range of techniques, which allow an improved therapeutic ratio in the treatment of prostate cancer by increasing the dose to the tumor for better tumor control, while reducing the dose to adjacent critical organs for lower morbidity. This goal drives much of the research performed in the field of radiation medicine and promises to improve outcomes and QOL for patients.

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## 135

# High-intensity Focused Ultrasound of the Prostate

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## Introduction

Since 1998, prostate cancer has been the most prevalent malignancy in men in the United Kingdom [1]. As a malignancy, its mortality is second only to that of lung cancer [1]. With any cancer, the optimal end goal is to cure or control the disease with minimal side-effects or complications. To achieve this, one must balance the number of quality years of life gained against any potential morbidity of any particular treatment and appropriately match that to the risk that any particular cancer poses to a patient. This creates an immediate dilemma in prostate cancer. This particular malignancy often has a long natural history before culminating in lethality, even in the absence of treatment, and hence there is often innate difficulty when deciding whether or not treatment is necessary in a particular treatment, and if it is, in what manner should that treatment be advocated? Such a conundrum in prostate cancer is further compounded by the intrinsic urinary and sexual side-effects that are associated with our treatment armory and which many men find displeasing. Furthermore, an increasingly easy access to prostate specific antigen (PSA) screening has led to a clear downward stage migration at diagnosis, with contemporary men being much more likely to be diagnosed at earlier, organ-confined stages [2]. Nevertheless, many men with low- and intermediate-risk disease will inevitably choose curative therapy rather than active surveillance [3–5]. There is no single cause for such decisions. They are likely due to both the psychological impact of a diagnosis of malignancy and the psychological burden of active surveillance for men alongside a physician's concern over potential disease progression. Thus, despite many of these men having disease which would be unlikely to impact their life expectancy they elect to undergo radical treatments which, despite their excellent curative potential, carry significant urological and sexual morbidity.

In contemporary surgical practice, there is an evident movement toward the use of increasingly minimally invasive techniques. Within prostate cancer this is clearly demonstrated by the recent introduction of new laparoscopic and robotic-assisted techniques. In addition, novel techniques such as high-intensity focused ultrasound (HIFU), cryotherapy, and radiofrequency ablation (RFA) offer a more discrete delivery of treatment and allow for a cancer to be destroyed along with a margin of healthy tissue rather than an inevitable destruction of the entire gland. Such an approach confers a reduction in the side-effect and complication potential seen after established radical therapies. These novel techniques represent an additional therapeutic choice for men with low- to intermediate-risk disease in whom the side-effects of radical therapies are unacceptable despite their excellent curative potential [6]. Because of this, the existence of a clinical niche, which offers curative intent alongside reduced side-effects, is undeniable. Such a niche is not isolated within the field of prostate cancer. For example, wide local excision for ductal breast carcinoma has clearly replaced the radical mastectomy, along with its defeminizing side-effects, as the treatment of choice in localized disease, from both the patient and physician perspective [7]. Clearly, there is a valid comparison to be made here with the sexual side-effect profile associated with the radical treatment options in prostate cancer.

Such techniques are potentially very attractive when used as focal therapies. Most prostate cancers are multifocal, however, around 15–20% are unifocal [8]. In addition, the concept of an index lesion, usually the most

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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voluminous and highest grade, which drives the metastatic process forward, leaving its less aggressive counterparts as spectators, has been proposed [8]. These oncological characteristics allow for a defined treatment of a defined area, offering good curative rates and a less severe side-effect profile when compared to radical therapies. Such a combination, as described by the Consensus Conference of Focal Treatment of Prostatic Carcinoma as “an individualized treatment that selectively ablates known disease and preserves existing functions, with the overall objective of minimizing lifetime morbidity without compromising life expectancy” [9] is the ultimate goal.

However, as we currently stand, a universally accepted set of indications for focal treatments of prostate cancer is still lacking. Patient suitability is based on their risk of bilateral or extraprostatic disease, and decisions made with guidance, such as that proposed by the National Comprehensive Cancer Network and advocated by the 2015 consensus meeting on focal therapy [10], which are based on clinical, radiological, and histological findings.

Although there are an increasing number of focal treatments available – HIFU, cryotherapy, RFA, photodynamic therapy, focal laser ablation, and injectable toxins – for the purpose of this text we will focus on HIFU of the prostate and its role in the treatment of prostate cancer.

## High-intensity focused ultrasound for prostate cancer

Since the early 1930s, we have known that HIFU has the ability to destroy living tissue [11]. However, at the time of this discovery, the existing imaging technology available was simply inadequate and it would be some time before cross-sectional computed tomography (CT) or magnetic resonance imaging (MRI) was in regular use. Likewise, diagnostic ultrasound imaging was not yet even in its infancy and because of this the use of HIFU remained obscure, along with the intraprostatic lesions that were unable to be identified accurately or treated. However, the translational potential of HIFU as an ablative technology was further explored in the 1970s and 1980s [12, 13]. After some conceptual success there was a natural move to assess its potential as a therapy for use in malignancies. In particular, the urological community was an especially prominent proponent and since the 1990s numerous highly accurate commercially available devices were developed. In some uro-oncology centers the technique is in regular use for the noninvasive, focal or salvage treatment of prostatic carcinoma.

Ultrasound is an inaudible (to humans) high-frequency mechanical vibration wave that in clinical practice is emitted by a transducer. The ultrasound waves are absorbed by the prostatic tissue and agitate the molecules within [14]. The consequential friction generates heat that can cause the temperature within the affected area to rise to above 80°C in a matter of seconds [14]. The lower frequency ultrasound waves utilized by HIFU, when focused precisely on a single point, result in tissue destruction by coagulative necrosis induced by cavitation and heat injury [14]. The heat causes denaturation of lipoprotein and protein structures in the sarcolemma and the intracellular organelles and associated machinery contained within [15]. Cavitation is a destructive mechanism caused by microbubble formation and collapse in targeted tissue, which causes further tissue destruction [16].

The aim of HIFU is the irreversible destruction of prostatic tissue. This is achieved by the focused deposition of energy on a single point within the gland. This increases the temperature within that minimal area to a degree sufficient to cause discrete destruction of tissue [13, 14]. Mechanically, in order to achieve this, HIFU generally uses ultrasound frequencies of 0.5–7.0 Hz, in comparison to the frequencies of 2.0–12.0 Hz more usually used [17]. Thus, the energy levels delivered to the tissue in a focused HIFU beam are typically 10 000 times greater than a modern diagnostic ultrasound beam [18]. This level of energy rapidly increases the temperature of the beam’s focal point to over 80°C. Such a temperature is more than adequate to induce cell death [14]. However, outside of the focal point, little tissue damage occurs due to a rapid drop-off in temperature. The resultant post-HIFU lesion shape and volume is dependent on the design of the transducer, the “on” and “off” time of the beam and the power (W) that is delivered [19]. This focus of discrete destruction is small in volume but reproducible. Each pulsed cycle of energy results in a rice-shaped ellipsoid (3 mm × 3 mm × 10 mm) of ablation [20]. This can be repeated by refocusing the piezoelectric crystals on further areas of prostatic tissue until the desired predefined treatment area has been fully treated.

The safety and efficacy of HIFU is vital if effective treatment is to be achieved. A key part of this quality control is optimal intraoperative monitoring, which both accurately targets disease and actively monitors the effects of treatment. Currently, either ultrasound or MRI may be used to monitor HIFU treatment [21, 22]. However, given the mobility and accessibility of ultrasound and the significantly higher costs of MRI, the former modalities are clearly the more popular choice. Usually, the imaging ultrasound transducer is mounted in the treatment probe, making real-time intraoperative monitoring possible. The intraoperative gray-scale image can be monitored for hyperechoic changes (Uchida changes) [22], which represent microbubble formation (in effect, steam) [23] and the operator can react to them accordingly. However, this can also be a disadvantage as the bubbles cause appreciable ultrasound artifacts that confer additional difficulty to the interpretation of often already poor-quality images [24]. This is of particular concern when tissue in front of the target zone is being treated.

Both *in vitro* and *in vivo* studies have demonstrated that HIFU can target and destroy prostatic malignancies transrectally without inducing metastatic spread [25, 26]. When planning treatment, physical parameters that should be considered include ultrasound frequency (MHz), energy intensity (W), its duration of action and the interval between pulses [11]. In addition, the architecture of the prostate and the location of lesions pose additional difficulties. Because of this, the distance between lesions and the penetration depth should be considered when planning treatment. Current HIFU devices are typically equipped with transducers with adjustable focusing systems. These are moved mechanically, and allow for a large volume of prostate tissue to be treated in a single treatment session [27, 28].

## HIFU treatment devices

Currently, there are two existing commonly used commercially available devices for use in the treatment of prostate cancer: the Sonablate® system (Sonacare Inc., Indiana, IL, USA) and the Ablatherm® HIFU device (EDAP TMS, Lyon, France). Other prototype devices in various changes of development exist, but they are not in common clinical use outside of clinical trials.

The Sonablate device is minimally invasive and mobile (Figure 135.1) with an operating frequency of 4 MHz that has been developed to treat prostate cancer via an endorectal probe (Figure 135.2). The endorectal probe has the advantage of real-time imaging of the prostate during treatment and also has an added option of ultrasound/multiparametric MRI (mpMRI) fusion. This combined imaging and treatment allows the operator to view the treatment effect following each treatment cycle. Furthermore, monitoring of the rectal wall temperature is incorporated within the system which, along with the cooling system (Figure 135.3), gives an added degree of safety and the user interface has been developed to allow for accurate treatment planning and monitoring (Figure 135.4). Using this interface, the operator can acutely target the intended treatment area and adjust the depth of the wave penetration to 3 cm, 4 cm, or 4.5 cm [29]. The energy delivered to the tissue can be monitored by color changes viewed within the targeted area, which allows for a great degree of clarity regarding target accuracy and the cell death contained within.

The Ablatherm device is a semi-automated device that also treats prostate cancer via an endorectal probe; however, the patient must be positioned in the right lateral cubitus position [30]. The unit consists of a treatment module (Figure 135.5), a control module (Figure 135.6) and the endorectal probe (Figure 135.7). The probe contains both imaging and treatment ultrasound transducers

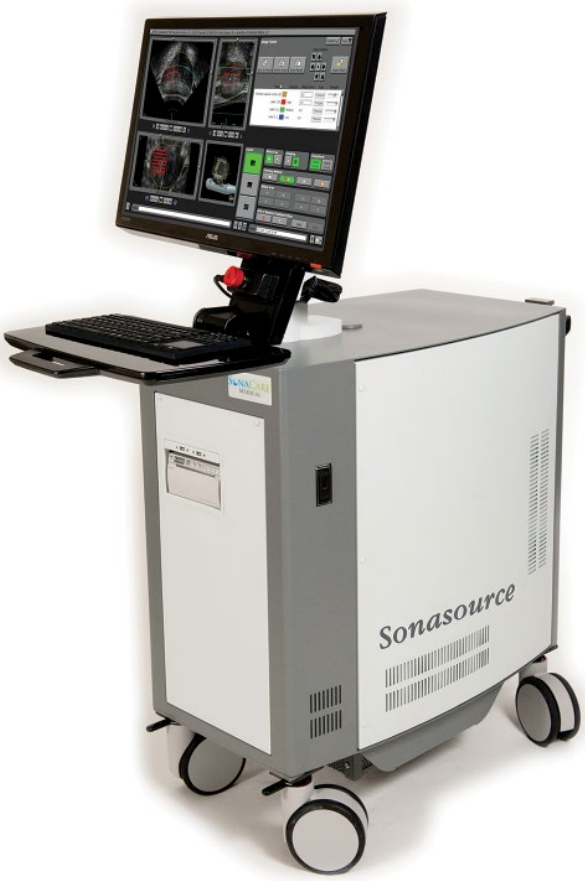


**Figure 135.1** The Sonoblate™ high-intensity focused ultrasound system, including endorectal probe, control module, and cooling system. *Source:* Sonoblate, North Carolina, USA. Reproduced with permission of Sonoblate.

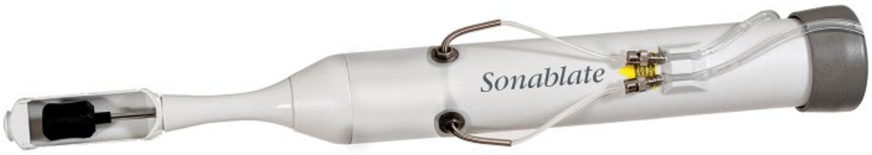


**Figure 135.2** The Sonoblate™ endorectal treatment probe. *Source:* Sonoblate, North Carolina, USA. Reproduced with permission of Sonoblate.

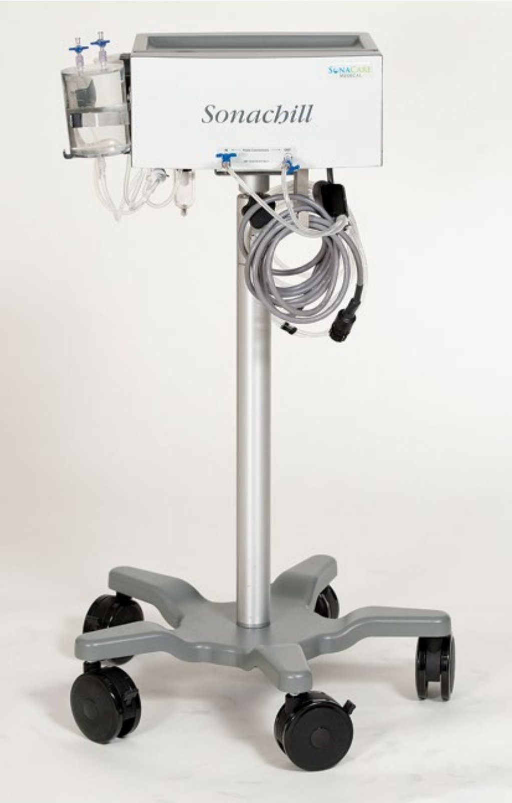


**Figure 135.3** The Sonochill™ rectal cooling system. *Source:* Sonoblate, North Carolina, USA. Reproduced with permission of Sonoblate.

and therefore allows for accurate treatment planning and offers real-time intraoperative imaging with real-time energy delivery adjustments [30]. This combination allows for highly precise energy delivery that creates posttreatment lesions 19–26 mm in diameter, determined by predefined power protocols. Safety features are incorporated and include a patient-monitoring device, real-time rectal wall temperature monitoring, and a rectal cooling system [30]. When this device is used, the HIFU treatment is often combined with transurethral resection of the prostate in order to reduce prostatic volume and the subsequent risk of stricture formation.

## Indications

The most accepted clinical use for HIFU is in patients with localized prostate cancer. These patients either profess a preference for focal therapy due to personally finding the side-effects of radical therapy unacceptable, or they are unfit for radical surgery [11]. However, as focal therapy moves from its infancy to adolescence, our greater clinical experience and conclusions from research have demonstrated clearer safety and efficacy and as such these indications have clearly broadened in scope. Currently, HIFU is indicated in focal therapy for low- to intermediate-risk prostate cancer [31] as well as salvage treatment in radiorecurrent disease [32]. Furthermore, the lesion to be treated should be visible on mpMRI and concordant with histopathological analysis. Importantly, if the disease is to be treated, it should be clinically significant (i.e. the lesion should have a histological Gleason score of 3 + 4 or higher and a volume of greater than 0.2 ml). Contraindications to HIFU are relatively limited but include an absent or severely strictured rectum or a damaged rectal wall [10].

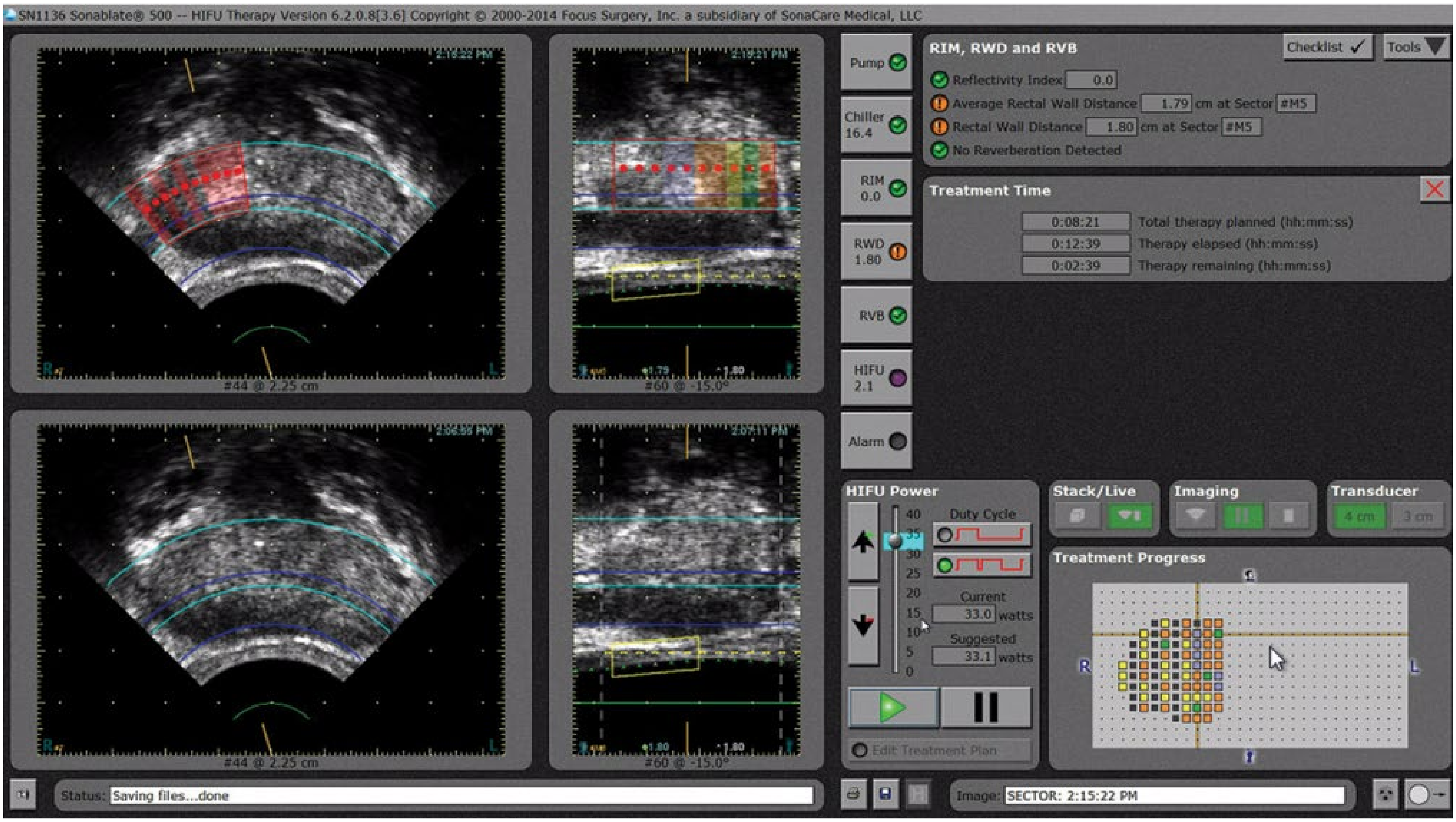
## The procedure

First, the procedure must be planned in advance of the surgery. An mpMRI should demonstrate a visible lesion that is concordant with histopathology. The mpMRI is then used to map the pattern of disease from which a treatment plan is devised, taking the form of a zonal ablation (demonstrated in Figure 135.8). The intension is to destroy the target lesion while preserving as much healthy tissue as is possible.

Unless there are perioperative concerns or a patient's comorbidities demand otherwise, treatment with HIFU is performed as day-case surgery. Full bowel preparation is unnecessary, but an enema an hour prior to the procedure will usually be sufficient to optimize perioperative ultrasound imaging. In general, antimicrobial prophylaxis is unnecessary, but this should be guided by local policy and sensitivities. Intravenous broad-spectrum, Gram-negative, and anaerobic cover is acceptable and furthermore a postoperative course of oral antibiotics is recommended.

HIFU should be performed under general or spinal anesthetic. The latter will require deep sedation as any untoward patient movement renders the treatment significantly more difficult. Furthermore, if there is evident heavy breathing and this is causing movement of the prostate, the patient should be paralyzed and mechanically ventilated.

Once the anesthetic induction is completed successfully, the patient is either placed into the right lateral decubitus position (Ablatherm), or the extended lithotomy position (Sonablate) and the perineum exposed. A urethral catheter may be inserted to help with treatment planning by giving an obvious landmark on ultrasound imaging. This may be removed prior to starting treatment. Suprapubic catheters are an acceptable alternative preferred by some surgeons, and in certain circumstances necessary; however, naturally they carry their own complications. Following this, a digital rectal examination – sometimes augmented by a proctoscope – is performed to ensure an


SN1136 Sonoblate® 500 -- HIFU Therapy Version 6.2.0.8[3.6] Copyright © 2000-2014 Focus Surgery, Inc. a subsidiary of SonaCare Medical, LLC

RIM, RWD and RVB

Reflectivity Index 0.0
Average Rectal Wall Distance 1.79 cm at Sector #M5
Rectal Wall Distance 1.80 cm at Sector #M5
No Reverberation Detected

Treatment Time

0:08:21 Total therapy planned (hh:mm:ss)
0:12:39 Therapy elapsed (hh:mm:ss)
0:02:39 Therapy remaining (hh:mm:ss)

HIFU Power

Current 33.0 watts
Suggested 33.1 watts

Status: Saving files...done

Image: SECTOR: 2:15:22 PM

2:15:22 PM
2:15:21 PM
2:06:55 PM
2:07:11 PM
#44 @ 2.25 cm
#60 @ -15.0°
#44 @ 2.25 cm
#60 @ -15.0°
R
L
Pump
Chiller 16.4
RIM 0.0
RWD 1.80
RVB
HIFU 2.1
Alarm
Checklist ✓
Tools
Duty Cycle
40
35
30
25
20
15
10
5
0
Edit Treatment Plan
Stack/Live
Imaging
Transducer
4 cm
3 cm
Treatment Progress
R
L

**Figure 135.4** The Sonoblate™ user interface. *Source:* Sonoblate, North Carolina, USA. Reproduced with permission of Sonoblate.

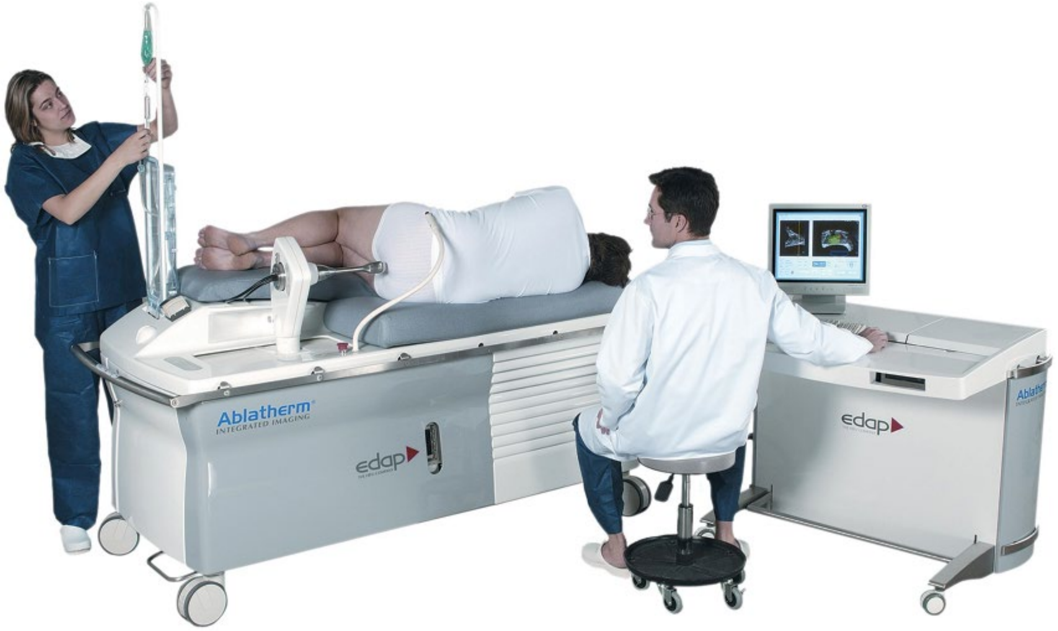


**Figure 135.5** The Ablatherm™ treatment module. *Source:* Maude Davageau, France. Reproduced with permission of Maude Davageau.

Ablatherm
HIFU INTEGRATED IMAGING
edap tms

**Figure 135.6** The Ablatherm™ control module. *Source:* Maude Davageau, France. Reproduced with permission of Maude Davageau.

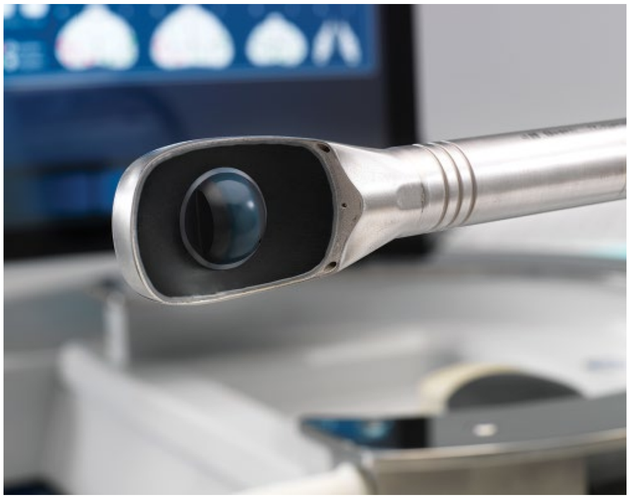
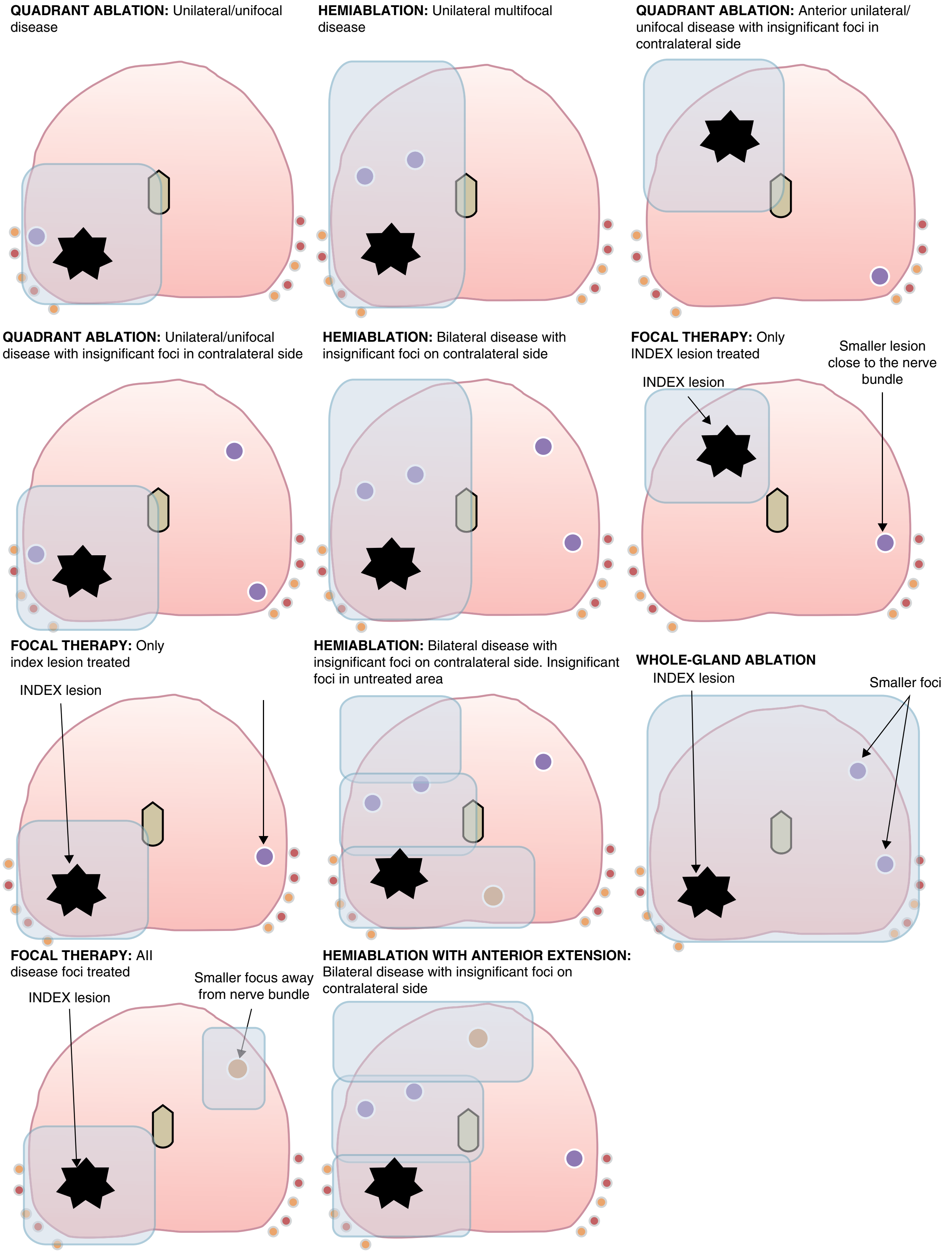


**Figure 135.7** The Ablatherm™ endorectal probe. *Source:* Maude Davageau, France. Reproduced with permission of Maude Davageau.

empty rectum and the endorectal HIFU treatment probe is introduced to the rectum. The position of the probe should be manipulated until the ultrasound images are satisfactory. Once this is acceptable, the prostate can be mapped and the treatment zone defined. The rectal cooling system is then started and the treatment begins. The operator carefully monitors the treatment area, rectal wall distance, reflectivity index, and any reverberations on the user interface to ensure safe delivery of the treatment. If there is concern that structures such as the rectum are at danger of injury, or if any swelling has altered the position of the treatment zone, the treatment can be stopped. The rate of energy delivery (power) differs between devices. It can either be preset (Ablatherm), or it can be changed intraoperatively (Sonablate), dependent on tissue changes observed



**QUADRANT ABLATION:** Unilateral/unifocal disease

**HEMIABLATION:** Unilateral multifocal disease

**QUADRANT ABLATION:** Anterior unilateral/unifocal disease with insignificant foci in contralateral side

**QUADRANT ABLATION:** Unilateral/unifocal disease with insignificant foci in contralateral side

**HEMIABLATION:** Bilateral disease with insignificant foci on contralateral side

**FOCAL THERAPY:** Only INDEX lesion treated

INDEX lesion
Smaller lesion close to the nerve bundle

**FOCAL THERAPY:** Only index lesion treated

INDEX lesion

**HEMIABLATION:** Bilateral disease with insignificant foci on contralateral side. Insignificant foci in untreated area

**WHOLE-GLAND ABLATION**

INDEX lesion
Smaller foci

**FOCAL THERAPY:** All disease foci treated

INDEX lesion
Smaller focus away from nerve bundle

**HEMIABLATION WITH ANTERIOR EXTENSION:** Bilateral disease with insignificant foci on contralateral side

**Figure 135.8** A diagram demonstrating preoperatively planned ablation zones.

during treatment. A standard urethral catheter should be left in place for between 5 and 10 days.

Usually, patients are discharged on the day of surgery. Antibiotics are prescribed as discussed previously. In addition, alpha-blockers are given for 14 days post procedure to reduce postoperative lower urinary tract symptoms and the risk of urinary retention. Postoperative pain following HIFU is generally mild. Because of this, patients' analgesic requirements are usually fulfilled with simple oral analgesics.

## HIFU in focal therapy

Initially, focal HIFU was not truly focal, but subtotal. For example, in 2008 Muto et al. published a series of men who underwent a bilateral peripheral zone as well as a unilateral transition zone ablation following a diagnosis of localized disease after template biopsy [33]. Of this group, postoperative biopsy was performed at 6 and 12 months, revealing residual disease in 10.7% and 23.5% of men respectively [33]. Following this there was a clear move to treat in a truly focal manner and in 2009 Ahmed et al. published the first series in which men with low- to intermediate-risk prostate cancer were treated with HIFU hemi-ablation [34]. Prior to being treated, each patient underwent a full assessment with mpMRI and template biopsy [34]. Transperineal biopsies were performed at 12 months following the procedure and these demonstrated residual disease in 11% of cases [34].

Since then, further case series have been published that demonstrate the efficacy of focal HIFU in treating localized prostate cancer [33–44] (Table 135.1). Centers using the Ablatherm device have reported 5-year biochemical survival rates (according to the Phoenix criteria) of 59–77% [35–37]. Similarly, series that use the Sonablate system have demonstrated 5-year biochemical survival rates of 45–84% [33, 38–41].

Postoperative negative biopsies are a good indicator of treatment success. Success rates according to this parameter vary by study in their timing and technique, but range from 64% to as high as 94% in those where the Ablatherm device is used [10, 35, 37, 42–44]. Similarly, studies in which the Sonablate system is used typically demonstrate 12-month postoperative negative biopsy rates of between 77% and 84% [33, 38, 40]. Retreatment rates are reported in the literature. An exact retreatment rate is difficult to quantify at present due to confounding by studies in which men underwent a second treatment as planned. However, current consensus is that a retreatment rate of 20% within the first 5 years of the primary treatment is acceptable [10].

Negative postoperative biopsies combined with low postoperative PSA nadirs represent the best results and these have been achieved most commonly in men with low-grade disease [36]. Such results compare well with external beam radiotherapy [45], although long-term results are currently lacking and thus optimism must be somewhat restrained. Moreover, the question of what constitutes or defines biochemical failure in men who have undergone HIFU remains essentially unanswered. This is partially due to the inherent difficulty in estimating the ideal posttreatment PSA nadir following any focal treatment for prostate cancer.

## HIFU in salvage therapy

Men with prostate cancer treated in the first instance with external beam radiotherapy or brachytherapy are at varying risk of recurrent disease in the long term, depending on the disease profile at diagnosis. For example, in men with intermediate- to high-risk cancer, the risk of biochemical recurrence can be over 50% after 10 years of follow-up [46]. These patients represent a cohort of men who are at high risk of disease progression to metastatic disease and, inevitably, death [47]. Of this group, up to 98% will receive systemic androgen-deprivation therapy (ADT) as part of their treatment of radio-recurrence, as well as the myriad of unpleasant side-effects that they carry [48]. Many of these patients, however, have solely organ-confined disease at the time of a diagnosis of radio-recurrence. These patients are suitable for focal salvage therapy, which has potential to prevent the need for ADT and its side-effects [49, 50].

Traditionally, salvage therapy is conducted in a whole-gland manner. However, regardless of the technique, this confers a substantial risk of urinary and sexual side-effects [49, 50] due to the previous radiation the region has been exposed to. We now know from histopathological studies that the site of recurrence often arises from the location of the index lesion that preceded treatment [51, 52]. Thus, a focal rather than whole-gland approach, which, similar to primary focal treatment, aims to treat only an area of diseased tissue, may offer cancer control while significantly reducing the risk of complications and side-effects of salvage treatment. Indeed, a systematic review of focal salvage treatment found the complication rates to be either comparable or favorable [53]. Focal HIFU is currently used in this role, albeit mainly in the context of clinical trials.

The first such series was published by Ahmed et al. in 2012 [54]. Thirty-nine men were treated for localized radiorecurrent disease with focal salvage HIFU, 23 with quadrant ablation and 16 with hemi-ablation. PSA responses were observed in 87% of the patient group and in 44% it fell to a nadir of less than 0.5 ng/ml [54]. In the men in whom a PSA response was observed there was a

**Table 135.1** Results from existing studies of focal high-intensity focused ultrasound.

| Reference | Treatment | No. of patients | Mean preoperative PSA level | Gleason score | Biochemical failure | Biopsy type | Biopsy-proven recurrence | Potency | Continence | Adverse events |
|---|---|---|---|---|---|---|---|---|---|---|
| Muto et al. [33] | Zonal ablation | 29 | 5.36 | 5–10 | 2 year: Low: 16.7% Int: 46.4% | TRUS | 6-month: 3/28 (10%); 12-month: 4/17 (23.5%) | NA | 29/29 (100%) | None |
| Ahmed et al. [34] | Hemi-ablation | 20 | 7.3 | ≤4 + 3 | Not specified | MRI + saturation transperineal biopsy | 6-month: 2/19 (11%) in the treated lobe | 19/20 (95%) | 18/20 (90%) | Urethral stricture in single patient |
| Ahmed et al. [54] | Focal/bilateral 2 area ablation | 41 | 6.6 | ≤4 + 3 | Not specified | MRI + saturation transperineal biopsy | 6-month: 9/39 (23%), 3 (8%) with significant cancer | 31/35 (89%) | 38/38 (100%) | Urinary retention in single patient Urethral stricture in single patient |
| Barret et al. [58] | Hemi-ablation | 106 | 6 | 6 | Not specified | Transperineal saturation biopsy | NA | IIEF decrease 19 from 20 | 106/106 (100%) | Urinary retention in single patient |
| El Fegoun et al. | Hemi-ablation | 12 | 7.3 | ≤4 + 3 | Not specified | TRUS biopsy | 12-month 1/12 (8%) | NA | 12/12 (100%) | Urinary retention in single patient |
| van Velhoven et al. | Hemi-ablation | 50 | 6.6 | ≤4 + 3 | 2 year: 11% (Phoenix) | Unspecified | 12-month 6/50 (12%) | 24 (80%) | Transient: 7 (14%)<br>Persistent: 3 (6%) | Urinary retention in 4 (8%) Urethral stricture in 2 (4%) |
| Feijoo et al. | Hemi-ablation | 71 | 6.1 | ≤3 + 4 | 1 year: 6 (9.7%) (Phoenix) | TRUS | 12 month: 16.4% | IIEF decrease 15.4 from 17.9 | 71/71 (100%) | Urinary retention in 4 (6%) |

TRUS, transrectal ultrasound; IIEF, International Index of Erectile Function.

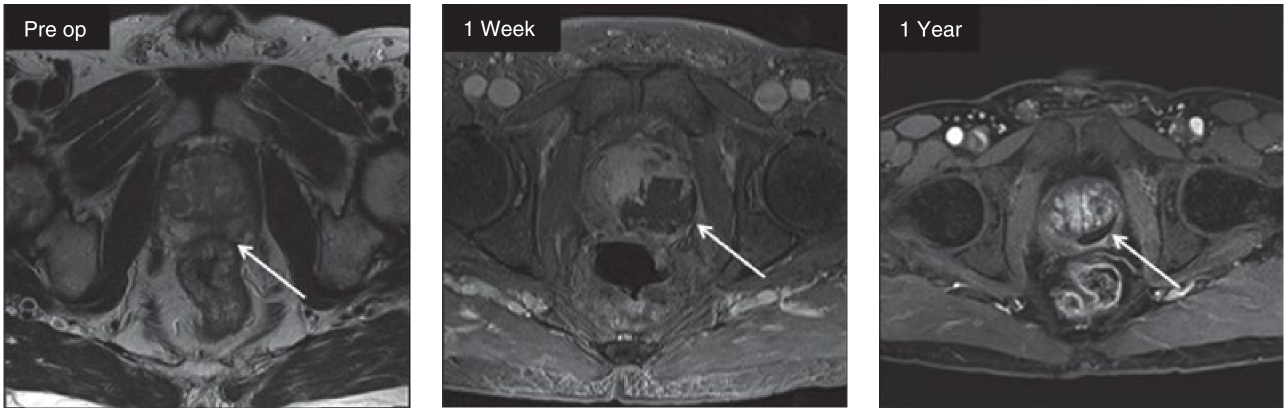


**Figure 135.9** Pre- and postoperative magnetic resonance images.

63% rate of biochemical survival at 3 years according to the Phoenix criteria [54]. Furthermore, in the men where no such PSA response was observed, the rate of biochemical survival at 3 years was 0% by the same criteria [54]. Unfortunately, two patients developed metastases ultimately requiring ADT [54].

The largest yet series of focal HIFU for radiorecurrent disease was published by Baco et al. in 2014 [55]. This two-center study enrolled 48 patients between 2009 and 2012 with a median follow-up of 16.3 months [55]. The mean PSA nadir was 0.69 ng/ml [55]. During follow-up, recurrence was observed in the untreated lobe in 4 of the group and bilaterally in a further 4 [55]. The biochemical survival according to the Phoenix criteria was 83% at 12 months and 52% at 24 months [55]. Six men developed radiologically proven metastatic disease and in 2 further men PSA levels continued to rise in the absence of radiological evidence of metastases [55].

The concept of focal salvage therapy is clearly interesting and adding further options other than ADT to our armory is of extreme importance. However, further investigation is required in this area. It is especially important to determine whether this treatment improves long-term survival when compared to watchful waiting and subsequent systemic therapy. Such studies are currently in progress.

## Postoperative follow-up

Currently, no consensus regarding a defined follow-up protocol exists. However, a suitable regime is three monthly visits for the first postoperative year, six monthly visits for the second postoperative year, and yearly visits thereafter. At these visits PSA monitoring should be performed, as well as lower urinary tract and sexual function, as measured by the International Prostate Symptom Score (IPSS) and quality-of-life questionnaire, and the International Index of Erectile Function 5 (IIEF-5) questionnaire, respectively. Of note, PSA values should be interpreted with caution early after treatment as it may take several months before it reaches its nadir. Furthermore, an optimal definition of biochemical failure following HIFU is lacking. Until the recent past, many centers commonly used the old American Society for Therapeutic Radiology and Oncology (ASTRO) criteria of three consecutive rises in PSA to define biochemical recurrence. However, as this was designed specifically for biochemical recurrence 5 years following radical radiotherapy its use here is not validated and questionable [56]. More recently, however, the Phoenix criteria have been more widely adopted due to the increased robustness in artifact reduction.

Multiparametric MRI is an essential part of post-HIFU follow-up and is usually required 12 months postoperatively (Figure 135.9). Dynamic contrast enhancement (DCE) MRI is of particular use in determining whether there has been adequate early cancer control. A lack of enhancement demonstrates clearly the presence of necrosis and there is good correlation with biochemical outcomes [57]. Posttreatment targeted biopsy of the treatment area is often performed. The best time for this is 12 months postoperatively following the initial posttreatment mpMRI. However, this may be brought forward if there is cause to be concerned [10].

## Complications

The potential complications and side-effect profile of HIFU are well documented. Common side-effects are fairly benign and include visible debris in the urine, new or worsening of existing lower urinary tract symptoms, dysuria, and acute retention of urine. However, these are inconsistently reported in the literature. As demonstrated in Table 135.1, the rate of postoperative retention of urine is reported at between 0% and 6%. Urinary tract infections and cases of epididymo-orchitis occur in between 5% and 10% of patients [33–44]. Hematuria and hematospermia may be present and may persist for some time. In particular, hematospermia may persist for up to 8 weeks. Retrograde ejaculation is common in around 50% and between 0.5% and 15.4% of men [33–44] will develop urinary incontinence requiring pads. Carrying a risk of 5%, a less common side-effect is the development of a urethral stricture (Table 135.1). In comparison to the radical treatments, erectile dysfunction is generally a less common complication. Existing case series demonstrate impotency rates of between 13% and 53% [33–44]. However, the degree of potency in these series is often inadequately assessed and as such directly comparing their results is problematic. The most serious potential complication of HIFU is the recto-urethral fistula that occurs in between 1 in 500 cases [33–44]. In reality, the rate of this complication is likely to be lower as most of these recorded cases are in earlier series with prototype devices. Finally, there is an acceptable retreatment rate of 20% [10] within 5 years of treatment. Subsequent radical therapy is regarded as a true failure of treatment [10].

## Conclusion

HIFU may be considered as a potential minimally invasive treatment for patients with localized low- to intermediate-risk prostate cancer. More favorable oncological outcomes are seen in patients with lower preoperative PSA levels and lower Gleason grades on biopsy. The technique can also be used for salvage treatment, for example in case of radio-recurrence following radical external beam radiotherapy. However, HIFU should be offered with some caution and patients should be carefully selected according to both premorbid and prognostic factors. HIFU is still in relative infancy and as with any novel therapy its efficacy should be evaluated further, particularly in the context of long-term oncological outcomes compared to established radical treatment options. Such studies are currently ongoing and in combination with further technological advances, we are optimistic that the role of HIFU in localized prostate cancer will continue to expand.

See accompanying Video 135.1.

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# 136

# Cryotherapy of the Prostate

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## Introduction

Human experience has definitively established that cold temperatures kill living tissues. Certainly, arctic explorers and polar bear swim clubs have learned about the manifestations of frostbite as frozen cells become ischemic from exposure to freezing temperatures. The medical applications of such low-temperature exposure was first developed for the management of malignancy in nineteenth-century England. Modern technology has provided a mechanism to percutaneously target and ablate clinically localized prostate cancer using the same lethal cold temperatures delivered with needle probes cooled by high-pressure gas-based systems. This chapter provides information about the basic principles of cryobiology, current indications for cryotherapy of the prostate, and procedural details, and summarizes the outcomes as reported in the literature.

## Cryobiology: general principles

### Cryogenic injury

All living cells possess mechanisms for managing exposure to cold temperatures. The limitation of fluid flow across cell membranes, the high concentration of solutes in the cytoplasm and various proteins can minimize the mechanical effect of low temperatures and freezing of water. However, these mechanisms can be ultimately abrogated as the ambient temperature falls below a value of approximately −10 °C. As tissue is exposed to lethally cold temperatures the cells are destroyed through one of several mechanisms. These mechanisms can be summarized into two categories: direct cellular injury and vascular cryogenic injury [1].

Direct cellular injury has been extensively studied in cell culture models and is based on the physics of water and ice formation within the frozen tissue. Two separate mechanisms of ice formation have been described. Initially, ice forms in the extracellular space and propagates through the tissue as temperatures decrease. Since only free water will freeze, the solute concentration rises in the extracellular fluid that has not yet frozen. Intracellular water moves out of the cells in response to this change in osmolarity, causing cellular dehydration with a corresponding increase in the concentration of intracellular solutes. This change disrupts protein function and enzymatic activity and can result in apoptotic cell death [2, 3]. This may be called a solution effect injury.

The next direct injury is a result of the development of intracellular ice crystal formation that only develops at very low temperatures (estimated to be below −40 °C). It is also likely that rapid rates of freezing are required to cause freezing of water that is entrapped within the cells before dehydration has occurred. Intracellular ice formation alters cell physiology by disrupting cell membranes and contributes to cell death by direct cryogenic injury. These cells then die through the mechanism of necrosis or direct disruption rather than the programmed cell death described above. Increasing the duration of exposure to lethal temperatures (<−40 °C) may enhance cell destruction since the limited amount of water that remains unfrozen at the periphery may also freeze [4].

Additional cellular damage is created as the tissue is allowed to warm following the initial freeze process. During thawing, recrystallization occurs when the temperature rises above −40 °C. In the recrystallization process smaller ice crystals coalesce into larger structures that can further disrupt cellular membranes and fracture the cells. Moreover, as extracellular ice crystals melt, a hypotonic extracellular environment is created such that

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free water now flows back into cells, causing cellular edema, swelling, and injury. It has been suggested that passive thawing may be more efficient in prostate cancer destruction.

The second category of cryogenic injury is the vascular mechanism. This type of cryogenic injury occurs preferentially in the microcirculation. Vascular endothelial cells are more sensitive to cold-based injury (as generally understood from experience with frostbite injuries to the extremities of cold weather explorers) and slough into the vessel lumen, resulting in increased vessel permeability and platelet aggregation with thrombosis. This results in tissue ischemia, inflammation, and cell death through necrosis [5]. In addition, thawing and reperfusion injury mediated by the release of free radicals augments the endothelial cell damage and can enhance the inflammatory process with enzymatic degradation of the cellular debris.

Cryogenic injury progresses as the temperature drops and is a time-dependent process. Although cell dehydration occurs at temperatures between 0 °C and −20 °C this is insufficient to produce permanent cellular injury and death. Intracellular ice begins to form at temperatures below −20 °C and is maximal at temperatures below −60 °C, which is uniformly lethal for cancer cells [6]. Importantly, tissue at the periphery of the freeze zone may be exposed to less cold temperatures, despite being included in the frozen tissue, and receive only sublethal injury. In this zone of damage cellular apoptosis is the primary mechanism for cell death and is not uniform. Cryobiologists have attempted to augment the cellular injury that results from exposure of cells to sublethal temperatures in an effort to increase the percentage of cancer cells that suffer programmed cell death. Clarke et al. have demonstrated that several different chemotherapeutic agents can potentiate the lethal impact of freezing cancer cells and may represent the optimal mechanism for destroying all cells within a target tissue volume [7].

### Cryoimmunology

The mechanical freeze fracturing of living cancer cells has been demonstrated to release tumor antigens into the microcirculation and initiate an immune response [8, 9]. This potential therapeutic mechanism has been demonstrated in rats treated with cryoablation of a prostate cancer with concomitant administration of BCG [10]. Despite these results, the clinical exploitation of this phenomenon has been limited, although recent studies have suggested that the immune response to the cryoablation of a malignancy within the prostate can be augmented with systemic agents [11, 12]. It remains possible that a multimodality approach using local cancer cryoablation with systemic immune modifiers may result in the treatment of metastatic prostatic cancer in the future.

## Indications for cryotherapy of the prostate

Primary cryoablation of the prostate is considered to be an option for the treatment of localized prostate cancer. The American Urologic Association's (AUA) Best Practice Statement considered cryosurgery to be an option for patients who either do not desire or are not good candidates for conventional treatment modalities [13]. The European Association of Urology considers cryoablation of the prostate to be investigational at this time [14].

The optimal candidates for primary cryoablation of the prostate for curative intent are men with likely organ-confined prostatic malignancy with prostate gland volumes between 25 and 80 ml without significant protrusion of the prostate into the bladder or the rectum. The AUA Best Practice Statement indicates that cryoablation is an option for low-, intermediate-, and high-risk clinically localized prostate cancer, setting no apparent limits to prostate specific antigen (PSA) values, clinical stage, or biopsy Gleason score. However, this document does not specifically address the suitability for cryosurgery of high-risk patients who may require multimodality treatment. It is likely that the optimal clinical stage for prostate cryoablation is cT1 or cT2 tumors. Cryoablation has been evaluated in men with clinical T3 cancers with mixed results [15, 16]. Therefore men with locally advanced prostatic cancers may elect for cryoablation but with the understanding that the risk of incomplete ablation and of associated toxicity is increased.

Prostate cryoablation has demonstrated the capability to destroy prostatic tissue with a reduction in the volume of the prostate gland following the procedure, suggesting that this modality can treat men with clinically localized prostate cancer and associated benign prostatic enlargement with voiding dysfunction [17]. Therefore, men with prostate cancer within the setting of benign prostatic enlargement may elect this treatment approach rather than alternatives that do not reduce the volume of prostatic tissue.

### Salvage cryoablation

Salvage prostatic cryosurgery after primary radiation therapy has been proposed as an alternative to salvage radical prostatectomy with the potential for reduced morbidity. Salvage cryoablation has been reported after interstitial brachytherapy as well as external beam therapy [18]. There have been no prospective comparison trials between salvage radical prostatectomy and cryoablation following initial radiation therapy but clinical case series have suggested that the surgically related toxicity is likely reduced with cryoablation [17]. In addition, the oncologic outcome of cryoablation in the salvage setting may be related to the location and volume of persistent malignancy within the prostate gland [19].

Therefore, candidates for salvage prostate cryoablation include men with a small volume of prostatic cancer, as identified on postradiation prostate biopsy, following evaluation for an elevated PSA following first-line therapy without radiographic evidence of metastatic disease. The optimal PSA level for salvage cryoablation has not been established but is likely similar to that of a salvage radical prostatectomy. A serum PSA value below 4 ng/ml has been associated with the highest likelihood of organ-confined prostate cancer that can be eradicated with a radical prostatectomy. It is possible that this value is similar for salvage cryoablation [20].

Radiation-persistent prostatic adenocarcinoma is associated with a higher incidence of seminal vesicle invasion and higher pathologic Gleason sum on prostate biopsy [21]. Although cryoablation is capable of destroying the malignancy irrespective of the histologic grade, successful management of invasive disease within the seminal vesicles is unlikely. Therefore, a seminal vesicle biopsy could be helpful in determining the correct candidate for a salvage cryoablation.

## Cryoablation procedure: whole-gland therapy

As technology has improved over the years, we discuss only the current third-generation technology, leaving the description of previous techniques (first and second generations) to historical reference.

Third-generation cryotechnology is based on dual-gas systems exploiting the Joule–Thomson principle of gas expansion to provide heat subtraction and delivery through small-caliber cryoprobes. The same effect is used in home appliances such as air conditioning systems and refrigerators. Briefly, these systems use pressurized argon and helium gases delivered to the cryoprobe in a closed circuit. When argon gas is allowed to expand through a pinhole opening at the tip of the cryoprobe, the gas changes its internal energy state as the pressure drops and the process consumes energy, thereby reducing the temperature. The inverse process happens during thawing, whereby helium is expanded in the cryoprobe, thus releasing energy and heating the probe. The opposite effects achieved with the two gases derive from different molecular properties (internal energy) of argon and helium gases, based on attractive and repulsive forces of gas molecules. The latest technology introduced an argon-only system whereby both freezing and thawing phases are achieved by altering the physical properties of argon, thus simplifying the technologic complexity of cryoablation and obviating the need for an additional gas.

The cryoablation suite consists of a console that monitors and controls the procedure, argon (and sometimes helium) pressurized gas tanks, a urethral warming device, and peripherals (transrectal stepper-mounted ultrasound, cryoprobes, and thermocouples). The system's user interface integrates ultrasonographic imaging that guides cryoprobe positioning and monitors the formation of the iceball, receiving input from the urethral warmer and the temperature probes.

Different numbers, positions and configurations of probes allow for sculpturing of the iceball with precision. Cryoprobes and thermocouples are positioned transperineally through a brachytherapy-like template (Figure 136.1). Currently, thin and ultrathin (17G, 1.5 mm) cryoprobes are available. Iceball formation is monitored both by temperature probe readings and by real-time ultrasound.

Cryoablation is typically an outpatient procedure and can be performed under general, spinal, or locoregional anesthesia. With the patient in lithotomy position, probes are positioned using the grid under the guidance of transrectal ultrasound. Thermocouples are typically positioned adjacent to the neurovascular bundles, sphincter, and Denonvilliers' fascia to assist with iceball monitoring. After probe positioning, flexible cystoscopy is used to verify that the probes have not penetrated the urethra or bladder. The urethral warming device is then introduced

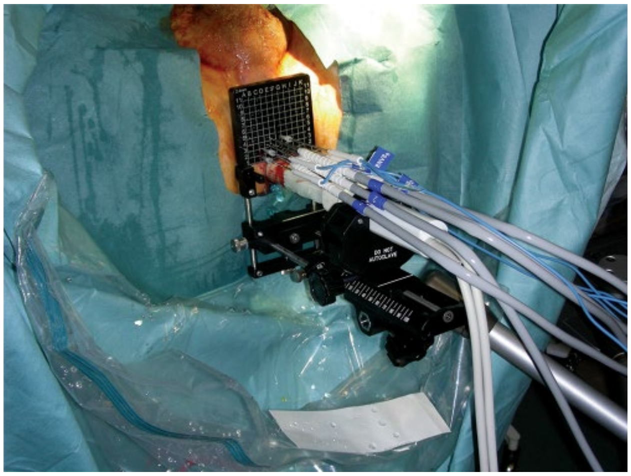

**Figure 136.1** Transperineal percutaneous prostate cryoablation under ultrasound guidance. Prostate cryoprobes are placed percutaneously into the prostate through a brachytherapy grid under ultrasound guidance.

over a super-stiff guidewire. Although some surgeons place a suprapubic tube to provide bladder drainage in the postoperative period, a urethral catheter can alternatively be utilized at the end of cryoablation, replacing the urethral warming device. Freezing proceeds in an automated manner, using dual freeze–thaw cycles, monitored by ultrasound and thermocouple readings.

Cryoablation results in acute swelling of the prostate that typically resolves in 1–2 weeks, during which time a urethral catheter (or a suprapubic tube) provides bladder drainage. After a successful voiding trial, the catheter can be removed. We recommend assessing voiding ability within one week postoperatively as in our experience most patients are able to spontaneously void by that time.

## Outcomes

### Oncologic outcomes of primary whole-gland ablation

The oncologic outcomes of primary prostate cryoablation have been extensively evaluated in both single-institution and pooled population studies and are presented in Tables 136.1 and 136.2. The reported clinical series suggest that cryoablation of the prostate can achieve acceptable long-term disease-free survival rates that are comparable to alternative options such as radical prostatectomy and radiation therapy. However, there have been no prospective trials that can provide more definitive information about the cancer control rates for cryoablation relative to these more established therapies. In addition, the definition of a successful ablation is variable and no specific PSA value has been established as a clear indicator for disease eradication. A pooled analysis of 1111 men demonstrated that 80% achieved a postcryoablation PSA nadir below 0.4 ng/ml. This achievement was then associated with a 90.4% progression-free survival for low-risk men, 81% for intermediate-risk and 73.6% for men with high-risk malignancy at 5 years [22]. Another pooled analysis demonstrated similar findings, with 14% of men having persistent cancer on a routine postcryoablation prostate biopsy [23]. Finally, cryoablation resulted in a 59.1% biochemical progression-free survival at 5 years following therapy in men with high Gleason score prostatic cancer, suggesting that this modality is a rational option for some men with high-risk disease [24].

### Oncologic outcomes of salvage prostate cryoablation

Pisters et al. reviewed the oncologic outcomes of 279 men treated with salvage prostate cryoablation after primary radiation therapy and found that 83% of men manifest detectable PSA levels but with a 58.9% biochemical recurrence-free survival at 5 years following treatment [20]. Since transperineal percutaneous prostate cryoablation is a very flexible treatment approach which can be alerted to individualize therapy for men based on cancer location, prostate anatomy and desire to reduce specific treatment-related side-effects it is possible to reduce the volume of the prostate tissue included in the ablation zone even in the salvage setting. A series of 91 men were treated with such a reduced ablation template, described as a focal ablation, for salvage therapy and achieved a 46.5% biochemical recurrence-free survival at 5 years [25]. These results suggest that the oncologic outcomes of salvage cryoablation are acceptable given the complexity of this patient population.

**Table 136.1** Oncologic outcomes of primary cryoablation.

| | | | Biochemical disease-free survival (%) | | | |
|---|---|---|---|---|---|---|
| **Study** | **No. of patients** | **Definition** | **1 year** | **3 years** | **5 years** | **7 years** |
| Hubosky et al. [39] | 89 | ASTRO | 94 | – | – | – |
| | | ≤0.4 | 70 | – | – | – |
| DiBlasio et al. [26] | 78 | ASTRO | 97.9 | 95.7 | 71.1 | – |
| Prepelica et al. [27][a] | 65 | ASTRO | 83.3[c] | – | – | – |
| Cresswell et al. [28] | 31 | ≤0.5 | 60 | – | – | – |
| Donnelly et al. [29] | 117 | Nadir + 2 | – | 82.9 | 75 | – |
| Bahn et al. [30][b] | 590 | ASTRO | – | – | – | 89.5 |
| Jones et al. [23][b] | 1198 | ASTRO | – | – | 77.1 | – |

[a] High-risk patients.
[b] Not pure third-generation technology.
[c] Median follow-up of 35 months.

**Table 136.2** Oncologic outcomes of salvage cryoablation.

| | | | Biochemical disease-free survival (%) | | | |
|---|---|---|---|---|---|---|
| **Study** | **No. of patients** | **Definition** | **1 year** | **3 years** | **5 years** | **7 years** |
| Ng et al. [31] | 187 | Nadir + 2 | – | – | 56 | – |
| Ghafar et al. [32] | 38 | Nadir + 0.3 | 86 | 74 | – | – |
| Ismail et al. [33] | 100 | ASTRO | 83 | 59 | – | – |
| Cresswell et al. [28] | 20 | ≤0.5 | 66.7 | – | – | – |
| Bahn et al. [34][a] | 59 | ≤0.5 | – | – | – | 59 |
| Pisters et al. [20][a] | 279 | ASTRO | – | – | 59 | – |

[a] Not pure third-generation technology.

**Table 136.3** Complication rates after primary cryoablation of the prostate using third-generation technology.

| | | Complication rate (%) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Study** | **No. of patients** | **Slough** | **Perineal pain** | **Urinary retention** | **UTI/ sepsis** | **Urethral stricture** | **Fistula** | **incontinence** | **ED** |
| Bahn et al. [30] | 210 | NR | NR | 3 | NR | NR | 2.4 | 9 | 41 |
| Shinohara et al. [36] | 102 | NR | 3 | 23 | 3/3 | NR | 1 | 4 (15[a]) | 86 |
| Han et al. [37] | 106 | 5 | 2.6 | 3.3 | 0 | NR | 0 | 3 | 87 |
| Wake et al. [35] | 100 | 1 | NR | 20 | NR | 2 | 0 | 8 | NR |
| DiBlasio et al. [26] | 78 | NR | NR | NR | NR | 1 | NR | 7.7 | 84.6 |
| Cohen [38] | 98 | 2 | NR | NR | NR | NR | 0 | 0 | NR |
| Prepelica et al. [27][b] | 65 | NR | 0 | 3.1 | NR | NR | 0 | 3.1 | NR |
| Hubosky et al. [39] | 89 | 2 | 6 | 4 | 1/0 | NR | 1 | 2 | NR |
| Donnelly et al. [29] | 117 | NR | NR | 15.4 | NR | NR | NR | 32.5 | 70.9 |
| Chin et al. [40][c] | 33 | NR | 32 | NR | NR | NR | NR | 7 | 29 |

[a] Including patients who underwent transurethral resection of prostate following cryoablation.
[b] High-risk patients.
[c] Locally advanced disease.
UTI, urinary tract infection; ED, erectile dysfunction; NR, not reported.

## Complications of whole-gland primary cryoablation

Percutaneous transperineal prostate cryoablation is performed under transrectal ultrasound guidance and was developed to specifically avoid some of the side-effects related to radical prostatectomy and radiation therapy options. In fact, it is the hope for a reduction in overall toxicity that makes cryoablation an attractive option for men with clinically localized prostatic adenocarcinoma. However, there are several associated side-effects from cryoablation that should be exposed to the patient during the informed consent discussion.

Minor self-limiting complications include transient scrotal edema, penile edema with ecchymosis, and possible penile paresthesia [35]. These symptoms typically develop immediately following the procedure and resolve within 2–3 weeks. Table 136.3 gives a summary of the complications after primary whole-gland cryoablation.

Urethral mucosal sloughing is rare and in most series is reported to occur in less than 5% of patients. The incidence of rectourethral fistula today is also low (0–2.4%). Urinary incontinence requiring pads has been reported to occur in less than 10% of patients and is typically transient. The incidence and presentation of incontinence has been reported using various definitions, with most studies not distinguishing between stress, urge, and mixed incontinence, making it challenging to derive precise conclusions. The incidence of urinary retention has varied widely across the literature and requires further evaluation as technical differences may have accounted for this discrepancy between studies. However, the majority of urinary retention events are transitory and resolve within 2–4 months. The more recent series suggest urinary retention may occur in less than 5% of cases [25, 35].

A recent report based on the CaPSURE database analyzed the incidence of urethral stricture after primary therapy for prostate cancer. The overall incidence of stricture after primary cryosurgery was 2.5%. At 1, 2, and 4 years, 96%, 95%, and 87%, respectively, of cryotherapy patients were stricture free. These data compare favorably to other treatment options: incidence of stricture formation 1.1% for watchful waiting, 2% for androgen-deprivation therapy 2%, and 8.4% for radical prostatectomy.

Currently, the available data are limited both due to many of the reported series being updates of previous studies and because data collection has not been standardized, thus precluding a detailed and accurate description of complications after cryoablation. Researchers should strive to better collect follow-up information to delineate accurately the complications profile and determine risk factors for these adverse events.

## Complications of whole-gland salvage cryoablation

A summary of complications after salvage cryoablation is outlined in Table 136.4. Overall, the toxicity profile appears similar to that of primary cryoablation with the exception of increased rates of urinary incontinence and pelvic pain. Overall, salvage cryoablation offers a complication profile that compares well with other salvage techniques. A recent review of the literature concluded that salvage cryoablation represents a viable alternative to the technically challenging salvage radical prostatectomy and can be recognized as an established option for radiopersistent or recurrent prostate cancer [41].

## Functional outcomes: urinary continence and erectile function

Information about urinary incontinence and erectile dysfunction following whole-gland primary and salvage prostate cryoablation are given in Tables 136.3 and 136.4. Erectile dysfunction is highly prevalent after whole-gland therapy and should be expected in the salvage setting. Importantly, although erectile dysfunction in previously potent men would be universal in the immediate postoperative period, with whole-gland primary cryoablation longer term follow-up suggests that as many as 46.8% of men will regain erectile function by 24 months [43]. This recovery was confirmed in a prospective trial comparing cryoablation to high-frequency ultrasound ablation [44]. Therefore, the changes to erectile function should be discussed with men prior to the selection of this treatment approach; many men with normal preoperative erectile function can expect recovery of this state over time.

The accurate placement of cryoprobes into the prostate through a brachytherapy grid under transrectal ultrasound guidance allows for the development of an individualized ablation template that can minimize injury to the pelvic floor and urethral sphincter. In fact, this technical possibility is one of the more attractive aspects of this surgical approach for many men with clinically localized prostate cancer. The manufacturers of cryoablation equipment have developed cryoprobes with short iceball lengths or even adjustable iceball lengths that allow for the targeted ablation of prostatic tissue while reducing the risk of injury to the sphincter.

**Table 136.4** Complication rates after salvage cryoablation using third-generation cryotechnology.

| | | Complication rate (%) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Study** | **No. of patients** | **Slough** | **Perineal pain** | **Urinary retention** | **UTI/ sepsis** | **Urethral stricture** | **Fistula** | **Incontinence** | **ED** |
| Ng et al. [31] | 187 | NR | 14 | 21 | 10 | 2.1 | 2 | 40 | NR |
| Han and Belledugrun [42] | 29 | NR | NR | NR | NR | NR | 0 | 7 | NR |
| Ismail et al. [33] | 100 | 2 | 4 | 2 | NR | NR | 1 | 13 | 86 |
| Pisters et al. [20][a] | 279 | NR | NR | NR | NR | NR | 1.2 | 4.7 | 69.2 |
| Ghafar et al. [32] | 38 | 0 | 39.5 | 0 | 2.6 | NR | 0 | 7.9 | NR |
| Cresswell et al. [28] | 20 | NR | NR | 4 | NR | NR | 0 | 4 | 86 |
| Bahn et al. [34] | 59 | NR | NR | NR | NR | NR | 3.4 | 8 | NR |

[a] Series includes a portion of cases treated using second-generation technology.

UTI, urinary tract infection; ED, erectile dysfunction, NR, not reported.

Urinary continence rates are as high as 98% at 24 months following whole-gland ablation [43, 45].

## Future modifications of prostatic cryoablation: focal or individualized therapy

The incorporation of transrectal ultrasound guidance into the performance of transperineal prostate cryoablation has provided an opportunity to more fully understand the individual patient's prostate anatomy as well as the location of the known prostatic cancer. In addition, retrospective evaluations of whole mounted prostate specimens from radical prostatectomy series have identified the most likely location and volume of all lesions within the prostate of men with clinically localized adenocarcinoma [46]. Therefore, the technical flexibility of the ablation approach coupled with improved information about cancer volume and anatomic location should allow a more precise destruction of the malignancy while avoiding injury to adjacent structures. This concept of a targeted ablation has become known as an individualized ablation, or more commonly, focal ablation. Figure 136.2 depicts one such ablation template with a focus on a left side cancer within the prostate.

Prostatic adenocarcinoma has been established as a multifocal disease process within the prostate gland of aging men. However, early detection strategies have resulted in the identification of prostate cancer with a smaller volume of malignancy and a reduced number of satellite lesions [47]. Onik and co-workers provided the first report of a focal ablation, defined as a less than total ablation of the prostate directed at the known malignancy, in 2002. They documented effective reduction in the postoperative PSA with negative follow-up prostate biopsy in a total of nine men associated with retained urinary control and erectile function [48]. The authors advocated for the term “male lumpectomy” to describe this technical approach [49].

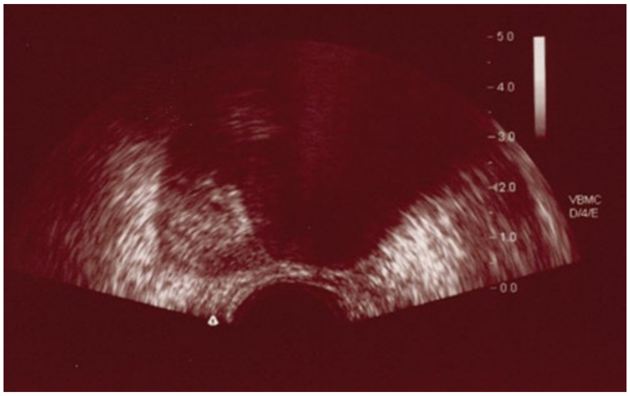

**Figure 136.2** Focal prostate cryoablation. A less than total focal prostate cryoablation is performed for a left side prostatic adenocarcinoma designed to avoid injury to the right side neurovascular bundle.

Since that publication a number of other investigators have pursued focal ablation as a viable treatment option to maintain oncologic efficacy while reducing treatment-related intensity and toxicity. A pooled analysis in 2012 identified 1160 men who had been treated with a focal ablation [50]. Approximately 3.7% of these men were found to have persistent prostate cancer on follow-up biopsy, suggesting that a less than total ablation of the prostate has only a small risk for incomplete disease eradication in properly selected men. It also appears that there

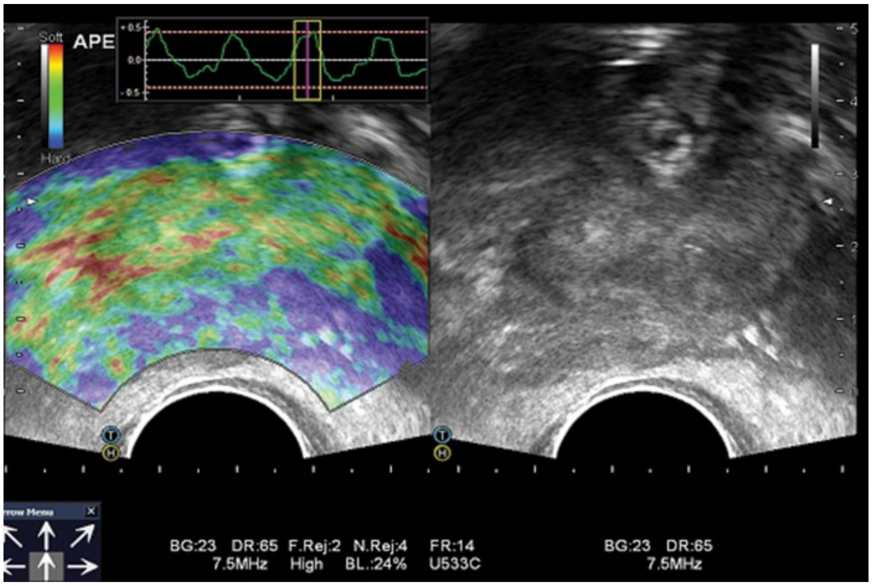

**Figure 136.3** Elastography for prostate cancer. Transrectal ultrasound of the prostate with strain elastography identifying a region of increased stiffness (blue) in the left lateral base.

is a reduced risk of urinary incontinence as well as a high rate of return of satisfactory erectile function [51, 52].

Focal or individualized prostate cryoablation designed to eradicate the known cancer while avoiding injury to the adjacent neurovascular bundles and pelvic floor represents an attractive technical advance in the management of clinically localized prostate cancer. It is possible that this treatment will improve further as new imaging modalities such as multiparametric prostate MRI and multiparametric prostate ultrasound using Doppler and elastography (depicted in Figure 136.3) provide improved localization of the prostatic cancers within the prostate gland [53, 54].

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# 137

# Cryosurgical Ablation of the Prostate

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## Introduction

Cryosurgery involves the use of ultra-low temperatures, below the freezing point of water, which causes thermal tissue damage and cell death. Cryoablation of the prostate is a minimally invasive treatment option for prostate cancer that offers shorter hospital stays, minimal risks of bleeding, and can even be offered to patients who are not good surgical candidates.

In 2004 almost 25% of patients underwent minimally invasive primary treatment of prostate cancer and of these 2.8% underwent cryoablation [1]. In 2010 this number had risen to 4% [2], and from the Cryo-On-Line Database (COLD) registry data we note that over 50% of patients who underwent cryoablation did so as a primary treatment modality for prostate cancer.

## History of cryoablation

Cryoablation actively uses the Joule–Thomson effect. When a compressed gas undergoes sudden expansion it causes a change in temperature. Many gases cause a cooling effect, but helium causes warming (Figure 137.1). This physical effect of cooling during cryoablation was first achieved using nitrogen and then, later, argon. With the demonstration that freeze–thaw cycles cause a more sustained and predictable cell death, the newer generation machines for ablation started using argon–helium combination. From when prostate cryoablation was first described in the 1960s, the technology and technique have undergone a process of steady evolution.

One of the earliest descriptions of cryosurgery involved the use of salt solutions to achieve subzero temperatures in order to induce tissue destruction in easily accessible cancers like those of the breast and uterine cervix. Subsequently cotton swabs soaked in liquid nitrogen were described for the treatment of skin lesions [3].

In 1961, Cooper and Lee first described the use of a hollow cannula constructed of stainless steel with an outer and inner tube. The length of the cannula was electrically insulated using copper wire and this was kept at body temperature, but the tip itself was noninsulated and was used for delivery of iceball measuring 8 mm in size in their experiments [4].

Prostate cryosurgery was first described by Gonder et al. in the 1960s [5, 6], and since then many technical refinements have continued to occur. The third-generation devices now use the argon–helium gas combination to produce the freeze–thaw cycles. Ablation probes have also decreased in size, and fine 17 gauge cryoprobes can now deliver precise iceballs measuring 8–10 mm in diameter.

The use of transrectal ultrasound (TRUS) to monitor the "cryolesion" or iceball was developed and popularized by Onik et al. in 1988 [7], and subsequently the same group described the use of a urethral warming device in 1993 to protect the urethra against injury [8].

Techniques aimed at improving the efficiency of cryoablation while minimizing complication rates followed. Onik et al. reported that raising the TRUS probe to push on the posterior wall of the rectum caused the anterior rectal wall to be pulled away from the prostate, creating a spatial separation between the prostate and the rectum [8]. Onik later described another technique to further accentuate this separation by injecting saline into the layers of the Denonvilliers' fascia [9] to minimize the chances of a rectal injury and rectourethral fistula. They also showed that the use of 6–8 cryoprobes results in better prostate tissue destruction than the original five-probe technique [9].

Prostate cryoablation devices are now into the third generation. The first-generation devices used liquid nitrogen and the probes were larger. The total time required for the procedure was also longer and

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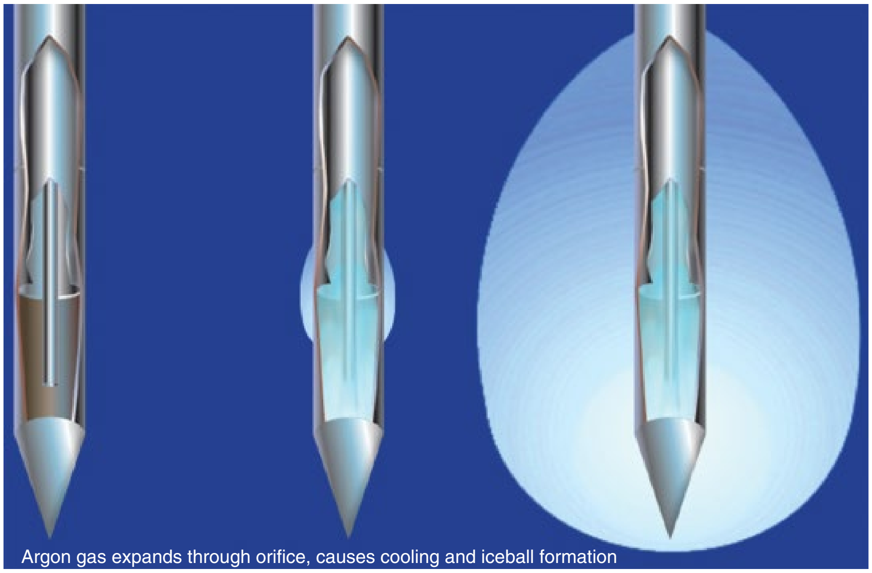
Argon gas expands through orifice, causes cooling and iceball formation

**Figure 137.1** Ultrathin needle probes: Argon gas expands through the orifice and causes cooling (Joule–Thomson Effect). *Source:* Endocare Inc., a subsidiary of HealthTronics Inc., Texas, USA. Reproduced with permission of HealthTronics, Inc.

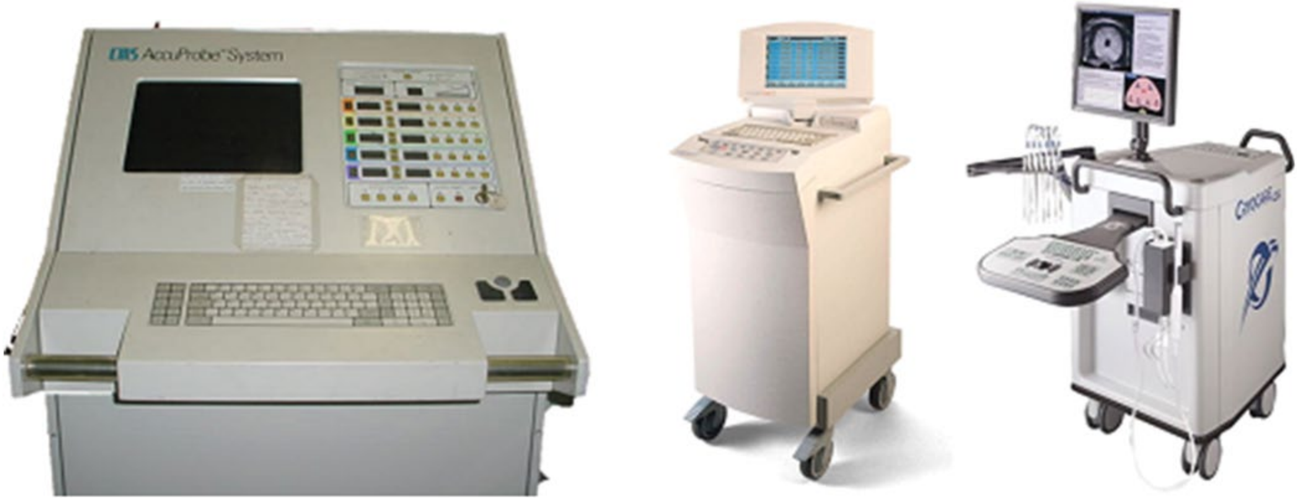

**Figure 137.2** First- (left), second- (center), and third-generation (right) cryoablation machines. *Source:* Endocare Inc., a subsidiary of HealthTronics Inc., Texas, USA. Reproduced with permission of HealthTronics, Inc.

temperature monitoring was not possible. The machines were also bigger and lacked mobility (Figure 137.2). The second-generation machines were more compact, and used freeze–thaw cycles with helium gas for the thaw cycles. The third-generation machines incorporated the technology into ultrathin 17G probes, along with temperature monitoring (Figure 137.2).

## Mechanism of tissue injury and cell death in cryoablation

Cryoablation causes cell damage through a drop in temperature that causes freezing. The aim of cryoablation is to cause destruction of the tumor by creating overlapping cryoablation zones to encompass the entire volume of tumor, while minimizing collateral damage to surrounding normal tissues. Various studies have looked at the minimum temperature required to achieve destruction of tumors, and the mechanisms of injury, importance of cooling rates, and time of contact, as well as the effect of freeze–thaw cycles.

In their review, Cooper summarized five mechanisms that are responsible for tissue destruction: dehydration and change in electrolyte concentration due to removal of water from solution, crystallization with rupture of cellular membranes, permanent change in the protein molecules of the cell membrane causing irreversible loss of semi-permeability, thermal shock, and vascular stasis and coagulation [10].

Today we understand the importance of intracellular ice formation which causes the secondary osmotic shifts from structural damage to the semipermeable membrane. This has been postulated to be an important mechanism of cellular rupture and death in cells in contact with, or very near to the cryoprobe and its iceball. However, there is a rise in temperature more peripherally and in this zone other mitochondrial and cytokine-mediated cellular injury occurs [11]. Studies have shown that Bax, a cytoplasmic protein that promotes apoptosis, is increased in the cytoplasm on thawing, [11], but it is the ratio of the Bax to the Bcl-2 (a mitochondrial membrane antiapoptotic protein) that determines whether a cell can survive the effect of marginal freezing that does not cause direct cell rupture [12].

Robilotto and colleagues have performed *in vitro* studies describing possible apoptotic pathways responsible for cell death using PC-3 prostate cancer cell lines and by analyzing caspase activity. Caspase-9 is considered a key component of the intrinsic pathway that follows release of mitochondrial proteins and cytochrome *c*, whereas caspase-8 is a marker of the Fas pathway death-induced signaling complex (DISC) [13]. Robilotto et al. showed that cell death started within 30 minutes of freezing to temperatures <−30°C, peaked at 90 minutes and was complete within 6 hours. Cell death in this model occurred predominantly through membrane-mediated pathways [13]. Apoptosis was more delayed in cells that were exposed to temperatures over −30°C occurring between 6 and 24 hours, and the mechanism was believed to be through an intrinsic or mitochondrial pathway [13].

Other *in vitro* cryoablation models have been conducted in the laboratory for the purpose of determining the causes of cell death and also to refine ablation techniques (i.e. to optimize the number of freeze–thaw cycles). Temperatures of −15°C to −20°C are achieved before ice crystals start to form [10]. However, Neel et al. showed that even −28°C is not uniformly lethal to tumor cells [14], and recommended repetitive freezing to temperatures below −60°C for effective tumor ablation [15]. Staren et al. studied the effect of cryoablation on breast tumors, and found that when the temperature at the periphery of tumors was maintained at −40°C for <7 minutes, there was good response in tumors <1.5 cm, but there was viable tumor cells at the periphery with larger tumors. When the temperature was further dropped to −70°C, there was still no significant difference in the outcomes even with the addition of a two-freeze, passive thaw cycle, until the freeze time was increased to 15 minutes [16].

A general consensus exists that temperatures of −40°C, have been shown to cause adequate cell destruction. The mechanism of cell death is different at different freezing rates: at rapid freeze rates of over 25°C per minute it is due to rapid intracellular ice formation, but at slower freeze rates of less than 5°C per minute, changes in the chemical composition of the cells were the main mechanism of cell death [17].

Since intracellular ice formation is an important component of cryoablation, it is essential to understand the factors that affect it: rate of cooling and the endpoint temperature can be controlled extrinsically, but the water content of tissues and the presence or absence of nearby heat sinks (such as major blood vessels that can transfer energy rapidly and prevent achievement of target temperatures) are intrinsic to the tissues being ablated. The cooling rate and endpoint temperature achieved are also interrelated. A more rapid cool rate of 25°C/minute can achieve cell death at higher temperatures of −19°C and the endpoint temperature does not need to go all the way down to −40°C [17].

Ice is a bad conductor of heat and, as more ice forms, it starts to prevent further propagation of the iceball. There are, therefore, limits to the size of the iceball that can be achieved for a given rate of cooling, and for cooling rates more than 25°C/minute, an iceball equilibrium is achieved at 8–10 mm in size [17].

Today's latest generation machine can achieve adequate intracellular ice formation through double or even triple freeze–thaw cycles [17, 18], and by ensuring the correct cooling rate for a given endpoint temperature.

## Types of cryoablation

The commonly used cryoblation techniques are shown in Figure 137.3. Targeted ablation is not often used since a conventional biopsy cannot detect all tumors. Targeted ablation is ablation of a well-defined lesion, proven on biopsy. The ablation aims to destroy the tumor and a part of surrounding normal prostate similar to the partial nephrectomy model. (Figure 137.3 left side of prostate) This form of ablation can have a good nerve-sparing effect, but the risk of recurrent or residual cancer is higher. Targeted ablation would be optimal for repeat or second ablations in patients who have had a primary ablation. Zonal ablation is a slightly more extended form of ablation that involves more prostate tissue and aims to encompass all areas with biopsy-proven cancer. In general, zonal ablation involves contiguous areas, but can be combined with targeted ablation of a single focal lesion too. Hemigland ablation (Figure 137.3 right side of the prostate) involves ablation of one lobe of the prostate and whole-gland ablation involves ablation of the whole prostate.

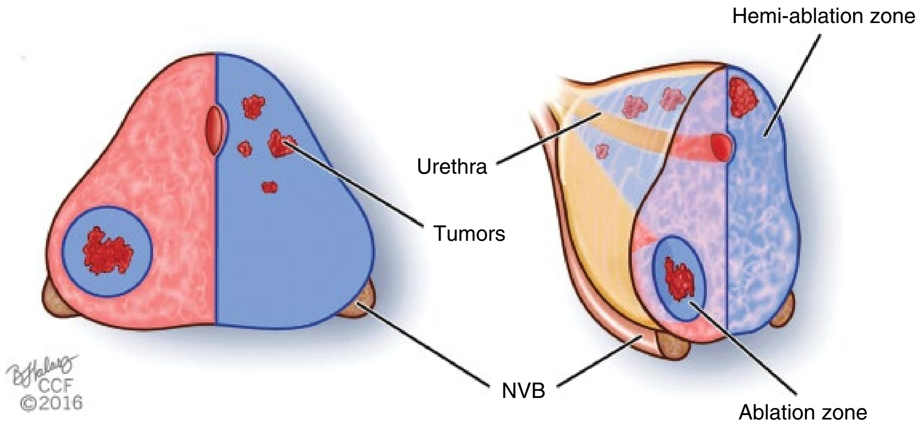

**Figure 137.3** Types of cryoablation: Targeted ablation on the left side of the prostate and hemiablation on the right.

## Patient selection

Prostate cryoablation is now being offered in the primary and salvage setting. Appropriate case selection is essential for ensuring optimal results, better biochemical relapse-free survival, and lower complication rates.

An ideal treatment model relies on the accurate and consistent identification of tumors in their entirety, and treatment delivery that consistently and predictably eliminates all of the cancer without causing any collateral damage to normal tissues. Cryoablation for prostate cancer does not consistently conform to the ideal treatment model. First, assessment of the anatomical extent of disease in terms of tumor location and volume cannot be accurately or consistently performed in all cases. Second, cryoablation, as a technology, has some limitations in how consistently and predictably it can eliminate prostate cancer without affecting the urethra, external sphincter, and neurovascular bundles. Lastly, there are challenges with following patients after nonexcisional treatment such as cryoablation, since we continue to rely on surrogate markers of recurrence used after radiation therapy.

Since the aim of treatment is to provide oncologic cure, while minimizing complications, it is extremely important to identify any parameters that are statistically associated with higher failure rates or with poorer clinical outcomes. In general, patients with high-volume or aggressive disease, such as extraprostatic extension or seminal vesicle involvement, will demonstrate poor clinical outcomes as a result of higher rates of residual disease and/or higher rates of complications.

On the other hand, patients without high-volume or high-risk disease are potential candidates for focal treatment, which has lower complication rates compared to whole-gland cryoablation. A study on salvage cryoablation showed higher rates of urinary incontinence (13% vs. 0%), erectile dysfunction (100% vs. 71%), and fistulas (4% vs. 0%) in patients undergoing total cryoablation as compared to focal ablation [19].

Prostate cancer is often multifocal, as found in 79.5% of whole-mount prostate specimens after radical prostatectomy [20]. Cancer proximity to the urethra is also another cause for concern since urethral warming devices, designed to prevent cryo-injury to the urethra can potentially result in undertreatment in select patients. Studies have shown that in up to 66% of cases, foci of cancer were found within 5 mm of the urethra [20] with a mean distance of 3 mm from the urethra (17% of them in contact with the urethra) [21]. The prostate apex is another area that is at risk for residual cancer after cryoablation, with some studies suggesting that up to 74% of patients have apical cancers [21].

Results from salvage prostatectomy series also reflect similar patterns, with multifocal cancers seen in 28% of men, apical recurrences in 95% of men, and 65% of cancers found to be within 5 mm from the urethra (7% involving the urethra) [22]. In fact, radiation-resistant cancers show high incidence of extraprostatic extension (43%) and seminal vesicle involvement (28–62.5%) [22, 23], and such patients are not suitable for cryoablation with curative intent.

Routine prostate biopsies often do not detect the extent or volume of prostate cancer, and studies have demonstrated multifocal bilateral disease in 70.7–72.0% of men diagnosed with unilateral cancer on biopsy after review of the final radical prostatectomy specimens [24, 25]. Moreover, extracapsular disease was seen in 5% of men who underwent prostatectomy, on the side deemed to have completely benign pathology at biopsy [24]. More extensive saturation biopsies, in theory, may appear to be able to improve detection rates. This may then improve concordance between biopsy and radical prostatectomy [26], but other studies have not confirmed this. True unilaterality was inaccurately noted in 90% of patients (35 of 39) and 1–3 prostate cancer foci were missed on the saturation biopsy, of which 76% were determined to be clinically significant [27].

Multiparametric magnetic resonance imaging (mpMRI) fusion biopsy is increasingly being used and is now a recommendation for the workup of patients undergoing focal therapy as part of clinical trials [28]. Siddiqui et al. showed that there is good concordance between mpMR fusion biopsy and standard biopsy (69%). More specifically, mpMRI-targeted fusion biopsy demonstrate a 30% improvement in the detection of significant cancer over standard 12-core biopsy, and a combination of mpMRI-targeted and standard template biopsy had an overall sensitivity of 85% for detecting prostate cancer [29]. However, mpMRI technology is relatively new, with a significant economic cost of adoption, and results will vary based on physician experience. In addition, some tumors are not visible on mpMRI, and technical errors such as patient movement or mismatches in registration and/or fusion can cause inadequate sampling of the target lesion [30].

Conventional prostate cancer staging such as computed tomography (CT) abdominal sectional imaging and bone scans are inaccurate at the lower PSA levels commonly seen in the group of patients undergoing focal therapy. Overall, MRI staging accuracies of 71–72% have been reported [31]. However, there are some useful findings that MRI can provide with regard to disease staging. For example, the presence of suspected T3 disease on MRI is highly correlative, with metastatic disease in nodes as small as 0.8–1 cm, the accuracy of which improves when combined with staging nomograms [32]. The rates of micrometastatic nodal disease can be predicted with high sensitivity (88.9–100%) and specificity (65–94.6%) in the presence of clinical T3 (a and b) disease on MRI [31].

The role of a routine pelvic lymph node dissection (PLND) for staging prior to cryoablation has not been established. PLND can be done either by the conventional open technique or by laparoscopic or robot-assisted laparoscopic techniques. For PLND to be useful, enough lymph nodes, have to be sampled. The rate of residual cancer is about 13% in patients who undergo standard PLND when compared to extended templates which includes the presacral nodes [33]. An open extended PLND does blunt the advantage that a minimally invasive procedure such as cryoablation has to offer in the first place. Advances in minimally invasive surgical techniques provide additional options to open PLND that may confer the added benefit of less pain, improved cosmesis, and less hospital days with acceptable oncologic outcomes, but many of these studies demonstrated the efficacy of the minimally invasive technique when offered concurrently with the prostatectomy [34]. At this time standard open PLND is associated with a yield of 21–23 nodes [35], and minimally invasive approaches to PLND may potentially understage patients as a result of lower node counts on resection [36].

Assessing occult bone metastases can also be challenging. When the PSA is <10 ng/ml, bone scans have not been shown to be useful. Positive bone scans are seen with increasing PSA levels, rising from 8% for PSA levels between 20 and 50 ng/ml to 40% for PSA >50 ng/ml [37]. Other modalities, including NaF positron emission tomography (PET)/CT using $^{18}$F-sodium fluoride [38], MRI–diffusion-weighted imaging (DWI) and $^{11}$C-choline PET/CT [39], and fluciclovine ($^{18}$F) PET scans [40], are demonstrating promise in improving the detection of bony and other visceral distant metastases.

## Primary cryoablation

Prostate cryoablation is now being offered to more patients in the primary setting. When the COLD registry was reviewed as of December 2015, over 5000 patients were noted to have undergone primary cryoablation (Figure 137.4). A consensus study involving experts in the field of focal therapy looked at selection criteria for patients. There was a high level of agreement that focal therapy should now be used more in National Comprehensive Cancer Network intermediate-risk patients, and this is a shift over time, from previous policies restricting treatment to the low-risk group, due to concerns about “overtreatment” in the low-risk group [41]. There are other studies showing the effectiveness of focal therapy in the intermediate-risk group. Bahn et al. studied focal ablation in a selected group of 73 patients: 48 underwent biopsies after hemigland ablation for low and intermediate disease. Although 12 biopsies were positive, only 1 was positive on the treated side [42]. In their matched-pair analysis with radical prostatectomy, patients fared comparably to surgery, and there was no

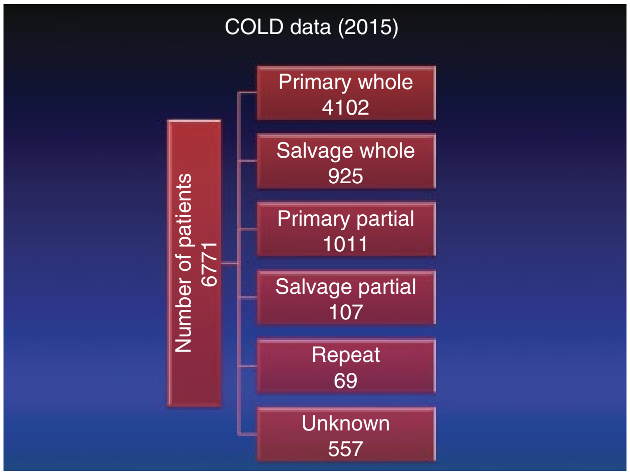

**Figure 137.4** Cryo-On-Line Database (COLD) data: Number of patients undergoing cryoablation as of December 2015 (data provided by Ahmed Elshafei).

statistical difference in the need for salvage treatment [42]. However, when there is evidence of locally advanced or clinical T3 cancer, a much higher rate of biochemical failure (48–52%) is noted compared to radical prostatectomy or radiation therapy [43, 44], with higher rates of rectourethral fistula [43].

Undiagnosed lymph node involvement (LNI) can occur and could be a cause of treatment failure. Accurately discerning the presence of LNI presents challenges to practitioners performing cryoablation, as positive nodes cannot be reliably identified by standard imaging modalities. For this reason, PLND is recommended for high-risk patients (i.e. those with higher PSA, higher grade disease, and shorter PSA doubling times).

Primary cryoablation should be offered to patients with acceptable risk criteria. Low-risk patients may be better followed on active surveillance and a recent study showed an actuarial cause-specific survival rate of 98.1% and 94.3% at the 10- and 15-year period, with 2.8% of patients developing metastatic disease [45]. Intermediate-risk patients with preexisting erectile dysfunction may be excellent candidates for cryoablation. Intermediate-risk patients with good preexisting sexual function should be aware that postprocedure sexual dysfunction is a possibility before proceeding with cryoablation. Although there are studies to demonstrate effectiveness of cryoablation for high-grade disease [43] routine use of cryoablation for patients with Gleason scores 8 or greater, tumor stage >T3, or those suspected of having LNI is not recommended.

### Salvage cryoablation

Similar criteria for patient selection applies to men undergoing salvage cryoablation after radiotherapy. The diagnosis of prostate cancer recurrence after radiotherapy needs to be confirmed and is aided by numerous imaging modalities, including MRI and confirmed by a biopsy. Pelvic MRI can utilize diffusion weighting and dynamic contrast enhancement to differentiate benign tissue from malignant disease. Magnetic resonance spectroscopy can be used to detect local prostate cancer recurrence [46]. In addition, mpMR has demonstrated increased accuracy in detecting prostate cancer in patients when compared to standard T2-weighted images, and consequently has significant utility in the detection of disease recurrence following radiotherapy [47]. These adjunctive imaging modalities can facilitate the selection of men for prostate biopsy who are at risk for local recurrence following radiotherapy.

Guidelines on the use of salvage radiation are often used for selecting men for cryoablation [48]. Specifically, these guidelines suggest that patients should demonstrate only localized recurrence without distant metastases, longer time interval (>2 years) between primary treatment and recurrence, PSA levels <10 ng/ml, PSA doubling time of >6–9 months, and a life expectancy greater than 5–10 years. These guidelines have been standardized for salvage cryoablation, and a study panel recommended men should typically have a PSA <15 ng/ml, clinical tumor stage T1c/T2a, Gleason score 3 + 3 or 3 + 4, a life expectancy of more than 10 years, and any prostate volume [28].

## Procedure, operative considerations, and technique of prostate cryoablation

### General considerations and patient preparation

A complete preoperative assessment is recommended for patients undergoing cryoablation and this includes anesthesia clearance, and appropriate cardiac and respiratory testing. Strict exclusion criteria for treatment, based on our experience, include uncontrolled bleeding diathesis or anticoagulant therapy that cannot be discontinued perioperatively. For those who can hold anticoagulants, these medications should be resumed within 24–48 hours following the procedure or after the urine clears, whichever is earlier.

A limited bowel preparation may be used, at the discretion of the practitioner, to free the rectum, however, there is no evidence that a bowel prep decreases treatment efficacy or decreases the rates of postoperative complications, such as infection. Standard antibiotic prophylaxis should be provided for no more than 24 hours in accordance with guideline recommendations and started within 1 hour of starting the procedure. Urethral strictures may need an internal urethrotomy or dilation and anal stenosis may require dilation in order to facilitate the insertion of a Foley catheter and the rectal probe, respectively, at the time of the procedure. Patients without a rectum or anal opening, such as patients who have undergone abdominal–perineal resection, are not suitable for cryoablation and other treatment modalities should be considered.

The last consideration prior to cryoablative therapy is the prostate gland volume. Men with very large glands are at higher risk of requiring multiple probes and are at increased risk of undertreatment. In this setting, neoadjuvant androgen-deprivation therapy (ADT) can be used to reduce gland volume prior to treatment. Specifically, neoadjuvant ADT has been associated with a mean reduction in prostate volume of 35% and tumor volume reduction of 50% within two months of treatment, although this rarely downstages the existing disease [49]. In one retrospective study, neoadjuvant ADT in men undergoing primary cryoablation (compared with those who did not get neoadjuvant ADT) demonstrated no significant differences in treatment outcomes or complications, with the exception of intermediate-risk men who had improved 5-year disease-free survival [50]. For these reasons, in our experience, we limit whole-gland cryoablation to men with prostate volumes greater than 80 g. For larger glands, we have used neoadjuvant ADT for size reduction for six months in men who could wait without high risk of disease progression.

### Operating technique

The patient is brought to the operative room and anesthesia is induced at the discretion of the anesthesia team. The patient is then positioned in the dorsal lithotomy position with appropriate padding, avoiding hyperflexion to minimize neuropraxia or injury. The lower abdomen, genitalia, and perineum are prepped using a betadine-based solution, and draped in the standard fashion. At this time, a transrectal ultrasound probe is introduced into the rectum and the prostate is carefully inspected. Measurements are taken of the prostate to calculate prostate volume. The ablation machine is calibrated for treatment and the precise location of probe insertion is determined. The simulation provides probe targets, and adjustment are made if needed to ensure that the final probe locations are sufficiently far away from the urethra and rectum to minimize injury and fistula.

Next a cystoscopy is performed to assess the urethra. In the absence of stricture, a glidewire is inserted into the bladder under direct visualization. A warming urethral catheter is then inserted into the bladder over the wire using the Seldinger technique. Temperature sensors are usually inserted at the apex, external sphincters, and neurovascular bundle to monitor freeze cycles (Figure 137.5; see also Video 137.1). The Onik maneuver is used to inject a combination of saline and local anesthesia (i.e. bupivacaine), intrafascially in Denonvilliers' to separate the rectum from the prostate. Our standard practice is to apply two freeze–thaw cycles, which are monitored under direct ultrasonic visualization and by temperature probe with the urethral warming catheter in place and functioning (Figure 137.5 shows the placement of probes and warming catheter) At the completion of the procedure, a urethral catheter is inserted into the bladder and is kept in place for a minimum of one week postoperatively. The patient is typically discharged home on the day of the procedure, with analgesia and the urinary catheter in place.

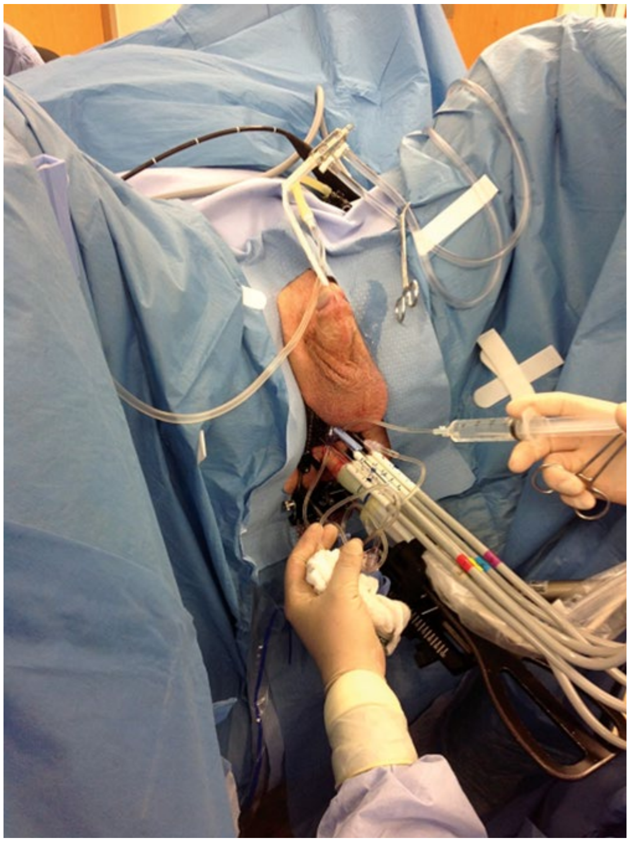

**Figure 137.5** Placement of probes and urethral warming catheter.

## Postoperative care

The most common complications in the more immediate postoperative period following cryoablation are urinary retention and pain, which can be managed with adjunctive medications at the discretion of the clinician.

### Follow-up: defining failure after cryoablation

Two major challenges are encountered in the follow-up of patients after cryoablation. With nonexcisional treatment for prostate cancer, like cryoablation, PSA does not completely become undetectable. Consequently, there are variable definitions of acceptable PSA levels following treatment, and current research is focused on defining PSA levels and kinetics that can better identify failure of therapy. The other challenge is deciding what triggers and criteria to use for ordering a prostate biopsy and how to interpret biopsy results after treatment. Lastly, these parameters differ in patients treated with partial or whole-gland therapy.

### PSA monitoring after cryoablation

Radiation therapy for prostate cancer currently relies on two criteria for identifying biochemical failure. The

ASTRO definition [51] has a sensitivity and specificity of around 60% and 72%, respectively [52], and the authors also looked at three other parameters that improved both sensitivity and specificity over the ASTRO definitions: a PSA > current nadir plus 3 ng/ml had a sensitivity of 66% and specificity of 77%; a PSA > absolute nadir plus 2 ng/ml was found to have a sensitivity of 64% and specificity of 74%; and two consecutive PSA increases of at least 0.5 ng/ml had a sensitivity of 67% and specificity of 78% [52]. The Phoenix definition was then described during a consensus conference in 2005 [53]. The ASTRO and Phoenix criteria, although widely used, have limitations and may delay detection of treatment failures [54].

Changing the PSA cutoff will understandably change the rates of biochemical failure. With the PSA cutoff set to >4 ng/ml, 68% patients were found to be free of biocchemical failure, but this dropped to 55% and 34%, respectively, when the PSA cutoff was lowered to >2 ng/ml or >0.5 ng/ml, respectively [55]. Bahn et al. also showed that when the PSA cutoff was raised from 0.5 ng/ml to 1 ng/ml, the biochemical disease-free survival rate rose from 59% to 69%, respectively [56]. An absolute PSA cutoff of <0.6 ng/ml has been recommended, and patients who demonstrated an initial PSA level of <0.6 ng/ml after salvage cryoablation had better (67% at 36 months) biochemical-free survival [57]. Others have suggested that a nadir PSA cutoff point of 0.4 ng/ml has better discriminating power [58, 59].

Biopsy-proven failures also correlate with PSA nadirs, and when the PSA nadir was <0.1 ng/ml, positive biopsies were noted in only 7%, but this rose to 60% when the PSA nadir was >0.5 ng/ml [60].

The Stuttgart definition of relapse was primarily developed in patients undergoing high-intensity focused ultrasound (HIFU), and is a variation of the Phoenix definition. Blana et al. stated that a PSA nadir plus 1.2 ng/ml and PSA velocity >0.2 ng/ml/year were found to be good predictors of recurrence [61]. A systematic review on salvage cryoablation noted that various series reported their results using PSA cutoffs of 0.3, 0.4, or 0.5 ng/ml, and the ASTRO and Phoenix definitions [62]. The Phoenix definition is more robust than the ASTRO definition, and correlated well with overall mortality [63], and is considered superior to ASTRO [54]. There is now a more sustained shift towards using the Phoenix definition for reporting on biochemical failure after prostate cryoablation.

PSA monitoring protocols have not been standardized. A recommendation by an international multidisciplinary consensus for design of clinical trials states that the PSA should be done quarterly for the first year, biannually for the second year, annually for the third year and then at the discretion of the center [28].

## Prostate biopsies

Prostate biopsies should become part of clinical trial protocols since almost 15% of patients could have cancer on the biopsy without having evidence of PSA recurrence [64]. Protocol biopsies are defined as biopsies that are done on all patients irrespective of the patient's PSA, at a certain point of time in their follow-up. The international consensus on trial design recommends a biopsy after initial inflammation has subsided and scar tissue has formed, and the authors suggest that this should be done 6–12 months after the cryoablation [28]. In a study on primary cryoablation, protocol biopsies were performed on all patients at six months and again as needed; 7.8% (8 patients) had elevated PSA and the biopsy was positive in only 1 patient [65]. Empiric biopsies are "without cause" biopsies that are done in the absence of a rise in PSA.

Biopsies should also be done when a biochemical failure is suspected, especially if the patient is being considered for salvage therapy. In a primary cryoablation study using the COLD registry, biopsies were performed in 28% of all patients: of these 38.4% were done for suspected recurrence based on PSA, while the remaining 61.6% were without cause biopsies done on an empiric basis [64]. When biopsies were done for suspected recurrence, 38% were found to be positive for cancer, while only 14.5% were positive for cancer in the empiric biopsy group [64].

The biopsies should be read and reported by an experienced genitourinary pathologist, since cryoablation-induced changes can pose challenges with interpretation. Studies have looked at biopsies after cryoablation, but many of these were done for suspected recurrence after salvage cryoablation, and the confounding effect of the previous radiation therapy induces bigger challenges in interpretation. Gooden et al. excluded patients with a prior history of radiation therapy and looked at biopsies in 30 patients who underwent primary cryoablation [66]. Recurrent or residual cancer was noted in 37% of patients, and these showed no therapy-induced changes. Unlike what is noted after radiation or after androgen-deprivation therapy, the effects of cryoablation mostly occur in the stroma, with acinar changes being uncommon [66]. Marked endothelial proliferation may, however, occur and special stains such as basal cell markers, AE1/AE3, and CD34/CD31 may be needed to differentiate between endothelial cells and cancer recurrence [66].

Since the pathologic changes mirror the necrosis and loss of glands with stromal fibrosis, residual glands may point to inadequacy of treatment in the corresponding areas. Studies have looked at the proportion of unchanged prostate epithelium in biopsies and this seems to correlate with residual cancer. Residual cancer was seen in

8,4% in biopsies having an average of 10% unchanged epithelium, but this rose to 43.6% when the normal epithelium per core was higher [67].

## Results

Results after primary and salvage cryoablation are summarized in Table 137.1. A review of literature has shown a lack of standardization in the reporting of treatment outcomes of different therapeutic options for prostate cancer. Perhaps this is one of the cancers where results should not be analyzed in isolation, as oncologic outcomes and postoperative complication rates are interrelated. Specifically, a wider field of treatment may lead to improved biochemical progression-free survival (BPFS), but at the expense of a higher complication rate. This is a result of the fact that cryoablation can induce collateral thermal damage to surrounding tissues. On the other hand, low complication rates noted with focal ablation are usually associated with higher rates of biochemical failure [19].

### Primary cryoablation

Primary cryoablation is increasingly being offered to many patients, and one recent large study looked at outcomes and predictors of biochemical failure [68]. In their study the overall BPFS at 5 years was 72.8% for 2242 patients who received primary cryoablation monotherapy.

**Low-risk category**

In the analysis of the COLD registry, 51.6% of patients had a Gleason score of 6 or less and 42.2% were classified as D'Amico low-risk patients, and the estimated 5-year BPFS for this group of patients was 82.6% [68]. In the study, the authors concluded that the pretreatment PSA, stage, Gleason score, and prostate volume were

**Table 137.1** Prostate cancer cryoablation and biochemical progression-free survival.

| Author, year (reference) | Type of study | No. of patients (range) | Median follow-up (mo) | Criteria used | 5-yr BPFS (%) | Comments |
|---|---|---|---|---|---|---|
| **Primary therapy** | | | | | | |
| Elshafei 2015 [68] | Pooled data COLD | 2252 | Mean 32.6 | Phoenix | 72.8 | |
| Rodriguez 2014 [93] | Single series | 108 | 100 | ASTRO | 80.4 | |
| Guo 2015 [44] | Single series all T3 | 75 | 60 | Phoenix | 48 | |
| Lian 2015 [70] | Single series | 40 | 63 | Phoenix | 90 | |
| Liu 2015 [94] | Single series | 114 | 24 | Phoenix | 74.6 at 24 mo | |
| Tay 2015 [59] | Pooled data COLD | 300 | 18.2 | Phoenix | 59.1 KM est | |
| Ward 2014 [43] | Pooled data COLD (T3) | 366 | NA | Phoenix | 51.9 | |
| Grossgold 2014 [50] | Single series | 1761 | 320 | Phoenix | 66.9 | |
| Bahn 2012 [42] | Single series | 73 | 44.4 | Phoenix | NA | 1/48 + Bx on treated side |
| COLD unpublished | Pooled, unpublished | 4102 | NA | Phoenix | 73.2 | |
| **Salvage therapy** | | | | | | |
| Siddiqui 2016 [95] | Single Series | 187 | 117 | Phoenix | 35.0% at 10 years | |
| Li 2015 [96] | Single series | 91 | 15 | Phoenix | 46.5 | |
| Chang 2015 [97] | Single series | 12 | 33 | Phoenix | NA | |
| Ahmad 2013 [98] | Single series | 283 | 23.9 | Phoenix | 44–55 | |
| Abreu 2013 [19] | Single series | 25 focal/<br>25 total | 31 | Phoenix | 54.4 | |
| Parekh 2013 [62] | Systematic review (16 studies) | 18–279 | 9–113 | Multiple criteria | 18–83 | |
| Nguyen 2007 [99] | Systematic review (9 studies) | 18–131 | 19-57 | Multiple criteria | 18–77 | |
| COLD unpublished | Pooled, unpublished | 925 | NA | Phoenix | 58.4 | |

BPFS, biochemical progression-free survival.

independent predictors of BPFS [68]. In another study on focal cryoablation, 56% of 41 patients were low risk, but the recurrence rate (biopsy or PSA criteria) described for the whole group of low- and intermediate-risk patients was 10%. In their study Bahn et al. reported on low- and intermediate-risk patients who underwent focal cryoablation. Of the 24 (33%) patients in the low-risk group, 6 had positive biopsies, but these were all found to be on the untreated side, reflecting an understaging effect of the pretreatment biopsy and the risk of focal therapy [42].

#### Intermediate-risk category

Cryoablation may have good efficacy in this group of patients. Bahn et al. described a biopsy-proven recurrence on the treated side in 1 out of 49 patients undergoing focal ablation for intermediate-risk disease [42]. They also noted five other positive biopsies in this group of patients, but these were noted to be on the contralateral, untreated side of the prostate [42]. Elshafei et al. described a 5-year estimated BPFS of 71.1% [68].

#### High-risk category

A recent study looked at 300 men with Gleason scores of 8 or more but localized T1 or T2 cancer, with failure defined using the Phoenix criteria. Their estimated 2- and 5-year BPFS was 77.2% and 59.1%, respectively, with continence in 90.5% and potency in 17% [59]. In another report from the COLD registry, the Kaplan–Meier 5-year estimate for this group was 57.8% [68]. For a group of 366 patients with clinical T3 disease, and using the Phoenix criteria, the estimated BPFS rates for whole-gland cryoablation, were 65.3% at 36 months and 51.9% at 60 months [43], and the use of neoadjuvant ADT improved these rates without reaching statistical significance [43]. Another study reported on 75 patients with cT3 disease and noted a 5-year BPFS of 48%, with BPFS of 55.6% for the T3a group compared to 36.7% for the T3b group [44].

### Salvage cryoablation

Many studies have looked at the results of salvage cryoablation, and BPFS rates range from 18% to 77%. However it is more common for the BPFS rates to be in the range of 45–55%. When the PSA nadir after treatment was set at <0.4 ng/ml, the 5-year estimated BPFS was 78.5% versus 17.9% when it was more than 0.4 ng/ml [58]. Compared with salvage radical prostatectomy, salvage cryoablation had a higher incidence of disease progression (23.5% vs. 16.7%) and a higher complication rate (23.5% vs. 16.7%), with urethral stricture being the commonest complication in this study [69].

## Complications and management

Cryotherapy-related complications are often due to unintentional thermal injury to adjacent tissues. We reviewed complications from available literature, and also looked at the COLD registry. Records of 6771 cases were available from 39 centers, and most of these had undergone primary cryoablation (whole-gland 4102, partial 1011).

The most commonly seen complication was erectile dysfunction with an incidence of 23.1–98.1% for primary and 50–100% for salvage cryoablation (Tables 137.1 and 137.2). Other common complications included perineal pain, tissue slough and urinary retention.

The wide variation in the incidence of erectile dysfunction and other complications is often due to lack of standardization in definitions, and difficulties seen with patient self-reported questionnaires such as the International Index of Erectile Function (IIEF-15) or the shortened version, the Sexual Health Inventory for Men (SHIM). Focal primary ablations demonstrate lower rates of erectile dysfunction [70] than salvage total ablations [71]; the etiology is multifactorial, with possible contribution from the effects' neurogenic and vasculogenic components. The effect of thermal injury to cavernous nerves [72], and the possible contribution from the vascular component [73], have been studied. Erectile dysfunction is more likely to occur with two freeze–thaw cycles than with one cycle (92% vs. 77%) [74], and recovery can be delayed up to 2–3 years after treatment and rarely even 5 years [75], with reported average recovery times of 16.4 months [76]. Recovery from erectile dysfunction depends on early penile rehabilitation, with multimodal therapy as needed (e.g. vacuum device along with regular use of oral medication for erectile dysfunction) [77].

Urinary retention is also more common after salvage cryoablation (0–21%) than after primary ablation (0–6%), and inflammation and prostate swelling [78] contribute to outlet obstruction. Indwelling urinary catheters and selective alpha blockade may help patients void reasonably following treatment. Clean intermittent self-catheterization may be required, but should be done with the understanding that in some cases it may cause urethral trauma and possible fistula formation. Some patients will require transurethral resection of the prostate (TURP), and suprapubic catheter placement for patients failing a second voiding trial is also an alternative [78].

Lower urinary tract symptoms, perineal pain, and symptoms secondary to tissue slough have common etiology arising out of direct effects of the freezing of the prostate and urethra, as a result of inflammation and tissue necrosis. Perineal and/or rectal pain has been

**Table 137.2** Complications of prostate cryoablation: pooled series.

| Author, year (reference) | No. of patients (range) | Impotence % | Pelvic/perineal pain % | Tissue slough % (range) | Incontinence % (range) | Stricture/urethral complications % (range) | Retention/ obstruction % | Fistula % (range) | Others % |
|---|---|---|---|---|---|---|---|---|---|
| **Primary therapy** | | | | | | | | | |
| Rodriguez 2015 [93] | 108 | 98.1 | 11.1 | 5.6 | 5.60% | NA | 1.9 | 0.90% | 1/9% Hematuria |
| Guo 2015 [44] | 75 | NA | 0 | 6.7 | 4 | 0 | 0 | 0 | |
| Lian 2015 [70] | 40 | 23.1 | NA | 0 | 2.5 | 0 | 2.5 | 0 | |
| Liu 2015 [94] | 114 | 88 | NA | NA | 1.6 | 3.3 | NA | 0 | TURP/OIU 8.8%, scrotal edema 74.7% |
| Tay 2015 [59] | 300 | 83 | NA | NA | 9.5 | NA | 3.3 | 1.3 | |
| Ward 2014 [43] | 366 | 69.6 | NA | NA | 2.6 | NA | 6 | 1.1 | |
| Grossgold 2014 [50] | 1761 | 69.6 | NA | NA | 1.6 | NA | 1.2 | 0.6 | |
| COLD unpublished | 3843 | – | NA | NA | 6.4 | NA | 9.7 | 1 | |
| **Salvage therapy** | | | | | | | | | |
| Li 2015 [96] | 91 | 50 | NA | 1.1 | 5.5 | NA | 6.6 | 3.3 | 1.1% TURP |
| Chang 2015 [97] | 12 | 100 | 0 | 8.3 | 8.3 | 0 | 0 | 0 | Salvage cryo after Primary cryo<br>LUTS 14% |
| Ahmad 2013 [98] | 283 | 83 | 4 | NA | 12 | NA | 7 | 1.8 | |
| Abreu 2013 [19] | 25 focal | 71 | NA | NA | 0 | NA | NA | 0 | |
| | 25 total | 100 | NA | NA | 13 | NA | NA | 4 | |
| Parekh 2013 [62] | 18–279 | NA | 15.6 (0–39.5) | 8.2 (0–52.2) | 16.4 (0–91.3) | 4.2 (0–44.4) | 9.9 (0–21.4) | 1.6 (0–11.1) | |
| Nguyen (2007) [99] | 18–131 | NA | 36 (5.6–44) | 11 (0–55) | 36 (4.3–83) | 17 (0–28) bladder neck contracture/retention | NA | 2.6 (0–11) | |
| COLD unpublished | 925 | NA | NA | NA | 28.2 | NA | 19.1 | 2.8 | |

OIU, optical internal urethrotomy; TURP, transurethral resection of the prostate.

described to occur in 0–11% after primary cryoablation and 4–44% after salvage cryoablation. Tissue slough is described to occur in 0–6.7% of cases, but in the salvage series it is reported in 1.1–55%. The use of the newer generation machines [79] and urethral warmers [74, 80] reduces the incidence of these complications, and we believe that limiting the freeze time on the anterior probes also reduces the incidence of perineal pain. The perineal pain syndrome can be troublesome, and is often described as a burning sensation that can be associated with frequent bowel movements or rectal irritation [81]. Perineal pain can represent a significant cause for patient dissatisfaction following treatment [74]. Associated lower urinary tract symptoms may be noted, including irritative and obstructive voiding symptoms. The International Prostate Symptom Score (IPSS) overall symptom score and urinary bother score worsen in the first six months after cryotherapy, but return to baseline in 12 and 18 months, respectively [82]. Perineal pain can be managed conservatively, but transurethral resection of the necrotic tissue slough can speed up recovery [81]. Tissue slough is one of the main causes of retention and sometimes requires a TURP. When TURP is offered, it is important to recognize the risks of over-resection due to altered anatomy [80], and the higher risk of long-term incontinence. TURP should not be done earlier than three months following cryoablation [80]. In fact, the authors and many others reserve TURP until at least 12 months post treatment, especially in the salvage setting.

Less commonly, patients may develop urinary incontinence (1.6–9.5%), rectourethral fistulas (0–1.1% primary and 0–3.3% salvage), or urinary strictures and/or bladder neck contractures (0–3.3% primary and 0–4.2% salvage; 17% in one pooled series).

The risk of rectourethral fistulas increases from the primary (1%) to the salvage (2.8%) setting based on review of whole-gland ablation data from the COLD registry (unpublished data). Fistulas develop from freeze injury of the rectal wall [79], and the incidence has markedly decreased with the improvement of ultrasonography for imaging iceball formation during the procedure. Freezing injury can be compounded by poor quality in prior irradiated tissues, which may explain higher rates of fistula in the salvage setting, reported as high as 11.1% in some series. It is important to note that the rates of fistula decrease in the hands of an experienced surgeon, with most of the fistulas occurring in the first 25 cases of most surgeons' series [79]. Patients with fistulous disease most commonly present with watery discharge per rectum or "diarrhea" [81]. In addition, patients may present with classic urinary symptoms such as recurrent urinary tract infection, fecaluria, or pneumaturia.

The diagnosis of rectourethral fistula starts with a thorough history and examination, followed by evaluation of the defect via a combination of imaging (i.e. CT cystography or retrograde urethrogram/cystogram). Cystoscopy, with possible sigmoidoscopy, can also be considered at the discretion of practitioners based on patient symptoms. Early management should involve drainage of the bladder with a urinary catheter. In fact, some series have demonstrated that small defects may heal with prolonged (up to three months) drainage [81]. Our own preference at our institution is urinary drainage for 6–12 weeks, and we have reported treatment of a postablation fistula with urinary catheter and temporary fecal diversion [83]. In patients requiring more complex repairs, two principles should be considered – urinary diversion [84] and fecal diversion [85] – in addition to repair and coverage of the defect with a flap (i.e. omental, gracilis, etc.).

The incidences of urethral stricture and bladder neck contracture also increase from the primary to the salvage setting. Stricture disease occurs due to tissue injury during therapy and may be affected by prior irradiation or concomitant infection at the time of treatment. Furthermore, fistulous disease may cause stricture disease, further complicating the clinical picture and future repair [84]. Warming urethral catheters have been show to decrease the rate of tissue sloughing after cryoablation [74, 80]. Treatment is dependent on the length of the stricture and assessment of the defect by retrograde urethrography should only occur after three or more months of urethral rest. Shorter strictures may be managed by dilation or urethrotomy; however, urethroplasty may provide a more efficacious and durable response for both short- and long-segment urethral strictures. Severe bladder neck contractures may require aggressive incision and artificial urinary sphincter for management.

Lastly, the rates of urinary incontinence have decreased dramatically with advances in cryoablative technologies [79]. And the fluctuation in the rates of incontinence reported by different series may reflect differences in the definitions of incontinence used [76]. Incontinence may result from various causes following cryoablation, including damage to the external sphincter mechanism and new-onset bladder overactivity. Similarly to the other complications, prior radiation can lead to higher rates of incontinence in men undergoing salvage cryoablation [80].

Urgency incontinence is reported in up to 80% of patients with long-term incontinence [78]. It is important to note that recovery of continence may be a long process, taking up to 6.1 months [76]. Care must be taken to avoid transurethral resection of tissue slough after cryoablation in men with obstructive symptoms, as resection may potentiate incontinence and complicate management [86]. A series by Cespedes and colleagues showed that 13 of the 15 patients who developed obstruction became incontinent either after a TURP or after spontaneous passage of slough [80]. Urethral warmers have been shown to be associated with less frequency and severity of incontinence [74, 80]. Management of incontinence should be conservative, starting with lifestyle modification, pelvic floor exercises and therapies, and overactive bladder medications (i.e. anticholinergic or beta-3 agonists). However, in patients who fail conservative therapies, full evaluation with cystoscopy and pressure-flow studies may be required prior to considering more invasive therapies such as artificial urinary sphincter [74].

Extremely rare complications of cryoablation have been described in the literature and include death [87], transient ichemic attack/stroke [81], acute renal failure [87], and hydronephrosis secondary to ureteral obstruction [81, 87]. In addition, a very small proportion of men have described a feeling of penile tingling/numbness [18, 88], which was managed conservatively. Other rare complications include hematuria [78], scrotal anomalies (i.e. swelling or hematoma) [78, 81], urethrocutaneous fistula [89], and infective complications such as epididymitis [87] and abscess [75, 78, 90–92].

## Conclusions

Cryoablative therapy is increasingly used for men with localized prostate cancer as a treatment option both in the primary and salvage setting (Tables 137.1 and 137.2). Treatment outcomes demonstrate an acceptable oncologic outcome with a durable response, as evidenced by recent publications with intermediate follow-up. However, more time is needed to assess the long-term impact of current ablative therapies on postoperative functional and oncologic outcomes. Nonetheless, in carefully and informed patients, cryoablation is an acceptable therapy for prostate cancer.

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# 138

# Contrast-enhanced Ultrasound in Urology

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## Introduction

Imaging in endourology is mainly composed of grayscale ultrasound, X-ray, computed tomography (CT), magnetic resonance imaging (MRI), and skeletal scintigraphy. All of these modalities have their own place in urology; however, in this chapter we focus on contrast-enhanced ultrasound (CEUS) as it compares with MRI and CT imaging.

CT scans are commonly used in the diagnosis, staging, and follow-up of urologic malignancies. In the diagnosis of kidney tumors, ultrasound is mainly used for a first screening and, in most cases, CT is utilized to make the final diagnosis. MRI is commonly used to evaluate adrenal tumors and cystic lesions in the kidney, and to stage renal cell and prostate carcinoma. For some of the urological indications, MRI is used when CT is contraindicated.

Drawbacks of CT and MRI relate to their costs, limited availability, and impractical use at the bedside. Furthermore, CT and MRI contrast agents can have side-effects [1, 2]. CT contrast agents are iodine-based and these agents can worsen the existing renal function in patients with renal insufficiency [1]. CT is also associated with radiation exposure. Although MRI does not expose patients to ionizing radiation, its contrast agents are often gadolinium-based and can cause nephrogenic systemic fibrosis in patients with severe renal failure [2].

Ultrasonography is a safe method to investigate the kidney, bladder, prostate, scrotum, and penis. It has high resolution, allows real-time imaging and is widely available, cost-effective, and highly compatible with therapeutic equipment.

For diagnosing scrotal abnormalities, ultrasound is the investigation of choice. When used appropriately, ultrasound can distinguish between the most common scrotal abnormalities [3]. Doppler ultrasonography allows further discrimination of these abnormalities, since it can directly evaluate testicular perfusion. However, the diagnostic accuracy of grayscale and Doppler ultrasound for malignant processes of the kidney, bladder, and prostate is low. For the bladder and for the kidney, it is mainly used as a screening tool, and for prostate cancer, its main role is to guide systematic biopsies.

Malignancies are associated with angiogenesis and neovascularization and, therefore, changes in perfusion [4, 5]. The visualization of this process may increase the sensitivity and specificity of tumor detection as well as the accuracy of staging. Suitable techniques for perfusion imaging are dynamic contrast-enhanced MRI, contrast-enhanced CT, and CEUS.

CEUS was first observed in 1968 during imaging of the aortic root [6]. After an injection of saline, it was noted that the small air bubbles, present in the saline, significantly enhanced the ultrasound signal. Attempts to use free air bubbles as an ultrasound contrast agent have been conducted, but the short lifetime of these bubbles proved to be a problem. More recently, small ($<8\,\mu m$) encapsulated gas-filled microbubbles have been developed as new ultrasound contrast agents. Because of the presence of a shell, these contrast agents have a lifetime of several minutes, allowing contrast visualization of organs with a simple intravenous injection. The first application of CEUS was in cardiology for the visualization of myocardial perfusion, but its usage is currently extended to image the liver, breast, kidney, and prostate [7].

When microbubbles are exposed to sound waves, they are compressed and subsequently expanded as a result of the changing ultrasound pressure. With low-energy ultrasound waves, the bubbles expand linearly and behave like additional bloodstream reflectors, resulting

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in increased reflected ultrasound energy. This mode is especially useful in Doppler ultrasound imaging [8].

With medium-energy waves, the bubbles expand nonlinearly, which results in reflected signals that not only encompass the transmitted ultrasound frequency, but also additional harmonics. Currently, contrast-specific imaging techniques are available that utilize these harmonics to distinguish between the reflections of the bubbles and tissue. Hence, sensitive imaging of perfusion is possible.

At high energy, still within the normal clinical range, the bubbles will disrupt in the imaging plane, providing the opportunity to visualize a new inflow of contrast *in situ*. This technique, which is very useful to assess perfusion, is referred to as destruction–replenishment [9].

A wide range of ultrasound contrast agents are commercially available [10]. These agents have been extensively used for years and only in very few cases have side-effects been reported. The most commonly reported side-effects are usually transient: altered taste, pain at the side of injection, and generalized flushing [10]. The most severe adverse effects were allergic reactions to the administered substance [11]. In general, ultrasound contrast agents are considered to be safe [10, 12].

## Contrast-enhanced ultrasound of the prostate

Prostate carcinoma (PCa) is the most common malignancy in the male population in the western world, and accurate diagnosis and staging is still a clinical challenge [13, 14].

Transrectal ultrasound (TRUS) was introduced in 1968 by Watanabe et al. [15]. Currently, TRUS is mostly used for guiding systematic biopsies. At first, only hypoechoic lesions were considered as target for biopsy to identify PCa. However, it was demonstrated that these lesions only have a 17–57% chance of being malignant and that up to 30% of the prostatic malignancies are isoechoic [16]. Hodge et al. described the introduced ultrasound-guided sextant biopsy protocol, with a sensitivity and specificity in the range of 39–52% and 81–82%, respectively [16, 17]. The guidelines currently recommend a ≥10-core biopsy protocol [18]. However, biopsies are associated with a considerable risk of complications [19] as well as underdiagnosis; in up to 30% of the patients that are referred for repeat biopsy after negative outcome in the first procedure, malignancies are found [20].

As stated previously, malignancies are characterized with angiogenesis and neovascularization, and therefore an increased microvessel density (MVD) [5]. Siegal et al. reported an approximate twofold increase in MVD in prostate carcinoma in comparison to benign prostate hyperplasia [21]. In 2001, Sedelaar et al. correlated the histologically determined MVD in radical prostatectomy specimens with three-dimensional contrast-enhanced power Doppler [22]. On average, the areas with increased enhancement had a 1.93 times higher MVD than unenhanced areas, and all enhancing areas contained PCa. Only small satellite lesions (1–2 mm) were not identified on CEUS. This study clearly demonstrated that the increased MVD as a result of PCa can be visualized with CEUS (Figure 138.1), opening the door to biopsy targeting by CEUS.

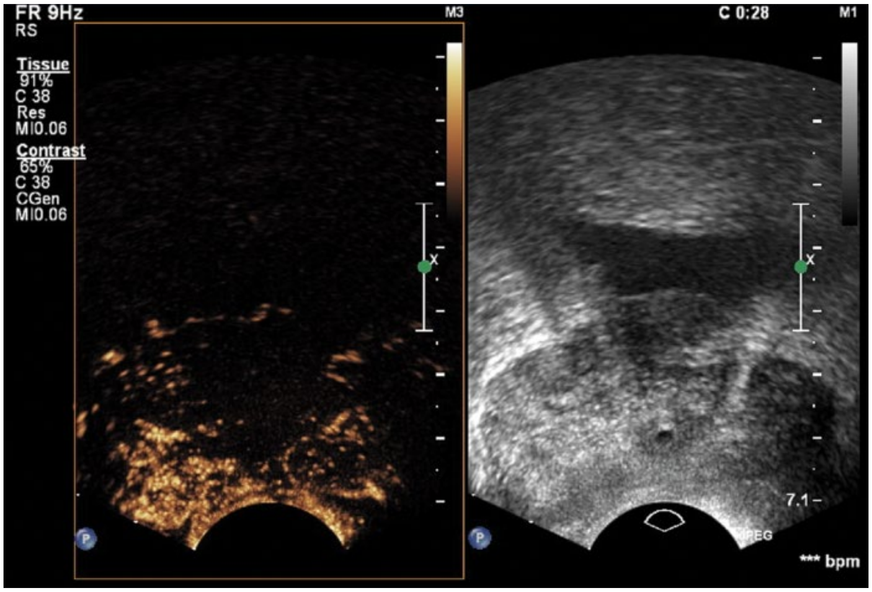

**Figure 138.1** Contrast-enhanced ultrasound investigation of the prostate with an enhancing lesion on the left side in the image. Histopathologic examination showed a Gleason 3+4 carcinoma.

## Targeted biopsies

The value of CEUS as a guiding tool for targeted biopsy has been extensively studied in recent years. In general, the PCa detection rate *per biopsy core* is significantly higher for targeted than for systematic biopsies. Zhao et al., for example, reported a per core PCa detection rate of 75% for CEUS-targeted biopsy, compared to 48% for systematic biopsy in 28 patients with confirmed PCa [23]. The sensitivity of targeted biopsy in the entire group of 65 patients with elevated prostate specific antigen (PSA) level and/or abnormal digital rectal examination was 79%; with false positives due to benign prostate hyperplasia and prostatitis, and false negatives for small-size or transitional zone foci. In a comparable study, Linden et al. found a similar relation for the detection rate per biopsy core (8.3% for systematic and 13% for targeted biopsy) in a group of 60 patients that were referred for biopsy [24]. These studies, however, also reported a small fraction of patients for whom PCa was only identified by systematic biopsy.

Contrast-enhanced Doppler ultrasonography was used in several studies on targeted biopsy. Peltzer et al. investigated 380 patients with a PSA level between 4 and 10 ng/ml and a free-to-total PSA level less than 18% with systematic and CEUS-targeted biopsies [25]. There was no significant difference (104 vs. 105 carcinomas out of 143 carcinomas), but the combination of CEUS and systematic biopsies was significantly more effective in detecting carcinoma than either modality alone. Mitterberger et al. compared the efficiency of 10-core systematic biopsy versus a 5-core targeted biopsy in 1776 men with a serum PSA concentration greater than 1.25 ng/ml [26]. The PCa detection rate of targeted biopsy (961 of 8880 cores) was higher than that of systematic biopsy (910 of 17 760 cores). Cancer was detected in 559 patients; in 149 cases only the CEUS-targeted biopsies returned positive, in 83 only the systematic ones. Another study on the use of contrast-enhanced Doppler (300 patients, PSA level greater than 2.5 ng/ml) did not find a significant difference in detection rate compared to systematic biopsy [27]. All of these authors concluded that for maximal detection, a *combination* of systematic and CEUS-guided biopsies is preferred.

In 2013, a meta-analysis on CEUS was published that incorporated 16 studies with a total of 2624 patients [28]. It was demonstrated that CEUS had high potential with an overall sensitivity and specificity of 70% and 74%, respectively. The technique was not yet considered sufficiently accurate to replace systematic biopsy. A more recent systematic review on targeted biopsy, incorporating a few CEUS studies mentioned in this section, indeed concluded that the combination between targeted and systematic is most reliable in terms of detection rate [29].

In summary, CEUS is a promising diagnostic tool for PCa localization. The PCa detection performance is comparable with that of systematic biopsies with fewer biopsies needed, and the detected cancers are of higher Gleason grade [30]. When CEUS is compared with histological specimens after radical prostatectomy, it frequently detects the index tumor. Prospective multicenter trials are still needed to confirm these results.

## Use in focal therapy

In the 2014 multidisciplinary consensus on trial design for focal therapy, CEUS is mentioned as one of the recommended imaging tools [31]. Due to its reliable assessment of tissue destruction, CEUS is increasingly used to guide and monitor the application of many focal therapeutic modalities. Here, we mention high-intensity focused ultrasound (HIFU), interstitial laser therapy, irreversible electroporation, and anti-androgen therapy.

Sedelaar et al. used CEUS to investigate the effectiveness of HIFU in the treatment of PCa [32]. In this study, CEUS was compared with whole-mount histology specimens from patients who underwent a radical prostatectomy 1–2 weeks after HIFU treatment for a T1 or T2 prostate carcinoma. Overall, a strong correlation of 0.98 between CEUS and pathology volumes of the lesion was found. In another study, Rouvière et al. found that the 30-day post-HIFU CEUS findings in 28 patients were in good agreement with biopsy outcomes and MRI acquisitions [33]. They concluded that CEUS was a promising tool to discriminate devascularized and viable regions after treatment. However, the interference of microbubbles with HIFU should be investigated before allowing immediate repeat of this procedure after CEUS.

Atri et al. applied real-time CEUS monitoring during interstitial laser therapy in 12 patients [34]. After one week, the treatment effect was quantified by means of the ablated tissue volume, which was in good correspondence with complementary MRI scans. Another study on laser photothermal focal therapy involved real-time CEUS to follow the size development of hypovascularized lesions, but also MRI in the follow-up [35].

In a study on irreversible electroporation by Van den Bos et al., involving 16 patients who were scheduled for prostatectomy, the treatment effect was monitored by both T2 MRI and CEUS [36]. The measured sizes of the ablated areas closely resembled those in the histopathological examination, with Pearson's correlation indices of 0.88 and 0.80, respectively.

These studies demonstrate that CEUS is able to reliably assess the treatment effect of focal therapies in real-time and follow-up monitoring. In view of this, CEUS has been hypothesized to be a suitable alternative also to contrast-enhanced MRI in cryotherapy and photodynamic therapy [37]. Up until now, however, the focal treatment of patients with localized PCa is not yet considered standard procedure due to the limitations in visualization and patient selection.

### Combined contrast-enhanced ultrasound

Recently, the use of CEUS in combination with other ultrasound modalities has been considered for the localization of prostatic malignancies [38].

After performing CEUS and grayscale TRUS, Matsumoto et al. were able to localize at least one focus in 40 of the 50 (80%) patients with biopsy-proven PCa. This was more than based on the grayscale (40%) or the contrast scan (62%) alone [39]. Also the combination of CEUS with grayscale TRUS and Doppler imaging was studied [40]. A PCa detection performance of 82% was observed after evaluation with a 10-biopsy protocol in 150 patients, compared to the detection rates of 51%, 48%, and 73% at cancer sites for TRUS, Doppler, and CEUS individually.

Promising results were also found for the combination between CEUS and elastography, which is the measurement of tissue stiffness upon cyclic manual compression. In a targeted biopsy study, the detection rate of this combination exceeded the rate that can be expected from systematic biopsies [41]. Alternatively, CEUS imaging of PCa regions that were marked as suspicious based on real-time elastography led to a decrease in histologically confirmed false positives, improving the positive predictive value from 65% to 90% [42].

All multiparametric or multimodality ultrasound approaches with CEUS, however, are still under development.

## Contrast-enhanced ultrasound in renal masses

The more frequent use of cross-sectional imaging has resulted in an increase of incidentally found renal masses. Renal masses are divided into solid and either simple or complex cystic masses. Approximately 10% of renal cell carcinomas present as complex renal cysts, but not all complex cysts are renal cell carcinomas [43, 44]. To characterize renal cysts, the Bosniak classification scale is generally used [45].

Conventional ultrasound imaging cannot perfectly differentiate between complex cysts that need surgery and those that can be observed. Currently, the decision is primarily based on the enhancement characteristics of the cyst and in most cases a contrast CT is used to image these characteristics. Contrast-enhanced MRI is traditionally utilized when CT is not possible, but also CEUS recordings are increasingly performed [46].

After administration of the ultrasound contrast agents, the kidney displays fast and intensive enhancement. In 2004, Thorelius used CEUS for various organs, observing a high sensitivity in the characterization of nonvascular lesions (e.g. cysts, infraction, and laceration) in the kidney [47]. The most recent EFSUMB guidelines on the clinical practice of CEUS recommend its use to differentiate solid lesions and cysts, discriminate tumors and “pseudotumors,” characterize complex cystic masses, and monitor ablative treatment [48].

### Diagnosis of renal masses

In the diagnosis of renal masses, imaging is primarily applied for the differentiation between malignancy (predominantly renal cell carcinoma) and benign lesions such as angiomyolipoma, oncocytoma, cysts, and “pseudotumors” [49].

Many studies found that CEUS was not inferior or even better to the traditional contrast-enhanced CT [49]. In a 2007 pilot study, Wink et al. performed CEUS in 18 patients and were able to classify all 20 renal masses correctly [50]. Of 13 masses for which histology was available, 12 proved to be malignant. Of the other 7 masses, 4 were classified as Bosniak I or II(F) cysts, 2 as angiomyolipomas, and 1 was suspicious of renal cell carcinoma. Figure 138.2 shows an example of CEUS of a renal tumor.

Quaia et al. investigated 26 patients with renal masses in whom they compared the CEUS recordings with histology or CT [51]. Of the 26 masses found, 19 were solid renal masses, of which 11 solid renal cell carcinoma, 7 angiomyolipoma, and 1 embryonal metanephric adenoma. CEUS and CT were equally good in the differentiation between solid renal cell carcinoma and angiomyolipoma.

Park et al. compared the performance of CEUS and CT in the diagnosis of cystic renal masses and found that 6 of the 19 patients with solid components were only identified with CEUS [52]. Furthermore, Ascenti et al. examined 40 patients with one or more cysts of Bosniak class II or higher and reported a complete concordance between CEUS and CT in discriminating between nonsurgical and surgical cysts [44]. In a study with 103 patients displaying complex cystic masses, Xue et al. found CEUS performed better than contrast-enhanced CT and ultrasonography in terms of visualizing the septa and wall thickness [53].

CEUS is also a valuable modality for the imaging of peritumoral pseudocapules, which are associated with low-risk tumors and are conventionally identified with MRI [54]. Ascenti et al. investigated CEUS in 32 patients with 40 renal masses, of which 26 were renal cell carcinoma [55]. On histological examination of the renal cell carcinomas in 14 of the cases, a pseudocapsule was

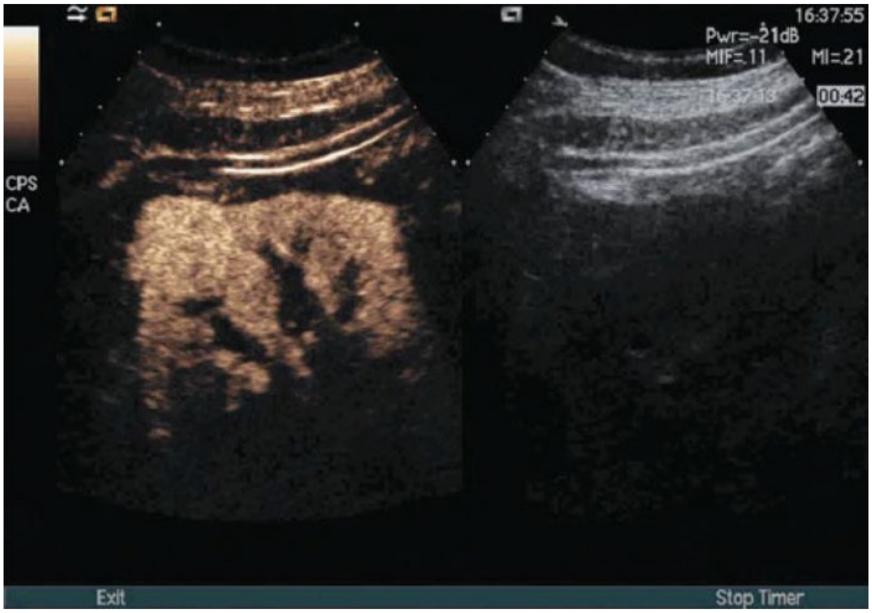

**Figure 138.2** Contrast-enhanced ultrasound investigation of a kidney tumor. On the left side in the image an enhancing lesion is seen.

present. Conventional ultrasound detected this in 3 cases with a sensitivity of 21%, and CEUS detected this in 12 cases with a sensitivity of 87.5%.

Larger scale studies also underline the value of CEUS in the diagnosis of renal masses. Barr et al. carried out a retrospective study from 1999 to 2010 on the performance of CEUS in 721 patients with indeterminate renal masses and evaluated the tumor detection in the 306 patients that received definite diagnosis [56]. Due to five false positives, they reported a sensitivity and negative predictive value of 100% and a specificity and positive predictive value of 95%. In addition, a recent meta-analysis on the ability of CEUS to detect renal cell carcinoma investigated 11 studies and 880 patients and found a sensitivity and specificity of 88% and 80%, respectively [7].

## Use in ablative therapies

As a result of the increasing incidence of small renal masses, of which a significant number are benign or low risk, nephron-sparing treatment modalities have been introduced. Along with partial nephrectomy [57], ablative treatments such as cryoablation [58] and radiofrequency ablation (RFA) [58] can be used. Similarly to the focal treatment of the prostate, CEUS could play a substantial role in the monitoring or follow-up of these treatments, by visualization of the resulting perfusion defects.

Meloni et al. compared CEUS with contrast-enhanced CT or MRI after RFA in 27 patients with 28 tumors. At baseline imaging, 27 of these tumors exhibited a hypervascular pattern and one a hypovascular pattern [59]. The concordance between CEUS and CT or MRI findings after RFA was 100% for the hypervascular tumors; the one case of the hypovascular tumor progression was missed on CEUS. In addition, Hoeffel et al. and Allard et al. compared CEUS versus CT in, respectively, 66 and 37 patients who were treated with RFA [60, 61]. The scans were interpreted by multiple independent, blinded radiologists and, again, high concordance was found between CEUS and the current gold standard.

CEUS was also tested as a surveillance tool after cryoablation treatment. Zhu et al. performed CEUS, CT, and MRI in three patients before and after the procedure [62]. The CEUS images demonstrated the same enhancement patterns as CT or MRI, but CEUS demonstrated a better visualization of the arterial feeding vessels. Wink et al. evaluated CEUS in the follow-up in seven randomly selected treated patients [63]. Even though the contrast recordings were not always taken on the same day as CT and MRI scans, a high concordance was found in the long-term follow-up. Also, Barwari et al. and Zeccolini et al. observed a high correspondence between CEUS and CT in the cryolesion assessment after (laparoscopic) renal cryoablation in 26 cases and 25 cases, respectively, and deemed the technique a proper alternative in the long-term follow-up [64, 65]. An example of CEUS after cryoablation is shown in Figure 138.3.

Especially for ablative treatment modalities, the latest studies suggest that CEUS is a viable alternative for contrast CT or MRI. The absence of perfusion can be visualized with a high sensitivity. Again, prospective multicenter trials are needed to fully establish the clinical additional value of this technique.

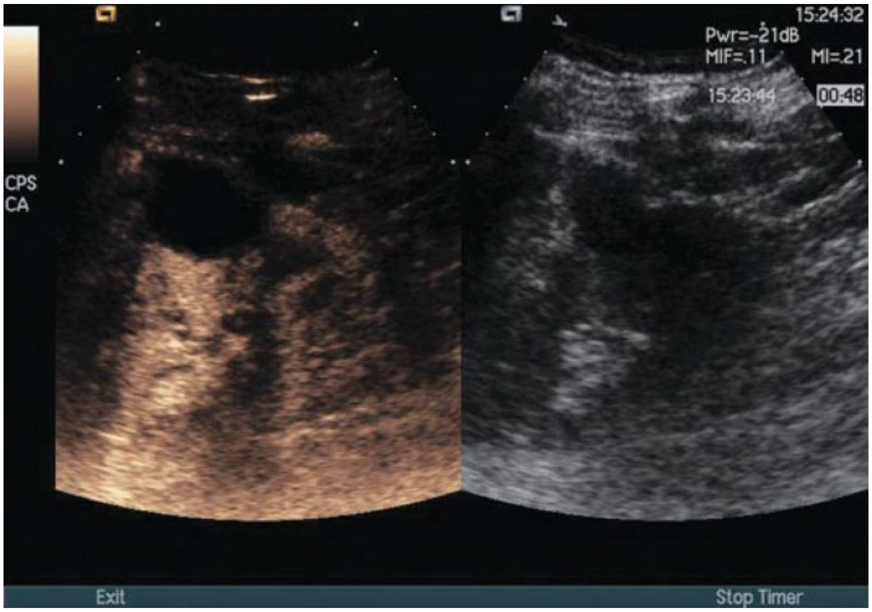

**Figure 138.3** Contrast-enhanced ultrasound image of a kidney after cyroablation. A clear avascular zone is visible in the location where the cryoablation was performed.

## Future developments

### Quantification

In general, the described use of CEUS permits a subjective determination of perfusion features by the investigators, and may therefore be subject to bias between centers and investigators. More well-defined and objective perfusion measures have been investigated. This quantification is often based on measured time-intensity curves (TICs) – the evolution of enhancement over time.

The crucial changes in the vasculature due to angiogenic PCa are reported to cause more rapid and strong enhancement compared to benign regions in the prostate [66]. This has been quantified by extracting features such as the bolus arrival time, maximum enhancement, and the wash-in gradient from the TICs [67]. A study by Goossen et al. indicated that the minimal time-to-peak enhancement was the most predictive factor to determine the affected side with malignancy in patients with proven PCa [68]. Postema et al. studied the wash-in rate to predict PCa biopsy outcome and found the use of this measure to increase the detection rate compared to the CEUS videos alone [69]. Instead of looking at the perfusion characteristics, the local dispersion kinetics of the contrast bolus can also be assessed. Several dispersion-related parameters were found to be excellent markers for PCa confirmed in corresponding radical prostatectomy specimens, yielding receiver-operating characteristic curve areas of 0.88 [70], 0.91 [71], and 0.92 [72]. An example is presented in Figure 138.4. These technologies are currently under investigation as a guiding tool for objective, standardized targeted biopsy.

Similar quantification techniques have been proposed for renal masses. The value of wash-in and wash-out characteristics to identify malignant and benign masses, for example, was evaluated by Eisenbrey et al. [73]. Indeed, Cai et al. found that correctly chosen thresholds for the enhancement intensity at 60 seconds and the wash-out time were able to discriminate malignant and benign masses [74].

Recent development of three-dimensional techniques to record or quantify CEUS measurements might boost its usefulness even more. Wei et al. showed that the application of CEUS in three dimensions visualized more intratumoral and tortuous branches in renal carcinoma [75]. Similar results are shown for acoustic angiography [76]. Furthermore, three-dimensional quantification, for example for dispersion imaging, is likely to improve the reliability of CEUS as a guiding tool for targeted biopsy of the prostate [77].

### Targeted microbubbles

Even more specific imaging of malignancy becomes possible with the development of targeted contrast agents (e.g. microbubbles with targeting ligands added to their coating). These adhesion molecules bind to biomarkers of angiogenesis, for example, such as vascular endothelial growth factor (VEGF) and $\alpha_v\beta_3$ integrin [78].

Particularly promising is the targeting of VEGF receptor type 2. In an *in vitro* study with mouse cell cultures with cancer and noncancer cells, Willmann et al. found that VEGF-targeted microbubbles adhered significantly more to the malignant cells than to a control sample of nontargeted microbubbles (2.1 bubbles per

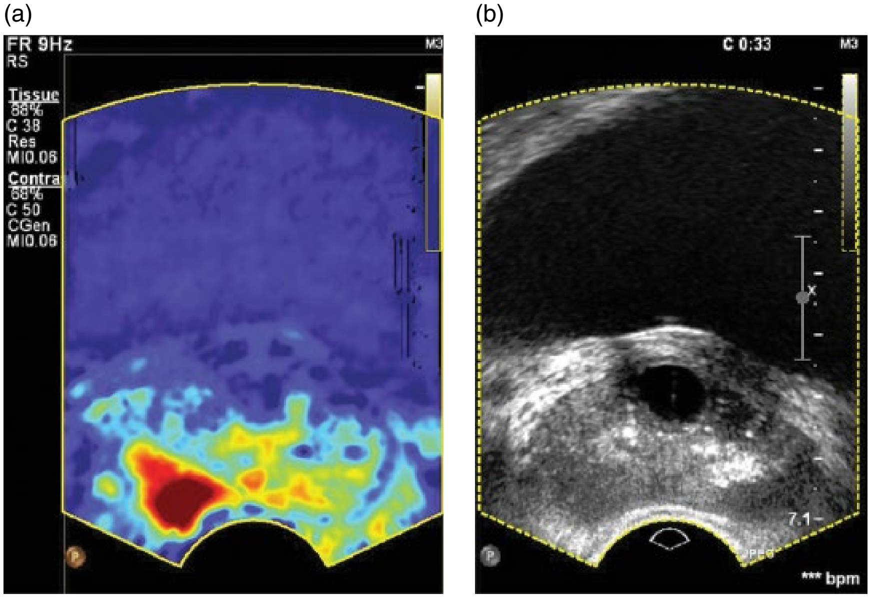

**Figure 138.4** Quantification of contrast-enhanced ultrasound with contrast ultrasound dispersion imaging. (a) Contrast-enhanced ultrasound with an overlay of the quantification results. The red areas are predicted to have a high chance of being malignant. (b) Normal B-mode grayscale image.

cell compared to 0.1–0.01 bubbles per cell) [79]. Cancer cells were also significantly more adhered to than non-cancer cells. Subsequently, these microbubbles were tested during CEUS measurements in *in vivo* murine models. Willman et al. [79], Lyshchik et al. [80], and Wei et al. [81] all observed a statistically significantly higher contrast intensity for the targeted agents than for the control agents in mice implanted with angiosarcoma, mammary carcinoma, and renal carcinoma, respectively.

In 2010, the VEGF-targeted contrast agent BR55 (Bracco Diagnostics, Milan, Italy) was introduced for use in humans [82]. After investigation in rat prostate and a successful Phase 0 trial [83], the first clinical trial for the diagnosis of prostate cancer using these targeted contrast agents has recently been carried out [84].

The amount of binding of these targeted agents (and thus the degree to which the targeted biomarkers are expressed) is usually assessed using destruction–replenishment techniques [79–81]. These methods involve a high-energy disruptive ultrasound pulse being delivered to the area after allowing the targeted microbubbles to fully bind. Since the subsequent contrast signal is only coming from freely circulating contrast agents refilling the vessels, the difference between the signal before and after said pulse can be used as a measure for the molecular binding (i.e. targeted differential enhancement) [85]. Promising new techniques for quantitative binding assessment are being developed by modeling the first-pass binding kinetics of these contrast agents [86].

## Drug delivery with ultrasound microbubbles

Manipulation of the contrast microbubbles also enables local ultrasound-mediated drug and gene delivery. This can be performed by either (i) using a high-intensity ultrasound pulse to destruct the microbubbles and locally rupture the capillary walls (sonoporation), resulting in the increased uptake of a drug that was co-injected in the bloodstream; or (ii) using the microbubble as a carrier and initiate bubble disruption with a high-output ultrasound pulse to release its payload [87]. For this, the pharmaceutic agents or plasmids can be encapsulated in the gas core or incorporated in the microbubble shell.

These approaches are especially important for gene delivery. The first approach was used by Koike et al. to nonvirally transfect rat kidneys with luciferase, while mixed with microbubbles under the application of ultrasound [88]. This way, up to 80% of the cells were transfected and this correlated well with the microbubble concentration. Lan et al. used a similar procedure and reported up to a 1000-fold increased transgene expression compared to non-ultrasound treatment [90]. Following the second approach, Haag et al. assessed whether a DNA particle could be transfected in to human prostate carcinoma cells [89]. Initial *in vitro* experiments revealed that 49% of the cells contained the DNA particles. Subsequently, ultrasound with contrast agents were successfully used to intratumorally and intravenously transfect DNA into mice with human PCa.

The relevance of ultrasound-mediated drug delivery techniques is expected to grow with the advances in drug treatments. The development of new microbubble contrast agents, such as nanoscale droplets that can be used both for imaging and therapy [90], also supports the progress of this kind of therapeutic modalities.

### Fusion imaging

Over the last years, CEUS has become a reliable technique for imaging of perfusion and associated diseases. New MRI developments for cancer detection and localization, such as multiparametric MRI for PCa [92], also show promising results in centers of expertise. The fusion of recorded MRI studies and real-time CEUS for PCa-targeted biopsy is technically feasible and has clinically acceptable accuracy [93]. First tests with targeted biopsy under MR/CEUS fusion guidance have been conducted with promising results [94].

In the same way, CT and ultrasound or CEUS can be combined. In 2008, Ukimura et al. used fusion imaging to guide RFA treatment of renal cell carcinoma [95]. They found that fusion imaging provided excellent anatomical visualization and a precise target of RFA. Even the combination of MRI, CT, and CEUS for imaging of renal cell carcinoma has been applied using electromagnetic field tracking [96], although this procedure is still in a very early stage of development.

## Conclusions

In centers of expertise, CEUS has shown promising results in diagnosis and treatment imaging of prostate and kidney cancer through the visualization of perfusion. The available results for monitoring and follow-up of focal (ablative) treatment modalities are also very encouraging, especially as it provides a safer alternative to ionizing renal CT acquisitions and the use of CT/MRI contrast agents that can cause renal failure. Large prospective and multicenter studies should provide the final evidence that CEUS has an additional clinical value. With the progress in targeted molecular imaging, the development of fusion techniques, and the introduction of standardized as well as objective quantification, the role of CEUS is expected to grow in the coming years, leading to even more accurate imaging of malignancies and ablative treatment effects.

See accompanying Video 138.1.

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# 139

# Principles of Prostate Magnetic Resonance Imaging

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## Introduction

Prostate cancer (PCa) is currently the most common solid organ cancer type among men in the western world, with a lifetime risk of approximately 1 in every 6 individuals. However, it is a slowly progressing disease; only around 1 of 36 diagnosed patients will eventually die from PCa [1, 2]. Early detection of PCa is important since treatment of localized disease can be curative. In the era of prostate specific antigen (PSA) screening, more patients are being diagnosed with PCa and these are often of the indolent type. This results from random biopsies of the prostate gland detecting low-grade, microscopic cancer that will take years to grow and may even never become symptomatic. One solution to this quagmire is to use imaging to detect only the most dangerous lesions.

Currently, most predictive nomograms fail to include imaging; they rely on demographics (age, family history) and clinicopathologic features (serum PSA, Gleason score at biopsy). However, such an approach, combined with random biopsy, can easily miss significant cancers while detecting many insignificant cancers. Conventional imaging techniques such as computed tomography (CT), transrectal ultrasound (TRUS) are of limited value for detection and staging of localized PCa. Consequently, multiparametric magnetic resonance imaging (mpMRI), which includes both high-resolution anatomic and functional pulse sequences, has begun to play a major role in the detection and staging of localized PCa [3, 4]. In this chapter, we will review the specific components of prostate mpMRI, how these can be used in the diagnosis and staging of localized PCa, guidelines for interpreting mpMRI, and use of mpMRI in targeted biopsy.

## Multiparametric magnetic resonance imaging

Multiparametric MRI has greatly improved the identification and staging of localized PCa. With the advent of higher field strength magnets (3 tesla), new coil designs (endorectal and multichannel phased array surface coils), modern MRI sequences have gained increasingly higher resolution. This not only allows for more accurate cancer detection, but also the ability to use sequences for guiding biopsies and therapy (Figure 139.1). In addition, the high signal derived from modern MRI units can enable high-quality scans to be obtained without an endorectal coil, which is considered important for the widespread use of prostate MRI. Regardless of whether an endorectal coil is needed or not, obtaining multiple parameters during the MRI improves the sensitivity and specificity of the scan. In this section the four basic parameters comprising a complete mpMRI will be discussed.

### T2-weighted magnetic resonance imaging

T2-weighted (T2W) MRI of the prostate is the backbone of mpMRI for lesion detection and local staging. It is best for clear delineation of prostatic zonal anatomy and visualization of surrounding structures, with superior soft tissue contrast [5–7].

PCa can be visualized as a hypointense focus on T2W MRI due to loss of normal glandular morphology. However, low T2 signal intensity in the prostate is not always indicative of PCa. Benign conditions such as prostatitis, benign prostatic hypertrophy (BPH), scars, or posttreatment changes (e.g. radiation, hormone ablation) may have a similar appearance [8, 9]. Post-biopsy hemorrhage can also appear hypointense on T2W scans,

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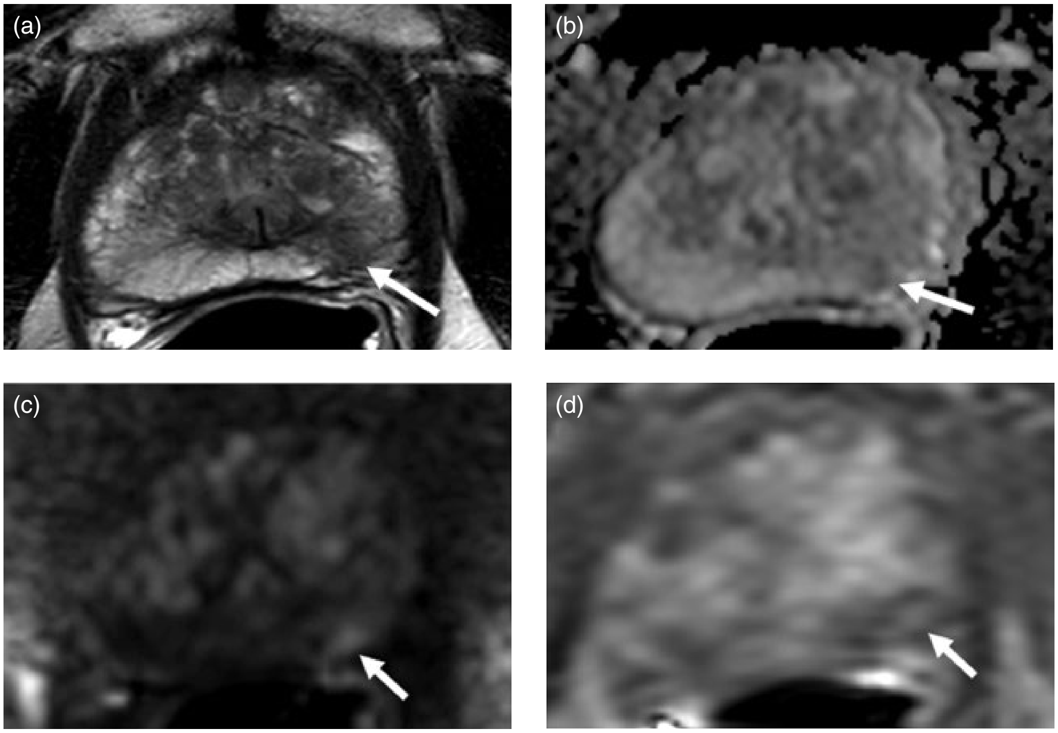

**Figure 139.1** A 67-year-old presented with PSA 4.67 ng/ml and underwent multiparametric MRI (mpMRI), which revealed PI-RADS v2 score 4 lesion in the left apical peripheral zone (arrows). Lesion was identified on T2-weighted MRI (a), apparent diffusion coefficient map of diffusion-weighted (DW) MRI (b), *b*-2000 image of DW MRI (c), and dynamic contrast-enhanced MRI (d). Subsequent transrectal ultrasound/MRI fusion-guided biopsy revealed Gleason 3+3 in 20% of biopsy core. Patient was offered active surveillance option with yearly monitoring using mpMRI and biopsy.

but is more easily distinguishable, as areas with hemorrhage correspond to hyperintense regions on T1-weighted MRI. Detection of PCa in the peripheral zone (PZ) is easier than it is in the transition zone (TZ). In the PZ, most PCa are hypointense against a background of high T2 signal intensity of the normal tissue. In the TZ, tumor is more difficult to differentiate because of the coexistence of BPH. Indicators of tumor in the TZ include homogeneous low to intermediate T2 signal intensity without a distinct capsule, ill-defined margins, and lenticular shape [6, 10].

T2W MRI can also be utilized for local staging. Extraprostatic extension (EPE) usually appears as a direct extension of the tumor out of the edge of the gland into surrounding hyperintense periprostatic fat. In most cases, EPE is subtle; secondary findings including asymmetry of the neurovascular bundle, tumor surrounding the neurovascular bundle, gland border irregularity or asymmetry, a relatively long contact of the tumor with the capsule, and obliteration of the rectoprostatic angle can be used to suggest EPE. If EPE is present, the patient is upstaged to T3a and this alters the treatment to a more aggressive approach [11]. Another part of staging is evaluating for seminal vesicle invasion (SVI), which is considered T3b disease. SVI can be seen as a low signal defect within the normally high-signal seminal vesicles. Two types of SVI are described: one is a direct extension of the tumor from its origin in the base of the prostate and the other is multifocal low signal intensity within the seminal vesicles not in continuity with the primary tumor. The presence of SVI upstages to T3b, and also affects subsequent treatment decisions [11] and likelihood of recurrence. Therefore, T2W MRI evaluation of EPE and SVI provides information regarding a patient's PCa that is vital to treatment planning.

T2W MRI has a wide range of sensitivities and specificities for detecting PCa (reported sensitivities: 27–100%; reported specificities 32–99%) as well as for staging (reported sensitivities 14–100%; reported specificities 67–100%). This range of performance in detection may be affected by significant variability of studied patient populations, as well as differences in the gold standard used (biopsy vs. surgery). T2W detection ability also depends on the sophistication of the MRI unit, experience of its operator, and experience of the reader. A large disadvantage of T2W MRI for accurate detection is that it is highly dependent on patient cooperation in order to minimize movement, and on the experience of the radiologist in subjectively determining signal differentiation [4]. However, even in ideal conditions, T2W MRI is not specific, and has demonstrated limited ability to diagnose PCa as a standalone method. A recent study from a top-rank institution demonstrated that T2W MRI alone at 3 T field strength revealed a detection accuracy of 80–90% for tumor foci larger than 1.0 cm in diameter [12]. However, for smaller tumors T2W MRI was far less accurate [13]. Nevertheless, for local staging, T2W is considered the most useful technique. The sequence is particularly useful for identifying EPE of a suspicious lesion. Bloch et al. evaluated the role of T2W MRI and dynamic contrast-enhanced (DCE) MRI in staging of PCa in a cohort of 108 patients and found an overall sensitivity, specificity, positive predictive value and negative predictive value for EPE of 75%, 92%, 79%, and 91%, respectively. In addition, for less experienced, moderately experienced, and highly experienced readers, they reported diagnostic accuracies for overall staging of 86%, 80%, and 91%, respectively, indicating that local staging based on these parameters is relatively easy to teach [14]. Staging using SVI identification on T2W images has proven successful as well. In a cohort of 573 patients of whom 28 had SVI, T2W MRI outscored all clinicopathologic variables in correctly predicting the SVI with an area under the curve (AUC) of 0.76 (vs. 0.62–0.73 for clinicopathologic variables) [15]. T2W combined with DCE MRI and diffusion-weighted (DW) MRI is even better, as unilateral atrophy, or calculi or clot within the seminal vesicles may mimic the appearance of SVI on T2 (Figure 139.2).

Although it is the backbone of mpMRI, T2W MRI is nonspecific; its use in combination with functional MRI can increase the accuracy of PCa detection and will be discussed next.

## Diffusion-weighted magnetic resonance imaging

DW MRI measures the random motion of water molecules within the tumor [16, 17]. Specifically, it measures water proton diffusion by utilizing apparent diffusion coefficient (ADC) [18]. Since this property is influenced by cellular density, membrane permeability, and extracellular space volume, DW MRI has the potential to explore several aspects of tissue microscopy [19, 20].

The basis of DW MRI is that stationary water protons will not acquire a phase shift when an external magnetic gradient is applied. Moving water protons, on the other hand, will acquire a phase shift proportional to the amount of motion, resulting in loss of signal. If this process is repeated for sequentially stronger external magnetic gradients (“*b*”-values), an estimate of the bulk water diffusion can be made with ADC values and represented on a voxel-by-voxel basis in the form of an ADC map [16]. Although the connection between random motion of water molecules and MRI was established many years ago, application of this principle to clinical imaging has only recently become feasible due to improved susceptibility artifact suppression [16]. First used for brain imaging in stroke, DW MRI has expanded its application to virtually every part of the body for oncology imaging, including the prostate [21, 22]. Cancers have significantly restricted water diffusion, which appears as a hypointense signal relative to surrounding tissue on ADC maps. This is due to cancer cells’ higher nuclear:cytoplasmic ratio, higher cellular density, and extracellular disorganization, which all contribute to trapping water more readily [21].

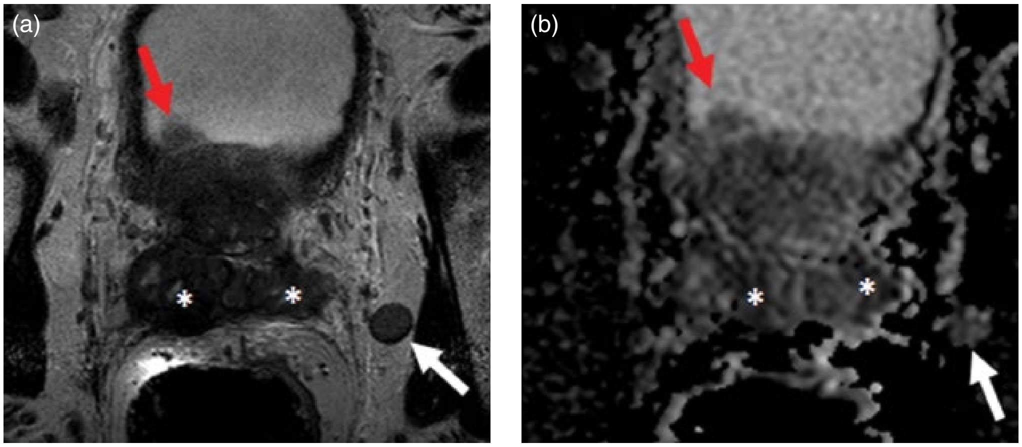

**Figure 139.2** A 66-year-old with serum PSA 48.90 ng/ml, diagnosed with Gleason 4+5 disease in the prostate base on TRUS/MRI fusion-guided biopsy. Multiparametric MRI exam was further evaluated for staging purposes, with axial T2-weighted MRI (a) showing evidence of seminal vesicle invasion (asterisks), bladder wall invasion (red arrow), and left iliac chain adenopathy (white arrow). These findings are further verified by apparent diffusion coefficient map of diffusion-weighted MRI (b).

DW MRI is obtained at various *b*-values ranging from 0 to 800 s/mm$^3$, which are postprocessed to create the ADC values that contribute to the final ADC map [23]. At *b*-values >1000 s/mm$^3$, a "high *b*-value" image can be produced [24]. This sequence displays as almost the inverse of the ADC map: areas with more diffusion restriction appear as hyperintense on the high *b*-value images, which are "raw" images and not processed. Therefore, tumors in the prostate appear as focal areas of hyperintensity relative to the surrounding tissue on high *b*-value sequences while on ADC maps the same areas appear focally hypointense. In general, high *b*-value DW MRI tend to have lower signal and therefore lower resolution, so suspicious areas should correspond to findings on other sequences of the mpMRI for more accurate detection. The high *b*-value images can either be directly acquired at higher magnetic gradient or calculated from lower *b*-value images using different decay models [25]. It has been shown that *b*-values >1500 s/mm$^3$ are best for maximizing lesion visibility for PCa detection on mpMRI [26]. With optimal high *b*-value imaging, sensitivities ranging from 78% to 94% have been reported. However, *b*-values >2500 s/mm$^3$ should not be used, as there is too great a compromise in signal-to-noise ratio in this range [27].

Advantages of DW MRI compared with other MRI techniques include DW imaging's short acquisition time and relatively high sensitivity and specificity for cancer [19]. DW MRI may also yield qualitative and quantitative information for predicting locally recurrent PCa post-therapy [28]. Active tumors tend to have lower ADCs while tumors undergoing therapy are observed to have progressively higher ADCs. In addition to enabling good detection and therapy monitoring, DW MRI could also play a role in active surveillance [16]. However, DW MRI has some limitations such as low spatial resolution, which hinders local staging. It is also prone to susceptibility artifacts, especially caused by rectal gas. Moreover, DW MRI findings of the TZ are more challenging as TZ is more heterogeneous due to BPH [29, 30]. TZ tumors and PZ tumors should have the same appearance on high *b*-value sequences and ADC maps. Based on diffusion signal alone, such lesions can be confusing; however, when they are placed in the anatomic context of a well-circumscribed BPH nodule, as seen on T2W MRI, it becomes easier to differentiate potential malignancy from benign tissue. DW MRI can also be falsely positive due to hemorrhage, prostatitis, dysplasia, and high-grade prostatic intraepithelial neoplasia, as well as posttreatment changes. In a study of 49 patients who underwent radical prostatectomy following MRI, Oto et al. analyzed the diffusion parameters of TZ PCa, stromal hyperplasia (SH), and glandular hyperplasia (GH) in the differentiation of TZ cancers from benign hyperplasia. Thirty-eight foci of carcinoma, 38 SH nodules, and 38 GH nodules in the TZ were localized on the basis of histopathologic correlation. Receiver operating characteristic (ROC) and multivariate logistic regression analyses were performed for the differentiation of TZ cancers from hyperplastic foci. They found the average ADCs as 1.05, 1.27, and 1.73, respectively, in TZ cancers, SH foci, and GH foci yielding AUCs of 0.99 and 0.78, respectively, for differentiation of carcinoma from GH and SH [29]. Thus, it may be possible to differentiate tumors from BPH nodules on the basis of their ADC value.

The addition of DW MRI to standard imaging protocols dramatically improves the overall diagnostic efficacy of MRI for PCa detection and for tumor recurrence [31]. For instance, Morgan et al. demonstrated a 93.8% sensitivity and 75% specificity, and AUC up to 0.992 for lesions >0.4 cm$^2$ when DW MRI was added to T2W MRI in the detection of local prostate tumor recurrence [17]. This is in contrast to T2-only detection of prostate tumor recurrence, reported with AUC of 0.67 by Petraki and Sfikas [32]. In a meta-analysis of 19 recent articles conducted by Tan et al., DW MRI both increased sensitivity and increased specificity for PCa detection compared to T2W MRI alone [19]. Rosenkrantz et al. studied 51 patients and showed that DW MRI and ADC maps had a greater sensitivity than T2W MRI for less experienced readers and that they improved detection of PZ lesions that were difficult to recognize on T2W MRI [33].

DW MRI may provide some additional information about the nature of the tumor detected as well. Studies have shown that in PCa, ADC values inversely correlate with lesion Gleason score on histopathology and can therefore play a role in risk stratification [34–36]. Hambrock et al. reported a negative correlation between the median ADC in the tumors and the PZ tumor Gleason grade in 51 patients [35]. Turkbey et al. found a similar negative correlation between tumor ADC values and Gleason scores in 48 patients scanned at 3 T. Moreover, they reported utility of ADC values in predicting D'Amico clinical risk scores [36]. The ability to predict tumor aggressiveness could be useful in selecting appropriate therapies. Thus, DW MRI is so far the most promising quantitative MRI technique for noninvasively accomplishing this. However, there remains overlap between Gleason scores and ADC values, thus limiting its predictive value in individual patients. Moreover, not all lesions found to have low ADC values are actually tumors. This underscores the need to obtain biopsies in patients with suspected lesions on MRI regardless of their ADC value.

## Magnetic resonance spectroscopic imaging

Proton MR spectroscopic imaging (MRSI) is a functional method capable of assessing prostate tissue metabolism. MRSI used to be more commonly included in mpMRI, but has recently fallen out of favor since its additive value is limited. Each volume of interest (voxel), acquired in a three-dimensional (3D) MRS image, contains a metabolite spectra. The spectra demonstrates the relative concentrations of the specific tissue metabolites citrate (Cit), creatine (Cr), and choline (Cho). Prostate tumors are characterized by increased levels of choline and decreased levels of citrate, whereas normal prostate tissues contain high levels of citrate and relatively low levels of choline and creatine. This allows for differentiation between the tissues with MRSI, and increases in ratios (Cho + Cr)/Cit and Cho/Cit serve as markers for likely PCa. The metabolic differences are likely secondary to increased cell membrane turnover, which results in high choline levels in prostate tumors, and abnormal functioning of tumor cells leading to low levels of citrate. Once the ratios are determined, a scoring method for metabolic ratios is used to characterize the tumor [37].

Metabolism is a unique measure in tumor detection. Several investigators have noted a correlation between metabolic ratios (e.g. Cho/Cit) and PCa aggressiveness [5, 38–41]. Kobus and colleagues studied the performance of MRSI alone and in combination with ADCs of DW MRI at 3 T. In this study, 54 patients with biopsy-proven cancer underwent MRSI prior to prostatectomy. They found significant correlation between pathology classification of tumor aggressiveness and (Cho + Cr)/Cit ratio, Cho/Cit ratio, and ADC values in PZ tumors (areas under the curve of 71%, 67%, and 81%, respectively). They also found significant correlation with (Cho + Cr)/Cit ratio and Cho/Cit ratio in the TZ (rho = 0.58 and rho = 0.60, respectively). Although further validation is needed, MRSI has the potential to be useful in assessment of tumor aggressiveness [42]. This is particularly useful as emphasis is placed on differentiating clinically significant tumors from lower grade tumors that may have no impact on the patient's longevity [43]. Multiple authors have incorporated MRSI into nomograms to help predict the aggressiveness of tumors [44, 45]. As an example, Shukla-Dave et al. studied 181 PCa patients using nomograms incorporating MRSI and nomograms based on clinical data alone. They found that when MRSI results used to distinguish low- and high-risk cancers were incorporated into nomograms, these predictions performed significantly better ($P \leq 0.05$) [44].

A prospective multicenter study performed by the American College of Radiology Imaging Network (ACRIN) to determine the benefit of combined endorectal MRI and MRSI concluded that T2W MRI alone and combined T2W MRI–MRSI had similar accuracy in PZ cancer localization (AUC, 0.60 vs. 0.58, respectively; $P > 0.05$). AUCs for individual readers were 0.57–0.63 for T2W MRI alone and 0.54–0.61 for combined T2W MRI–MRSI without significant difference [46]. On the other hand, in a recent study by Selnaes et al., the authors used a stringent segmental matching of histopathology and MRI. They found that combination of T2WI and MRSI had an AUC of 0.90, which was better than T2WI alone with an AUC of 0.85 [47].

MRSI has its limitations. It is technically challenging and time consuming, and adds to the expense of MRI studies. The spectrum is subject to artifacts. MRSI requires additional time for acquisition and separate postprocessing, decreasing clinical throughput and requiring skilled labor. Most vendors now supply a workable MRSI package for prostate imaging, but proper performance of the scan is still needed. For instance, proper MR shimming is needed to accentuate key peaks and suppress water, and lipid contamination to produce quality spectra. This often necessitates an onsite physicist. If the scan can be obtained, there are then challenges in interpretation. The large size of the MRSI voxel may cause partial volume effects, which can cause the image to be misread. Due to many of these limitations, MRSI has not gained the widespread popularity in clinical use that other mpMRI sequences have achieved. Currently, MRSI has largely been dropped from MRI protocols at most centers.

## Dynamic contrast-enhanced magnetic resonance imaging

DCE MRI is an important functional sequence of mpMRI. In DCE MRI, fast T1-weighted sequences are acquired before, during, and after the intravenous injection of an MRI contrast agent (such as low molecular weight gadolinium chelates). The rapid sequences are used to detect the arrival and uptake of the contrast into the prostate before washing out of the gland. This uptake provides a rough delineation of perfusion in the prostate, which can suggest regions of hypervascularity [48, 49]. Tumors are often hypervascular and enhance earlier and with more rapid wash-out than normal tissue. This is due to neoangiogenesis, a property of tumors that leads to rapid vessel growth and increased vascular permeability. Neoangiogenesis is thought to be related to tumor aggressiveness [50]. Usually, tumor foci within the prostate gland in the PZ tend to enhance earlier, faster, and to a greater extent than normal tissue and other benign conditions. Tumors also display a characteristic early contrast wash-out compared with healthy prostate. However, in the TZ, these abnormal enhancement patterns can also be seen in BPH nodules and inflammation, making assessment and detection of tumor more difficult [51]. In both prostate zones, smaller and low-grade tumor foci frequently do not demonstrate abnormal enhancement on DCE MRI [48, 52].

The most common evaluation method for DCE MRI is the qualitative approach, in which focal early and intense enhancement with early wash-out compared to normal prostatic tissue is visually detected. More quantitative approaches can be used as well. Pharmacokinetic parameters can be determined semi-quantitatively using different kinetic models which provide indices of vascular permeability. The most commonly used quantitative parameters based on a modified Toft's model are $K^{\mathrm{trans}}$ (transfer of gadolinium contrast from the vascular compartment to the tumor compartment representing forward vascular permeability and flow), $k_{\mathrm{ep}}$ (reverse transfer of contrast from the extracellular space back to the plasma space representing backward leakage) [53]. Higher grade tumors tend to have higher $K^{\mathrm{trans}}$ and $k_{\mathrm{ep}}$ parameters compared with normal surrounding prostate tissue. However, smaller and low-grade tumors often do not demonstrate abnormal enhancement on DCE MRI [52]. This information can be helpful to predict more aggressive disease and thus manage patients more appropriately. Additional semi-quantitative analysis can be based on fitting the time–gadolinium concentration curve to the two-compartment model. In addition to the calculated permeability parameters, the time–gadolinium concentration curve can be used to measure the AUC, time to peak enhancement, and initial slope. These enhancement curves can be classified into one of three types: type 1 persistent increase; type 2 plateau curve; and type 3 decline after initial upslope. Often, mixtures of different curves are found within lesions, but of these curves, type 3 is most commonly associated with PCa [54].

DCE MRI has high sensitivity, which can be useful for initial evaluation of potential tumor foci and has been routinely used to detect lesions, cancer aggressiveness, and monitor therapeutic response in clinic trial settings. The modality alone has a sensitivity and specificity range of 46% to 96% and 74% to 96%, respectively; as always, these ranges are highly dependent on patient selection, image acquisition and analysis technique, lesion size and diagnostic criteria [4]. A recent work by Puech et al. analyzed the performance of DCE MRI at 1.5 T in identifying and localizing intraprostatic cancer foci in relation to cancer volume at histology. The sensitivity and specificity of DCE MRI for identification of tumor foci of any volume were 32% and 95%, respectively. For identification of tumor foci >0.5 ml, the sensitivity and specificity were 86% and 94%, respectively, and the AUC was 0.874 [55]. Combining DCE MRI and T2W MRI resulted in a significant improvement of diagnostic accuracy of tumor detection up to 91% in 34 patients [56].

There are limitations in the performance of DCE MRI that should be considered. For instance, the TZ is a challenging area for tumor detection since a significant overlap is present between DCE MRI features of BPH and PCa. Therefore, previously published works on DCE MRI performance in the TZ are controversial. Some results have suggested potential usefulness of DCE in the TZ [57], while other studies failed to do so [58]. DCE MRI used with other pulse sequences for further anatomical and functional information can yield improved results for tumor detection in the TZ. In addition, staging accuracy and detection of EPE and SVI requires high spatial resolution for anatomic differentiation, which is why the use of combined endorectal/body phased array coils is needed. DCE MRI alone still suffers from relatively lower spatial resolution. It still can offer utility in identifying EPE and SVI; DCE MRI combined with a higher resolution pulse sequence such as T2W MRI is required to improve PCa detection and local staging. Bloch et al. found AUC 95% overall staging accuracy when DCE MRI was combined with T2W, up to a 3% and 11% AUC improvement compared with DCE MRI and T2W MRI alone, respectively [59, 60]. DCE MRI can play a role in staging to confirm suspicion of SVI detected via T2W MRI and/or DW MRI. Presence of an early enhancement within a seminal vesicle lesion can be meaningful for confirmation of invasion. Ogura et al. interpreted early enhancement within SVs at DCE MRI and reported that this finding has accuracy rates as high as 97% for SVI in a cohort of 38 patients [61].

## Interpretation of multiparametric MRI

Traditionally, interpretation of mpMRI has been quite subjective, with readers using signal findings to identify suspicious areas in the prostate. Different scoring systems for identifying lesions were utilized at each institution. As the role of MRI has continued to grow in PCa diagnosis and management, steps have been taken towards creating a standardized method of image interpretation. In 2015, the Prostate Imaging-Reporting And Data System version 2 (PI-RADS v2) was released as part of this effort. PI-RADS v2 is a set of guidelines that includes standardized imaging parameters for sequence acquisition as well as the PI-RADS v2 scoring system. The mpMRI sequences accounted for in PI-RADS v2 are multiplanar T2W MRI, DW MRI (ADC map and high $b$-value images ($b \geq 1500\,\mathrm{s/mm^3}$)), and DCE MRI with rapid acquisition of T1 images before, during, and after contrast administration. The scoring system utilizes characteristic signal patterns on mpMRI indicative of malignancy in the PZ and in the TZ [62].

Each sequence of mpMRI (T2W MRI, DW MRI, DCE MRI) receives its own score for each identified suspicious lesion. T2W MRI and DW MRI are scored on a scale of 1 to 5, while DCE MRI is recorded as positive or negative for enhancement. Each lesion is then given an overall score scaled 1 to 5, mostly influenced by what zone of the prostate the lesion is found in. In the PZ, DW MRI serves as the dominant sequence. This means that the score of DW MRI is considered first, and for scores 1, 2, 4, and 5, this serves as the overall score as well. If a PZ lesion is given DW MRI score of 3, the overall score can be upgraded to 4 if the lesion is also DCE positive. In contrast, in the TZ, T2W MRI serves as the dominant sequence. T2W MRI scores 1, 2, 4, and 5 serve as overall lesion score; T2W MRI score 3 can be upgraded to an overall score 4 if the TZ lesion of interest is given a DW MRI score of 5.

Overall PI-RADS v2 scores suggest probability of clinically significant cancer to be present in an identified lesion on imaging. Score 1 suggests very low probability, score 2 indicates low probability, score 3 indicates intermediate probability, score 4 indicates high probability, and score 5 indicates very high probability. Scoring determination for each sequence is based on signal findings consistent with tumor as described previously in this chapter. For T2W MRI scoring, heterogeneous or hypointense signal intensity can be suspicious in both the PZ and TZ. Heterogeneous signal intensity with obscured margins corresponds with a T2W MRI score of 3, while a circumscribed and homogeneous hypointensity corresponds with score 4 if it measures <1.5 cm in diameter, and score 5 if it measures >1.5 cm and/or shows suggestion of EPE. In DW MRI, the ADC map and high *b*-value sequence are evaluated together. For DW MRI score 3, a focal mildly or moderately hypointense area can be seen on ADC that corresponds with an isointense or mildly hyperintense area on the high *b*-value image. For DW MRI score 4, a focal markedly hypointense area on the ADC map and corresponding markedly hyperintense area on high *b*-value can be seen for a lesion <1.5 cm in greatest diameter; for score 5, the dimension of the lesion is >1.5 cm and/or there is indication of EPE. Finally, DCE MRI is positive if an area in the prostate focally enhances earlier than or synchronous with enhancement of adjacent tissue, and corresponds to a suspicious area on the other sequences of mpMRI. DCE MRI has the potential to upgrade the overall score of a PZ lesion scored 3 on DW MRI, but otherwise does not change overall scoring of lesions. Absence of early enhancement does not eliminate the potential of clinically significant cancer in a suspicious lesion found on other sequences. However, DCE MRI should be included in all mpMRI exams, as careful evaluation can help identify smaller foci of clinically significant cancer [62] (Figure 139.3).

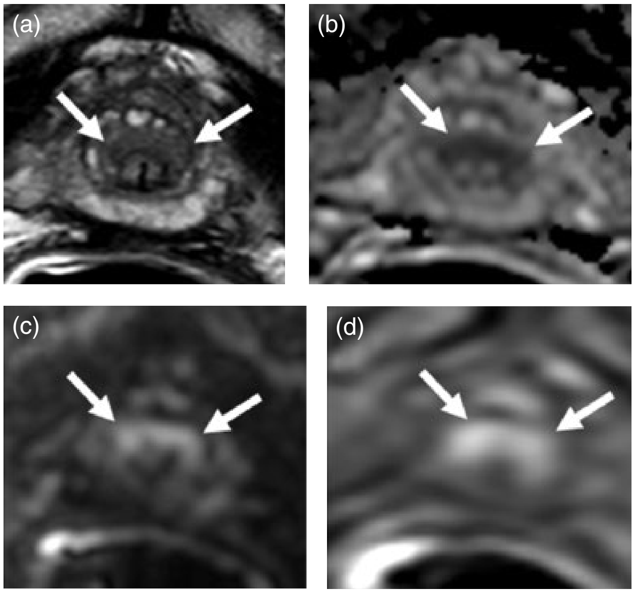

**Figure 139.3** A 75-year-old (serum PSA 14.60 ng/mL) with score 4 lesion identifed in the midline apical anterior transition zone on multiparametric MRI according to PI-RADS v2 criteria. This lesion was visualized as a uniformly hypointense area (arrows) measuring <1.5 cm on T2-weighted MRI (a), with a corresponding hypointensity (arrows) on the apparent diffusion coefficient map of diffusion-weighted (DW) MRI (b), a matching hyperintensity (arrows) on *b*-2000 DW MRI (c), and early enhancement (arrows) on dynamic contrast-enhanced (DCE) MRI (d). This TZ lesion received a PI-RADS v2 score 4 on T2-weighted MRI and DW MRI, and a positive score on DCE MRI. Patient underwent subsequent TRUS/MRI fusion-guided biopsy, yielding Gleason 3+4 prostate cancer diagnosis.

Since its introduction, many institutions have adopted PI-RADS v2 as the method of interpretation of their prostate mpMRI exams. However, while PI-RADS v2 is a large step towards standardization, it is still not optimal and there is variability among readers. In a multireader analysis, average sensitivity for lesion detection across five readers was 63%, with interreader agreement of 58%. This variability is also present in index lesion interpretation, with interreader agreement of 86% [63]. As PI-RADS v2 is based on expert opinion, complete validation of the system remains to be investigated.

## Use of multiparametric MRI for biopsy guidance

mpMRI is increasingly being used for identification of suspicious lesions. However, the mpMRI interpretation alone has little diagnostic value for a PCa patient. Only after the mpMRI findings are used to obtain a tissue diagnosis can a proper plan be implemented for patient management.

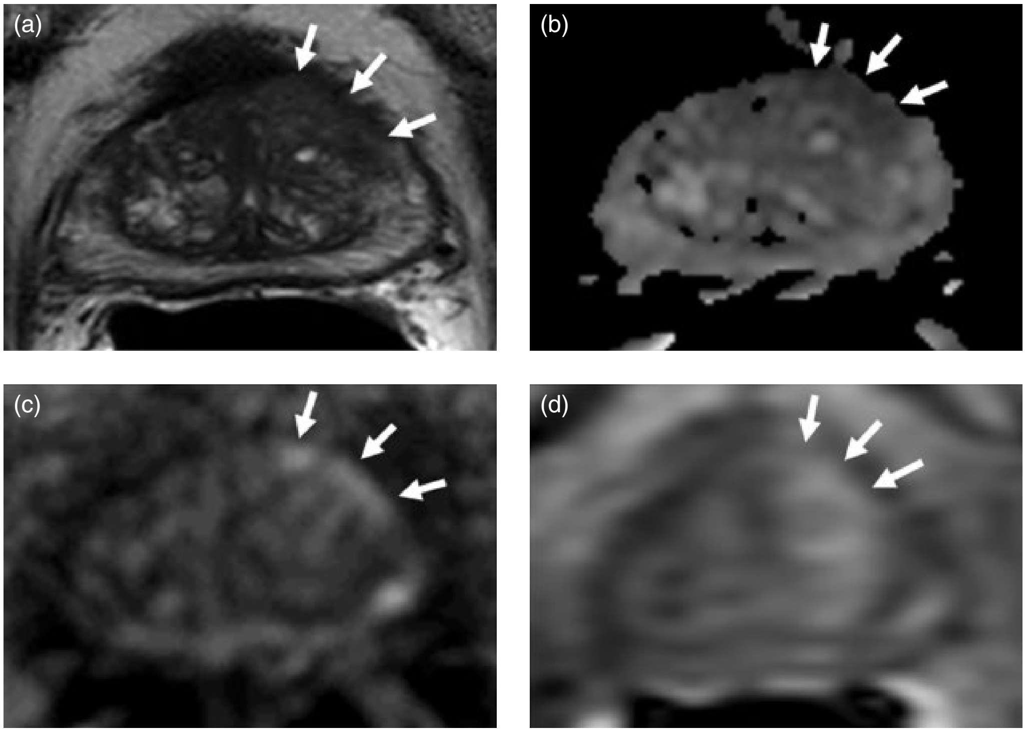

**Figure 139.4** A 67-year-old who presented in 2009 with initial PSA 5.90 ng/ml, and has had subsequent PSA measurements and negative systematic biopsies over the past 7 years. Patient had his first multiparametric MRI in 2016 which revealed a PI-RADS v2 score 5 lesion (1.6 cm) in the left mid anterior transition zone (arrows) shown on T2-weighted MRI (a), apparent diffusion coefficient map of diffusion-weighted (DW) MRI (b), *b*-2000 image of DW MRI (c), and dynamic contrast-enhanced MRI (d). TRUS/MRI fusion-guided biopsy yielded Gleason 3+4 prostate cancer. Following these new results, the patient was offered active management.

Traditionally, the standard of tissue diagnosis has been a 12-core systematic biopsy. However, the advent of TRUS/MRI fusion-guided biopsy has introduced targeted biopsy in PCa diagnosis. Common fusion systems include the UroNav, Artemis, Urostation, and BiopSee platforms. During the biopsy procedure, real-time ultrasound is fused with a previously acquired mpMRI to best target identified lesions. TRUS/MRI fusion-guided biopsy has been shown to increase detection of intermediate- and high-risk cancers, and decrease detection of low-risk cancers (Figure 139.4) [64–67]. For example, Siddiqui et al. demonstrated that tumors biopsied using mpMRI and subsequent fusion biopsy detect 30% more clinically significant cancers and 17% fewer insignificant cancers compared to traditional systematic biopsy [64].

## Conclusion

Accurate detection and local staging of PCa is important to deliver correct treatment approaches for patients. mpMRI can detect clinically relevant intraprostatic tumor foci and can provide valuable information about local staging and tumor aggressiveness. However, mpMRI is still a relatively recent addition to the PCa workup and its use is still controversial in some settings. As this modality migrates out into community practices it is important that attention is paid to issues of image quality, interpretation quality, adherence to international reporting standards (e.g. PI-RADS v2) and the quality of MRI/TRUS fusion-guided biopsy if this method is to provide uniformly positive benefits across all patients with PCa.

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# 140

# Male Lower Urinary Tract Symptoms and Assessment

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## Introduction

Benign prostatic hyperplasia (BPH) is an age-dependent pathoanatomic condition with an initial histopathologic development after 40 years of age, and prevalence rates of approximately 50% and 90% by 60 and 85 years of age, respectively. Cell proliferation associated with BPH is composed of both epithelial and stromal elements and may result in benign prostatic enlargement (BPE), bladder outlet obstruction (BOO), and a constellation of lower urinary tract symptoms (LUTS) that are commonly classified as voiding or storage symptoms.

In most instances, the patient has more than one complaint. It has generally been assumed that voiding symptoms are caused by prostatic obstruction and that storage symptoms are caused by inflammation or detrusor overactivity. Despite the logic implied, most clinical studies that document the relationship between symptoms and underlying pathophysiology have established no such correlation.

Although existing medical and surgical interventions attempt to reduce the obstructive component to provide symptomatic relief, the association between BPH, benign prostatic obstruction (BPO), and BOO is complex. For example, it is unclear whether urethral obstruction is the primary mechanism by which BPH causes symptoms. Nor is it known whether the relief of the obstruction is a prerequisite to successful treatment of symptoms. Likewise, the relationship between symptoms and commonly used indices (to measure LUTS suggestive of prostatism), such as uroflow and postvoid residual (PVR) urine, is unknown.

Recent evidence suggests that the etiology of prostatic symptoms is multifactorial involving (i) prostatic urethral obstruction, (ii) impaired detrusor contractility, and (iii) detrusor overactivity [1]. The best method to definitively diagnose BOO is the detrusor pressure–uroflow flow study (PFS), but there is much more to be obtained from urodynamics than simply diagnosing obstruction.

This chapter describes existing urodynamic techniques used in the diagnosis of BPH, and reviews the role of urodynamics in the evaluation of LUTS and urinary incontinence.

## Background

LUTS are generally categorized into storage, voiding, and postmicturition symptoms [2]. Storage symptoms include daytime frequency, nocturia, urgency, and urinary incontinence. Voiding symptoms are composed of slow stream, splitting or spraying, hesitancy, intermittency, and straining to void. Postmicturition symptoms include feeling of incomplete emptying and postmicturition dribbling. In men, BOO associated with BPH is only one of many causes of LUTS. Other causes include overactive bladder (OAB), neurogenic bladder, impaired detrusor contractility, low bladder compliance, and polyuria. It is not possible to make the diagnosis of BOO on symptom assessment alone. In patients with LUTS and BPH, urodynamic evidence of BOO exists in only 50–66% of patients [3–6]. Furthermore, a number of studies have demonstrated a lack of correlation between symptoms, the American Urological Association (AUA) symptom score or the Danish Prostate Symptom Score, and urodynamic data in patients with suspected BPH and BOO [7–10].

Determining the urodynamic abnormalities responsible for LUTS is important so that treatment can be directed at the underlying pathophysiology. Currently,

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

**Table 140.1** Relevant data before and after treatment.

| | |
|---|---|
| Structured micturition history | |
| Symptom severity score, such as the Lower Urinary Tract Symptom Score, American Urological Association symptom score, or ICIQmale LUTS | |
| Physical examination, including: | General examination |
| | Brief screening neurologic examination (to discriminate normal, paraplegic, quadriplegic, hemiplegic, dementia, etc.) |
| | Focused meurologic examination (perianal sensation, anal sphincter tone and control, and bulbocavernosus reflex) |
| | Prostate examination |
| A micturition diary including: | Time of micturition |
| | Description of symptoms |
| | Voided volume |
| Uroflow ($Q$) and postvoid residual determination (PVR): | Urodynamic parameters: the following parameters permit patients to be objectively classified as having prostatic obstruction or impaired contractility: |
| | i) Maximum uroflow ($Q_{\max}$) |
| | ii) Detrusor pressure at maximum flow ($P_{\text{det}}$ at $Q_{\max}$) |
| | Other useful urodynamic parameters include: |
| | i) Presence or absence of detrusor overactivity |
| | ii) Bladder sensation and ability to abort involuntary detrusor contractions |
| | iii) Bladder capacity |
| | iv) Voided volume |

the majority of medical and surgical interventions target the reduction or elimination of prostatic obstruction, yet only about two-thirds of men are actually obstructed according to urodynamic criteria. In fact, therapies should be specific for detrusor overactivity, urgency, and impaired detrusor contractility. Urodynamics are necessary to make the distinctions between these entities.

The most definitive method of diagnosing urethral obstruction and impaired detrusor contractility is the detrusor pressure–uroflow study, whereas only cystometry is necessary to assess urgency and detrusor overactivity. Although questionnaires, symptom analysis, uroflow, and postvoid residual urine volumes (PVR) all play a role in evaluating men with suspected BOO, only urodynamics can make the necessary distinctions to allow therapy to be tailored to the underlying condition.

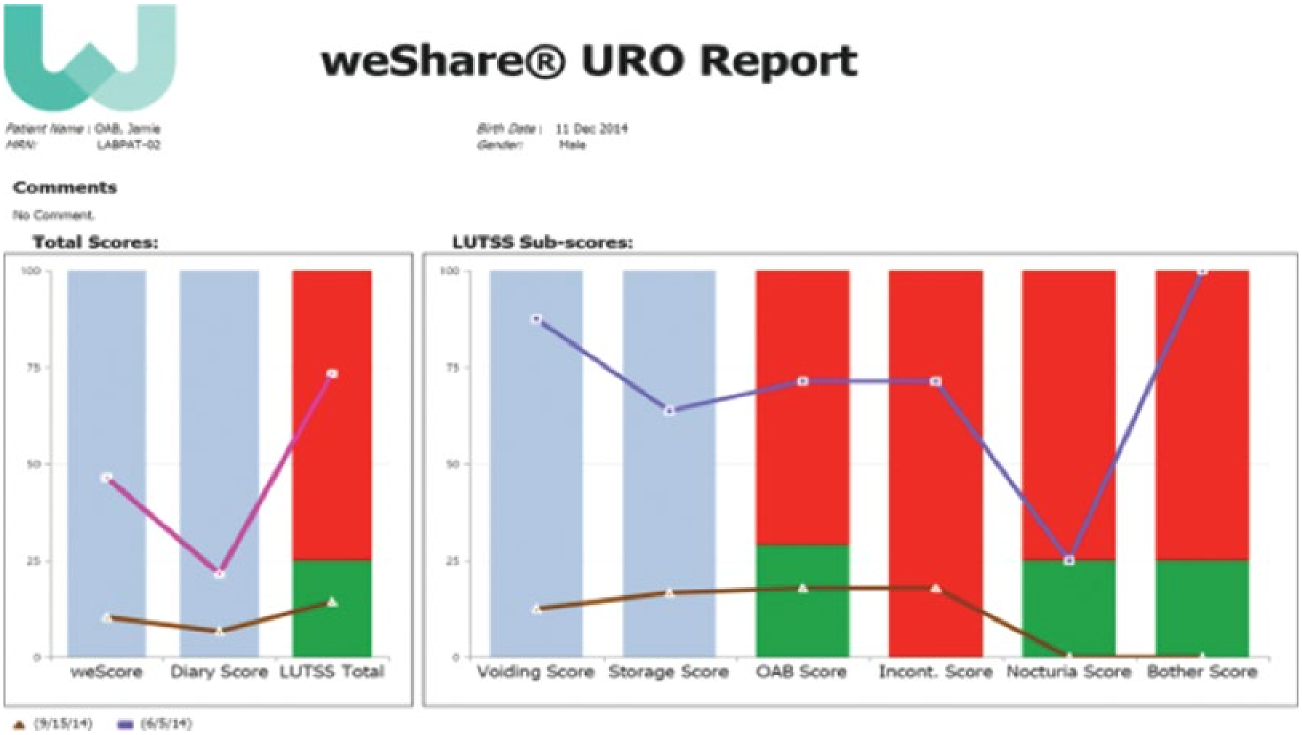
## Defining and quantifying symptoms

Defining and quantifying symptoms are important for two reasons. First, there is an imperfect correlation between symptoms, symptom severity, bother, and underlying pathophysiology. It is therefore important to quantify each of these variables separately in order to tailor the treatment to the individual patient's wants and needs. Second, in order to evaluate treatment outcomes in any meaningful way, it is necessary to tabulate this data before and after treatment (Table 140.1). There are numerous LUTS questionnaires and patient-reported outcome instruments, but no single questionnaire contains all of the domains necessary to define and quantitate the necessary data for clinical care or outcomes research. In our judgment, the two best are the ICIQmale LUTS-SF and the Lower Urinary Tract Symptom Score (LUTSS) [11, 12]. The latter is divided into six subscores: voiding, storage, OAB, incontinence, nocturia, and bother. It is also available as a mobile app that can be completed remotely by the patient and displayed in a graphic format that allows visual comparison of treatment outcomes (Figure 140.1).

## Preparation for urodynamic study

The main purpose of urodynamic evaluation is to document the underlying cause of the patient's complaints and to correlate symptoms with urodynamic findings. From a clinical standpoint, the purpose of urodynamic testing is to measure and record various physiologic variables while

(a)



## weShare® URO Report

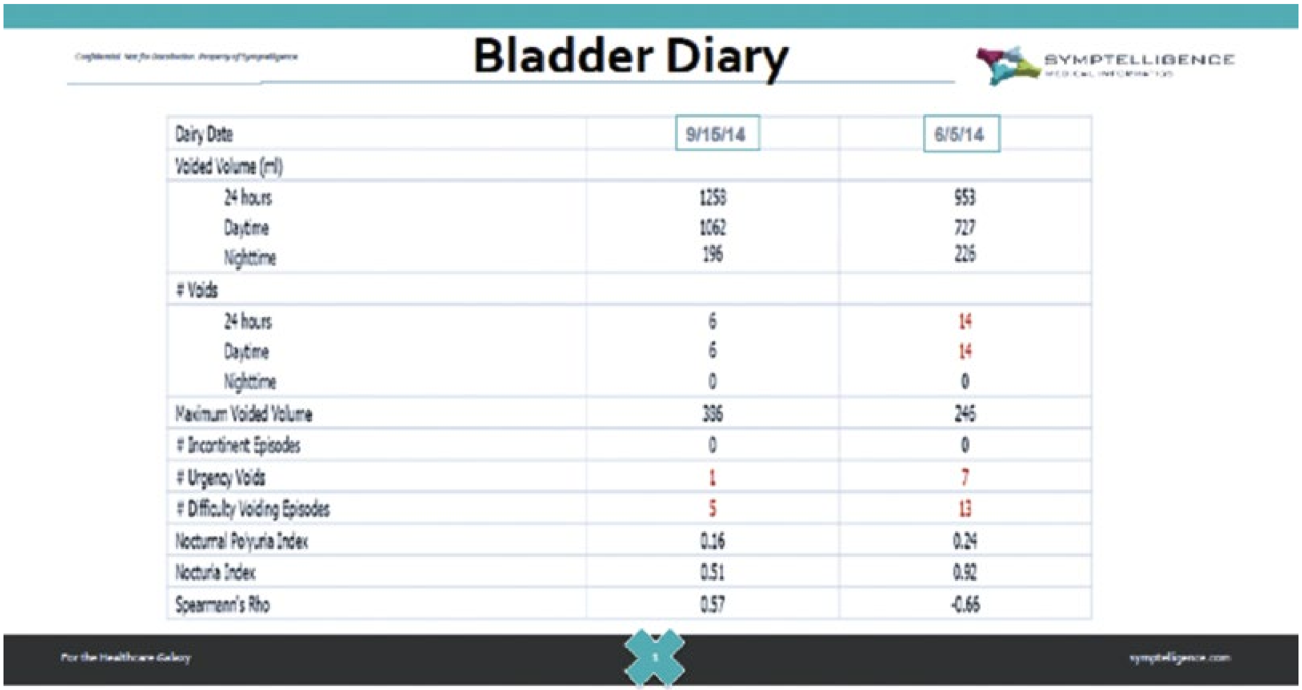
Patient Name : OAB, Jamie
MRN: LABPAT-02

Birth Date : 11 Dec 2014
Gender: Male

**Comments**

No Comment.

(b)



## Bladder Diary

| Dairy Date | 9/15/14 | 6/5/14 |
|---|---|---|
| Voided Volume (ml) | | |
| 24 hours | 1258 | 953 |
| Daytime | 1062 | 727 |
| Nighttime | 196 | 226 |
| # Voids | | |
| 24 hours | 6 | 14 |
| Daytime | 6 | 14 |
| Nighttime | 0 | 0 |
| Maximum Voided Volume | 336 | 246 |
| # Incontinent Episodes | 0 | 0 |
| # Urgency Voids | 1 | 7 |
| # Difficulty Voiding Episodes | 5 | 13 |
| Nocturnal Polyuria Index | 0.16 | 0.24 |
| Nocturia Index | 0.51 | 0.92 |
| Spearmann's Rho | 0.57 | -0.65 |

**Figure 140.1** Lower Urinary Tract Symptom Score (LUTSS) and bladder diary displayed via a mobile app. The patient is a 58-year-old man who presented with severe lower urinary tract symptoms. (a) Graphic representation of the LUTSS. The LUTSS is a 14-question questionnaire composed of six subscores: voiding symptoms, storage symptoms, overactive bladder (OAB), incontinence, nocturia, and LUTS bother. All scores are normalized on a scale of 0–100 (100 is the worst possible symptoms). The top graph in blue was competed prior to TURP; the bottom one in brown three months postop shows dramatic improvement in all scores. (b) Twenty-four-hour bladder diary pre and post TURP. Abnormal values are in red.

the patient is experiencing those symptoms that constitute his usual complaints. Thus, in this context, urodynamics should be considered to be a provocative test of vesicourethral function, and it is the responsibility of the examiner to ensure that the patient's symptoms are reproduced during the study. To this end, it is important that the examiner has all relevant clinical information prior to and during the urodynamic study. For example, the examiner should have results of fairly extensive evaluation including (i) a focused history (including symptom questionnaire), (ii) focused physical examination, (iii) urinalysis ± culture, (iv) a 24-hour bladder diary, (v) a 24-hour pad test (for patients with incontinence), (vi) uroflow, and (vii) PVR.

Furthermore, in order to interpret urodynamic studies more accurately, the following information should be available to the examiner before the start of the study:

- What symptoms are you trying to reproduce?
- What is the functional bladder capacity (maximum voided volume on the voiding diary)?
- What is the PVR?
- What is the uroflow? (Is there likelihood of either urethral obstruction or impaired detrusor contractility?)
- Is there a neurologic disorder that could cause neurogenic bladder?

The specifics of urodynamic techniques and parameters may confound the practicing physician, but in principle there are only five: cystometry, uroflow, leak point pressure, sphincter electromyography, and radiographic visualization of the lower urinary tract (if video is performed). Each technique may be performed alone or synchronously with one another. The tests are called multichannel urodynamics when done synchronously, and called video-urodynamics when performed with fluoroscopic visualization of the lower urinary tract. In the following section, use of each urodynamic technique in the evaluation of lower urinary tract symptoms will be explained.

## Evaluation of lower urinary tract symptoms

### Voiding symptoms with uroflowmetry

In general, voiding symptoms have one or more of three basic underlying etiologies: BOO, impaired or absent detrusor contractility, and/or trying to void when there is insufficient bladder volume. BOO is characterized by a detrusor contraction of adequate magnitude (pressure) and duration, and a diminished flow. Impaired contractility is characterized by a weak or poorly sustained detrusor contraction and a low flow. If a patient tries to void when there is an insufficient bladder volume, it may be difficult for him to initiate the stream and the flow is likely to be low because of the well-known correlation between bladder volume and urinary flow rate [13].

Uroflowmetry is a simple, objective, and noninvasive method to evaluate LUTS. Uroflowmetry is not used to evaluate filling symptoms. It should be performed in a private setting with the patient sitting or standing to reproduce normal voiding patterns. From simple uroflowmetry, the maximum urinary flow ($Q_{max}$), flow pattern, voided volume, and shape of flow curve can be obtained. After voiding, the PVR is recorded with ultrasound or catheterization if invasive urodynamics are to follow.

Uroflowmetry is best performed when the patient experiences a normal desire to void. A minimum urine volume of 150 ml provides an accurate study [13]. Existing nomograms provide values with age- and volume-adjusted flow rate [7, 8, 14]. A $Q_{max}$ of greater than 15 ml/s is considered normal, and approximately 95% of patients with this parameter will not be obstructed [15]. A $Q_{max}$ of less than 10 ml/s is considered abnormal, and of 10–15 ml/s is equivocal [15]. However, it should be noted that uroflowmetry cannot distinguish a low flow due to outlet obstruction from that due to impaired detrusor contractility [16]. A variety of normal uroflow tracings with normal curves and parameters are shown in Figure 140.2. Normal flow patterns have a bell-shaped curve, while patients with obstruction usually have a flattened curve. Interrupted flow patterns can be seen in patients with any of impaired bladder contractility, obstruction, or abdominal straining/voiding [17].

An equivocal uroflow may be seen in patients with significant obstruction and an abnormal flow may also be seen in those with poor detrusor function. It is obvious that BOO is usually accompanied by a low urinary flow rate, but a low flow may also be due to impaired detrusor contractility. In patients who are obstructed, uroflowmetry cannot differentiate between different types of urethral obstruction (BPH, urethral stricture, etc.). Figure 140.3 displays two similar abnormal uroflowmetry patterns despite their having different etiologies.

Despite these limitations, uroflowmetry remains a useful initial evaluation of men with LUTS. The AUA guidelines (2010; validated 2014) recommend uroflowmetry as an optional test in men with LUTS as initial diagnostic assessment or follow-up assessment after treatment. Ideally two flow rates should be obtained and each should have a voided volume of >150 ml [18]. However, the European Association of Urology Guidelines on BPH recommend uroflowmetry in the assessment and diagnostic workup of men with LUTS and it is considered mandatory prior to surgical intervention [19].

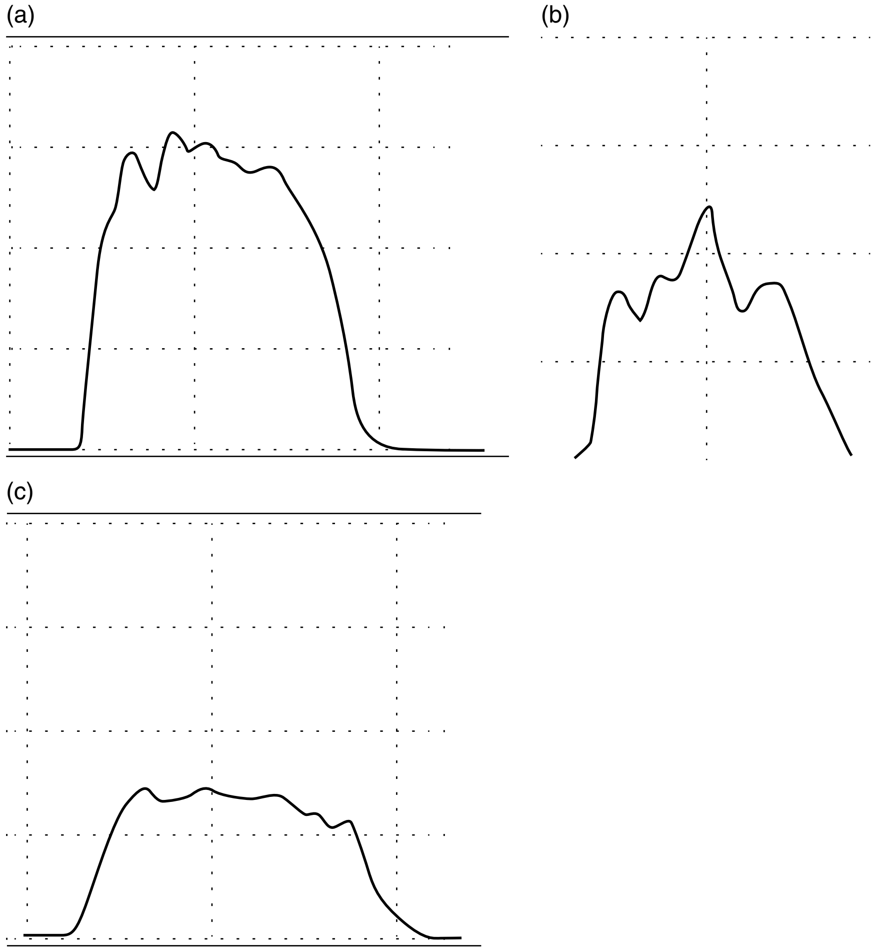


**Figure 140.2** Normal continuous uroflows. (a) Normal uroflow in a 52-year-old man. The pattern is continuous and the curve is very slightly fluctuating. Maximum flow ($Q_{max}$) = 31 ml/s; average flow rate ($Q_{ave}$) = 22 ml/s; voided volume = 269 ml; postvoid residual volume (PVR) = 0 ml. (b) Normal uroflow in a 53-year-old man. The pattern is continuous and the curve is fluctuating. $Q_{max}$ = 24 ml/s; $Q_{ave}$ = 13 ml/s; voided volume = 190 ml; PVR = 0 ml. (c) Normal uroflow in a 59-year-old man. The pattern is continuous and the curve is slightly fluctuating. $Q_{max}$ = 15 ml/s; $Q_{ave}$ = 10 ml/s; voided volume = 200 ml; PVR = 10 ml.

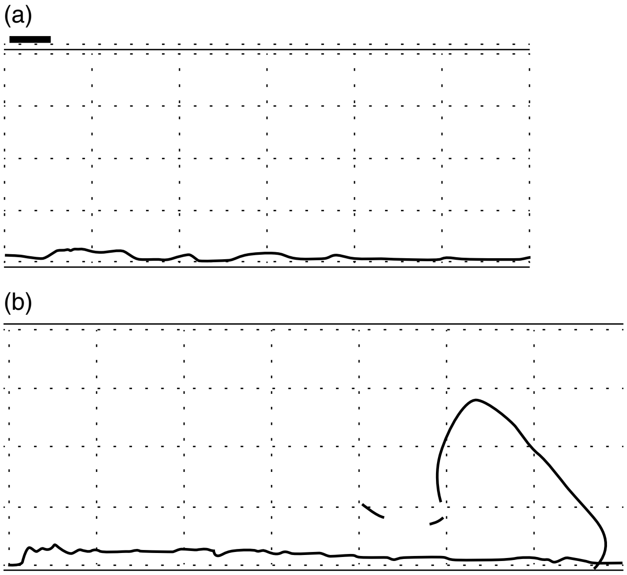


**Figure 140.3** (a) Low flow due to impaired detrusor contractility. Maximum flow ($Q_{max}$) = 2 ml/s; average flow ($Q_{ave}$) = 2 ml/s; voided volume = 58 ml; postvoid residual volume (PVR) = 120 ml. (b) Low flow due to urethral obstruction. $Q_{max}$ = 3 ml/s; $Q_{ave}$ = 2 ml/s; voided volume = 149 ml; PVR = 212 ml.

We recommend uroflow for all men as part of the diagnostic evaluation of LUTS and as an outcome measure when evaluating response to treatment.

## Filling symptoms with cystometry

Filling symptoms may be caused by detrusor overactivity, urgency, low bladder compliance, reduced bladder capacity, or polyuria. It is imperative to exclude other underlying causes of filling symptoms, such as urinary tract infection, bladder and prostate cancer, urolithiasis, and neurogenic bladder, prior to urodynamic testing. Polyuria can be caused by excessive fluid intake, diabetes mellitus, diabetes insipidus, and other less common conditions. Nocturia may be the result of abnormal drinking patterns, a reversal of the normal diurnal antidiuretic hormone cycle, congestive heart failure, venous insufficiency, sleep apnea, lower extremity edema, diabetes mellitus, or hypertension.

Filling cystometry is the only method that can document detrusor overactivity and low bladder compliance; however, it is not useful as a standalone procedure in men with LUTS. Currently, the AUA guidelines recommend

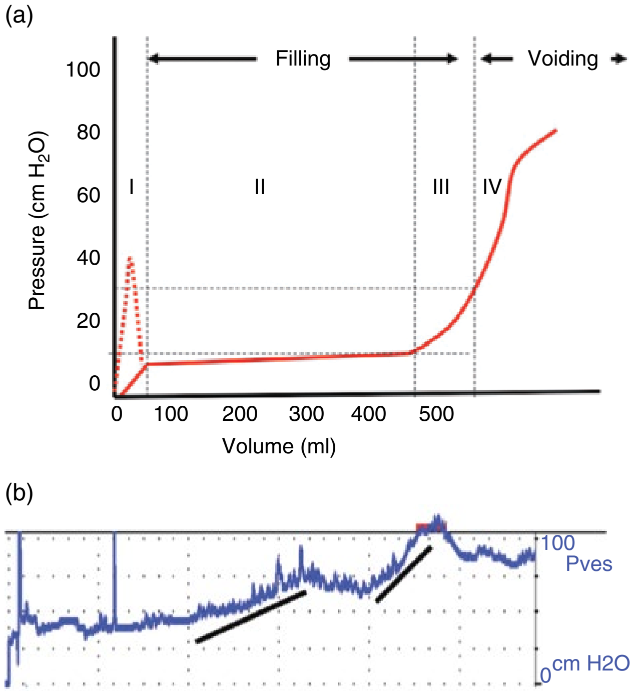


**Figure 140.4** (a) An idealized cystometrogram. The dashed red line in phase I is seen only with very rapid filling, such as that attained when $CO_2$ is used. It is attributed to the viscoelastic properties of the bladder wall. Note that bladder compliance changes at different bladder volumes. Bladder compliance during the tonus limb (phase II) = 400 ml/10 $cmH_2O$ = 40 ml/$cmH_2O$; at the end of phase III (500 ml) = 100 ml/20 $cmH_2O$ = 5 ml/$cmH_2O$. (b) This cystometrogram demonstrates two steep rises in vesical pressure ($P_{ves}$). The black lines parallel the pressure rises. Without further information, it is not possible to determine whether these are due to straining, detrusor contractions, or low bladder compliance.

that cystometry be done as part of the PFS. In men experiencing LUTS, up to two-thirds may be found to have detrusor overactivity. Despite poor physiologic explanation, resolution of detrusor overactivity can be expected in 50–70% of patients after outlet reduction [20, 21]. Figure 140.4 demonstrates an idealized cystometrogram as well as an actual cystometrogram from a patient: note that without abdominal pressure tracings, the cause of vesical pressure increase cannot be determined accurately.

## Multichannel urodynamics and video-urodynamics

The simultaneous measurement and display of multiple urodynamic parameters is the most precise diagnostic tool for evaluating abnormalities of micturition. As described earlier, the addition of radiographic visualization of the lower urinary tract with multichannel urodynamics is termed video-urodynamics. In these studies, radiographic contrast is used as the infusant for cystometry and other urodynamic parameters, including abdominal pressure, uroflow and sphincter electromyography, are recorded as well. By measuring multiple urodynamic variables, a better insight into the underlying pathophysiology is gained, as well as a better appreciation of their interrelationships and of artefacts. The International Continence Society has recommended standards for the performance of these studies [17, 22].

The main purpose of urodynamic evaluation is to recreate the patient's complaints and to correlate symptoms to the urodynamic findings. Thus, it is essential to understand the nature of a patient's complaints and to use the urodynamic evaluation as a provocative test to mimic those symptoms, as alluded to above. During the interactive process, the examiner should document whether or not the patient's symptoms are reproduced and, if they are, the underlying cause should be clearly understood before completion of the study.

## Urodynamic technique

A uroflow should be obtained prior to the urodynamic evaluation. Then, a 7 Fr double-lumen bladder catheter and rectal balloon catheter are passed into the bladder and rectum, respectively, to measure vesical and abdominal pressure. PVR is measured via the urethral catheter. Proper calibration is imperative to produce an accurate and clinically meaningful evaluation. Pressure transducers are zeroed to atmospheric pressure at the level of the symphysis pubis. Newer air-charged catheters have an air-filled balloon placed around a polyethylene catheter. Pressure measurements are made directly from the balloon to the air-filled catheter lumen and directly to the external pressure transducer; this conveniently eliminates the need for calibration to the symphysis pubis and flushing of the catheters, which was required in traditional fluid-filled systems. During calibration the patient should be asked to cough or Valsalva to ensure proper reading of instruments on the computer display. Vesical pressure ($P_{ves}$) and abdominal pressure ($P_{abd}$) are measured directly from the urethral and rectal catheters and displayed on a computer screen. Detrusor pressure ($P_{det}$) is electronically calculated by subtracting $P_{abd}$ from $P_{ves}$ and displayed on a third channel. Other channels display sphincter electromyelogram (EMG), infused bladder volume, filling rate, voided volume, and uroflow. For video-urodynamics, fluoroscopic images are sampled periodically as well as at times of events such as urgency and during voiding. Standard urodynamic parameters measured include bladder compliance ($C$ = change in bladder volume ($\Delta V$)/change in detrusor pressure ($\Delta P_{det}$)), maximum detrusor pressure, detrusor pressure at maximum flow ($P_{det}Q_{max}$), and bladder capacity. Bladder compliance should be measured with starting point at initiation of bladder filling and endpoint at either cystometric capacity or immediately prior to any detrusor contraction causing leakage based on International Continence Society (ICS) recommendations [2, 23]. Normal bladder compliance should be greater than 20 ml/$cmH_2O$, but there is no consensus on a strict value of normal or impaired compliance [23, 24]. The range in normal compliance is likely because compliance is highly dependent on bladder capacity. Impaired compliance is typically accepted as any value <20 ml/$cmH_2O$, but more importantly should be interpreted based on clinical context. The important components of urodynamic evaluation include presence of involuntary detrusor contractions, incontinence episodes, sphincteric coordination, and activity during storage and emptying, and bladder sensation. Bladder sensation is assessed at three standard points: volume at first sensation of bladder filling, first sensation of urgency, and strong sensation of urgency [23].

## Evaluation of filling symptoms

During bladder filling, the presence or absence of detrusor overactivity is noted and bladder compliance recorded. If detrusor overactivity is documented, the patient's awareness, concern, and ability to contract the sphincter, abort the stream, and prevent incontinence are noted. These characteristics are used to classify the type of overactive bladder [25] (Figure 140.5).

Detrusor overactivity is seen in over 50% of patients with BPH, but its presence does not correlate with urethral obstruction [1, 26–28]. A patient with clinical BPH may have detrusor overactivity in the presence of prostatic obstruction, but even in the absence of prostatic obstruction, detrusor overactivity may cause obstructive symptoms. For example, a patient may develop involuntary bladder contraction at a relatively low bladder volume, which is perceived as an urge to void. The patient rushes to the bathroom, however, by this time the involuntary contraction has subsided and there is no longer an urge to void. Attempts to void by the patient with straining and pushing will be unsuccessful due to the small bladder volume. Thus, once it has been determined that there are overactive detrusor contractions, it is important to determine the degree of the patient's awareness, concern, and control.

## Evaluation of voiding symptoms

BOO and urethral resistance are defined by PFS parameters. The BOO index (BOOI) is used to measure the degree of obstruction. It is calculated using the following formula:

$$\mathrm{BOOI} = P_{\mathrm{det}}Q_{\max} - 2Q_{\max}$$

where $P_{\mathrm{det}}Q_{\max}$ is the detrusor pressure at maximum flow. Men are classified as obstructed (BOOI >40), equivocally obstructed (BOOI >20–<40), or unobstructed (BOOI <20).

Multiple nomograms have been described to interpret PFS [15, 29, 30]. These plot detrusor pressure (at maximum flow) versus the maximum flow rate, and then divide results into unobstructed, obstructed, and equivocal categories. We prefer the Schafer nomogram because it provides a simple six-point obstruction scale: grade 0–1 is not obstructed, grade 2–3 is equivocal, and grade 4–6 is obstructed [22].

The urodynamic tracings, fluoroscopic images, and their application to a Schafer nomogram in Figures 140.6–140.8 demonstrate the role of each element in the differentiation of LUTS symptoms in three separate cases.

The Schafer nomogram also incorporates bladder contractility in addition to an obstructive index. The slopes of Schafer's contractility lines are obtained by the formula for bladder contractility index (BCI):

$$\mathrm{BCI} = P_{\mathrm{det}}Q_{\max} + 5Q_{\max}$$

A BCI greater than 150 is considered to be a strong contraction, a BCI less than 100 is considered to be weak, and a BCI of 100–150 is considered to be normal [31, 32]. However, for detrusor function to be normal, not only does it have to generate pressure, it also needs to sustain that pressure for long enough for the bladder to empty. Detrusor contraction duration (DCD) is a urodynamics parameter that is often overlooked and not well studied. Previous papers have defined it as "the bladder contraction in seconds from the first deflection from baseline during contraction until return to baseline detrusor pressure." Few studies have examined this parameter in men and even fewer in women. Kaplan et al. reviewed the urodynamic records of 120 consecutive patients (63 men and 57 women) who had moderate or severe AUA symptom score and found a weak correlation between DCD and BOO. DCD was longer in men with severe versus moderate AUASS (149.9 ± 62.3 vs. 109.3 ± 45.7 seconds) but this correlation was not seen in women [33]. This group also observed improved response to doxazosin in men with DCD >90 seconds [34]. Ameda et al. examined the urodynamic studies of 58 consecutive men with LUTS to assess the relationship between detrusor contraction duration, BOO, bladder capacity, detrusor contractility and symptoms to determine if DCD was a useful parameter for characterizing BOO [35]. In contrast to Kaplan et al.'s findings, this group did not observe a difference in DCD between patients with mild, moderate, and severe AUASS. Furthermore, there was no difference in DCD in patients who were obstructed versus those who were no obstructed (111.6 ± 53.7 seconds vs.

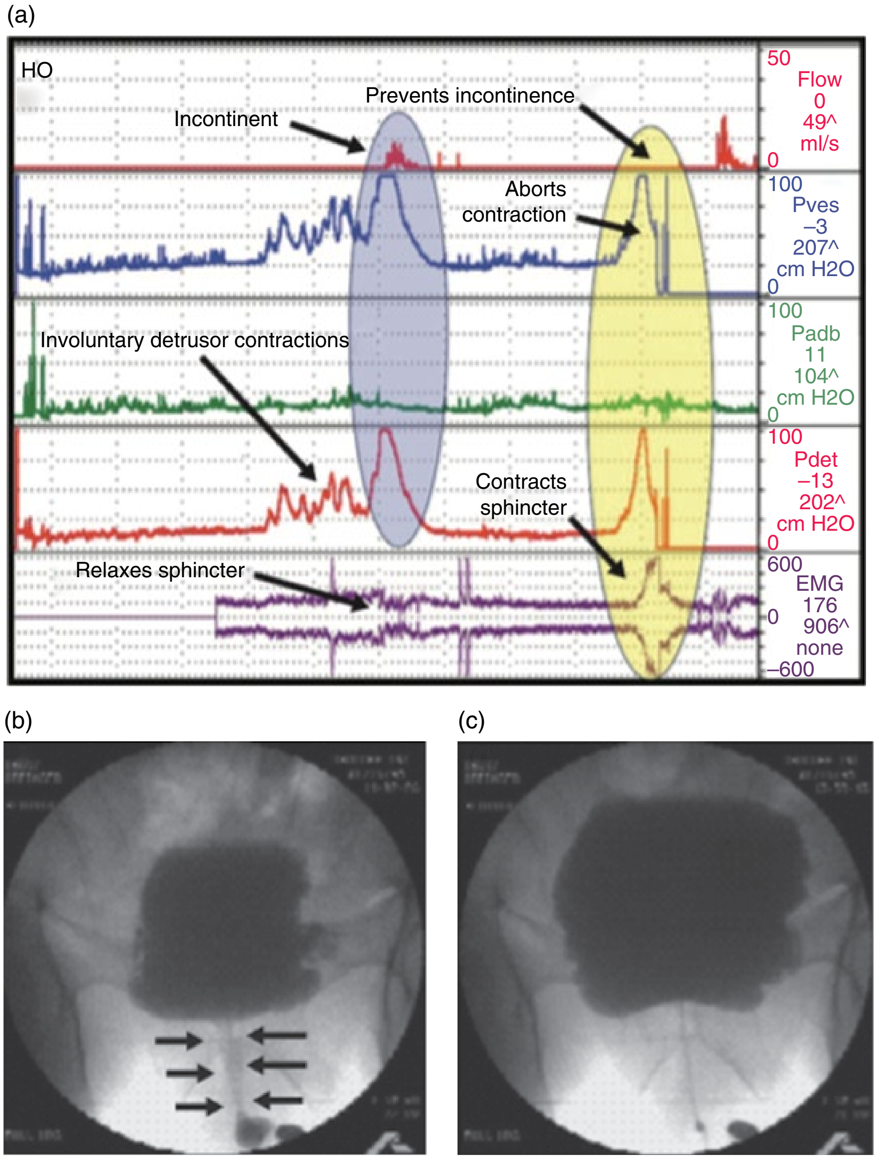

(a)
HO
Incontinent
Prevents incontinence
Aborts contraction
Involuntary detrusor contractions
Contracts sphincter
Relaxes sphincter
50
Flow
0
49^
ml/s
0
100
Pves
–3
207^
cm H2O
0
100
Padb
11
104^
cm H2O
0
100
Pdet
–13
202^
cm H2O
0
600
EMG
176
906^
none
0
–600
(b)
(c)

**Figure 140.5** (a) Urodynamic tracing of a type 2 overactive bladder and prostatic obstruction in a 53-year-old man with a 20-year history of refractory urgency, urge incontinence, and enuresis. During bladder filling the patient is instructed to neither void nor prevent micturition and to report his sensations to the examiner. There are a series of poorly sustained involuntary detrusor contractions (arrow) that he perceives as a severe urge to void, and then there is a sustained voiding contraction when he relaxes his sphincter and voids (blue oval). Detrusor pressure at maximum flow ($P_{det}$ at $Q_{max}$) = 100 cm$H_2O$; maximum flow ($Q_{max}$) = 8 ml/s (Schafer grade 5 obstruction). The bladder is filled again and there is another involuntary detrusor contraction. This time the patient is instructed to try to hold. He contracts his sphincter, obstructing the urethra, and the detrusor contraction subsides and he is not incontinent (yellow oval). (b) X-ray obtained at $Q_{max}$ shows a narrowed and faintly visualized prostatic urethra (arrows) characteristic of prostatic obstruction. The bladder is trabeculated and there are several small and medium-sized bladder diverticula. (c) X-ray obtained as the patient contracts his sphincter to prevent incontinence (gray oval). The contrast would be expected to stop at the distal prostatic urethra, but since the patient has prostatic obstruction that narrows the proximal urethra, no contrast is seen in the urethra at all.

91.5 ± 41.5 seconds). Our group measured DCD in 509 men and women who voided during urodynamics and observed that DCD tends to shorten with older age and that involuntary contractions are significantly shorter than voluntary contractions. (96.3 ± 41.7 vs. 63.4 ± 48 seconds). In addition, longer DCD was seen with higher detrusor pressure at maximum flow ($P_{det}$ at $Q_{max}$) and with higher maximum $P_{det}$ [36]. Further studies are needed to determine the role DCD plays in the mechanics of voiding and its clinical predictive value.

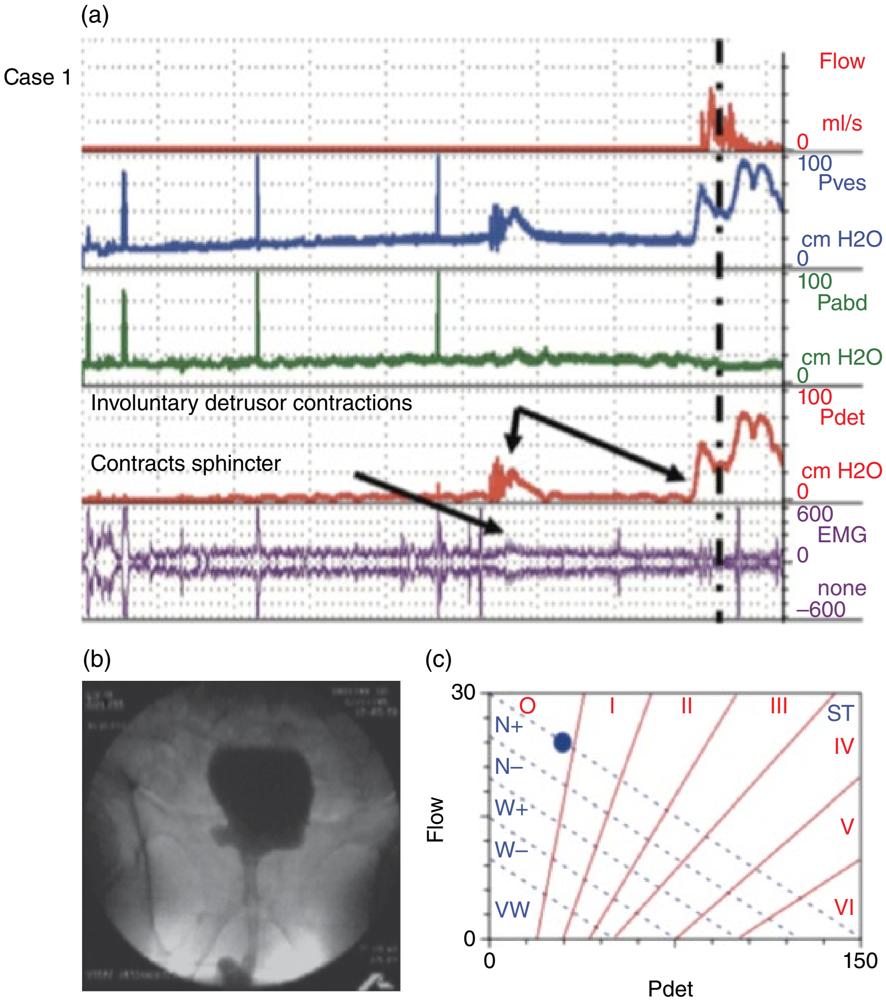


**Figure 140.6** Case 1. Urodynamic tracing of a man with two involuntary detrusor contractions; the terminal one causes incontinence. However, there is no bladder outlet obstruction. Maximum flow ($Q_{max}$) = 17 ml/s; detrusor pressure at maximum flow ($P_{det}$ at $Q_{max}$) = 22 cm$H_2O$. (b) Voiding cystourethrogram showing a wide open urethra during maximum flow. (c) Schafer nomogram plotting $Q_{max}$ versus $P_{det}$ at $Q_{max}$, yielding grade 0 voiding with excellent (N+) detrusor contractility.

## Cystoscopy

Urethrocystoscopy is recommended in evaluating men with suspected BPH with a history of microscopic or gross hematuria, prior lower urinary tract surgery, bladder cancer, and urethral stricture. It is not required and we do not recommend it in those patients who opt for medical therapy, unless there is another indication. AUA guidelines recommend use of cystoscopy in those patients where the “endoscopic appearance of the prostate may guide the choice of therapy in patients who have already decided to proceed with an invasive approach” [18]. This is particularly true in choosing newer minimally invasive therapies where the presence of a median lobe may be a contraindication.

## Detrusor underactivity (impaired detrusor contractility) and voiding dysfunction

The optimal management of patients with detrusor underactivity (DU) in the setting of voiding dysfunction deserves special consideration because, at the present time, there is no agreed method to determine whether or not the patient has BOO. Diagnosis and treatment are challenging for urologists.

DU is defined by the ICS as “decreased strength or duration of detrusor contraction that prevents timely and efficient bladder emptying” [37, 38]. The definition is highly subjective. Diagnostic tests used to help identify DU include mathematical calculations such as Watts factor,

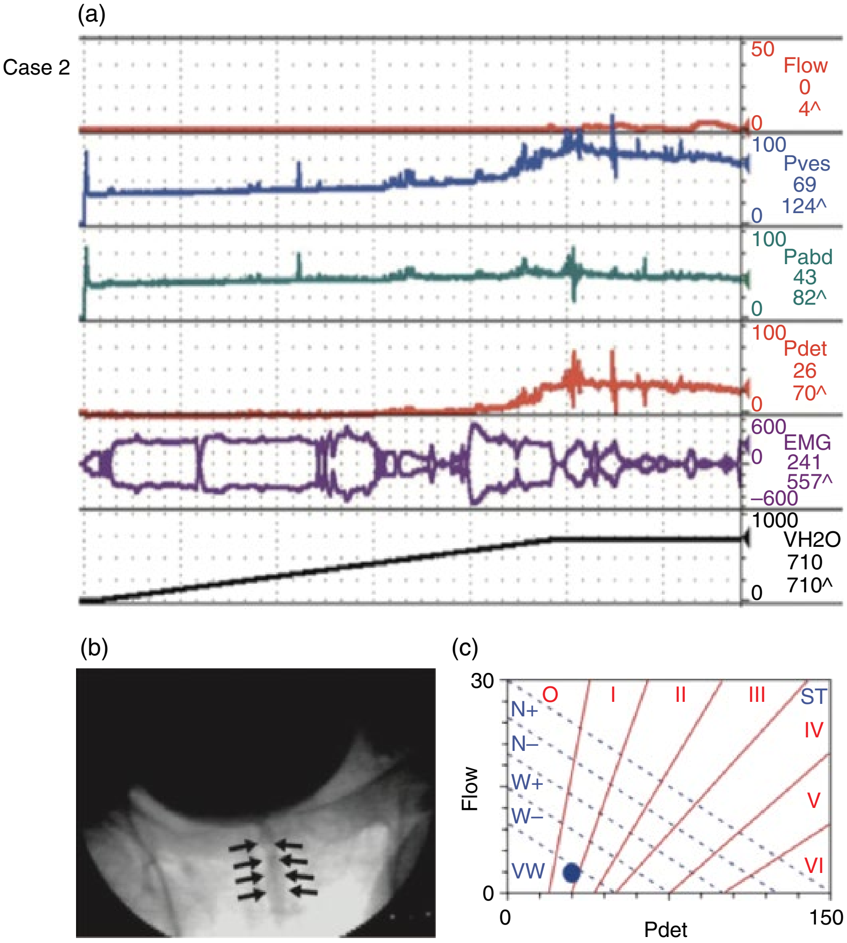
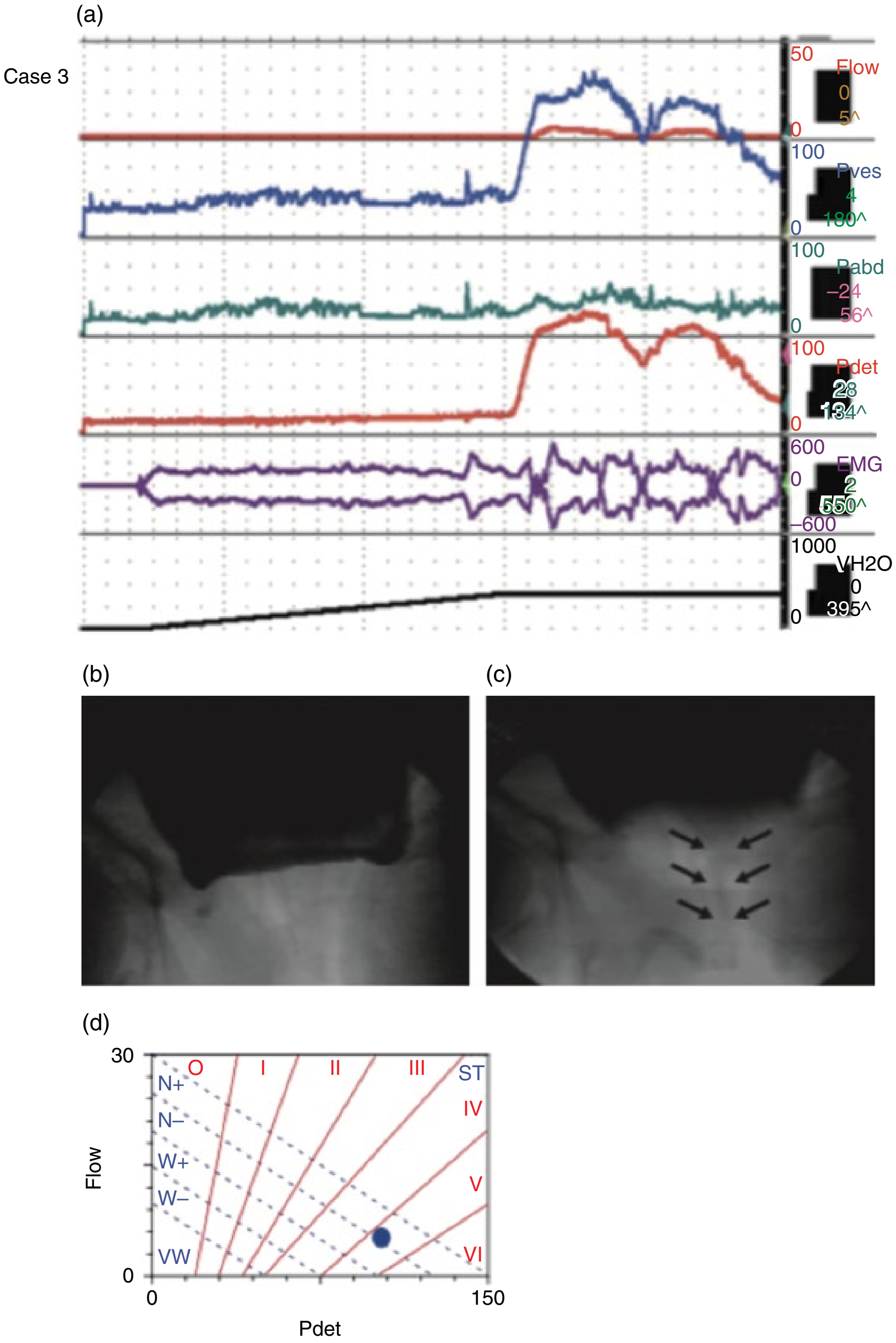


**Figure 140.7** Case 2. (a) Urodynamic study of impaired detrusor contractility (VW) in a 58-year-old man complaining of urinary frequency, urgency, occasional urge incontinence, hesitancy, and weak stream. First sensation of filling (FSF) = 272 ml; first desire = 491 ml; severe desire = 620 ml; bladder capacity = 710 ml; maximum flow ($Q_{max}$) = 6 ml/s; detrusor pressure at maximum flow ($P_{det}$ at $Q_{max}$) = 28 cm$H_2O$; maximum detrusor pressure ($P_{detmax}$) = 41 cm$H_2O$; bladder contractility index = 58; BOOI = 29. (b) X-ray obtained at $Q_{max}$ shows a narrowed prostatic urethra (arrows). (c) Nomogram reveals unobstructed voiding (grade 1) with very weak detrusor contractility. Bladder contractility index = 58.

indices such as BCI and bladder contraction coefficient, and urodynamic evaluation of $P_{det}Q_{max}$ and $Q_{max}$. None of these methods capture detrusor contraction duration (i.e. is the bladder contraction sustained sufficiently for complete bladder emptying?). Also, there is no objective definition of DU available [38]. DU describes defective detrusor function, while underactive bladder (UAB) refers to the symptoms resulting from decreased detrusor contractility. Such symptoms of UAB include sensation of incomplete emptying, double voiding, hesitancy, terminal dribbling, slow stream, prolonged voiding time, and intermittency [39–42]. DU is prevalent and identified in up to 48% of men and women during evaluation of LUTS [43, 44].

The main challenge in patients with detrusor underactivity and voiding symptoms is determining whether or not the patient has BOO. Standard pressure flow criterias for obstruction, such as the BOOI, require a $P_{det}Q_{max}$ >40 cm$H_2O$, but the vast majority of men with DU have $P_{det}Q_{max}$ <40 cm$H_2O$. When prostatic obstruction is encountered or suspected in the presence of DU, many surgeons hesitate to consider definitive surgical treatment of outlet obstruction because of fear that the procedure will be ineffective. Historically, studies had shown no benefit to outlet-reducing procedures in patients with both BOO and DU, but many recent studies have shown improvement in both subjective and objective outcomes. Improvements in IPSS and quality-of-life scores, reduction in postvoid residual volumes, increased $Q_{max}$, and elimination of need for clean intermittent catheterization (CIC) have all been reported [45–48]. Figure 140.9 shows a patient with severe LUTS and DU without diagnosable BOO who had successful outcome from transurethral resection of prostate (TURP). Those patients who have detrusor acontractility (DA) have a guarded prognosis with outlet surgery. Detrusor acontractility is the absence of any detrusor contraction during urodynamics. Such patients are unlikely to have return of volitional voiding after outlet surgery. Hence, UDS is invaluable in distinguishing between DU and DA, and identifying presence of BOO. We believe that most patients with combination of BOO and DU derive significant benefit from surgical treatment of their BOO.


(a)
Case 3
50
Flow
0
5^
0
100
Pves
4
180^
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100
Pabd
−24
56^
0
100
Pdet
28
134^
0
600
EMG
0
2
550^
−600
1000
VH2O
0
395^
0
(b)
(c)
(d)
30
O
I
II
III
ST
IV
V
VI
N+
N−
W+
W−
VW
Flow
0
0
150
Pdet

**Figure 140.8** Case 3. (a) Urodynamic tracing of a 63-year-old man with one episode of acute urinary retention on tamsulosin for 5 days. At a bladder volume of approximately 400 ml, the patient had a voluntary detrusor contraction. Maximum flow ($Q_{max}$) = 5 ml/s; detrusor pressure at maximum flow ($P_{det}$ at $Q_{max}$) = 117 cmH$_2$O (vertical line); maximum detrusor pressure ($P_{detmax}$) = 123 cmH$_2$O; voided volume = 215 ml; postvoid residual volume (PVR) = 174 ml. (b) X-ray obtained just prior to voiding shows a flattened bladder base characteristic of benign prostatic obstruction. (c) X-ray obtained at $Q_{max}$ (vertical line in (a)) reveals the prostatic urethra to be elongated and barely visible. (d) Detrusor pressure and uroflow plotted on the Schafer nomogram (grade 5 obstruction); BOOI = 107.

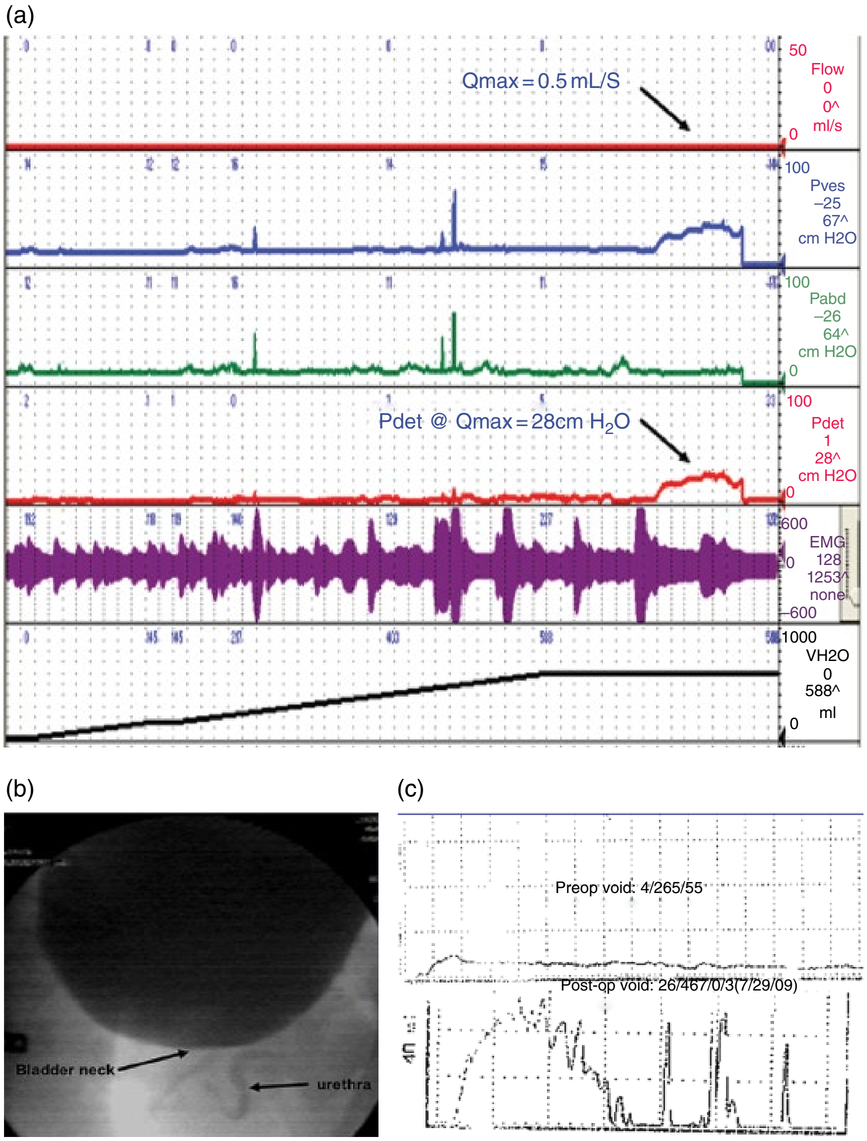
(a)
Qmax = 0.5 mL/S
50
Flow
0
0^
ml/s
0
100
Pves
–25
67^
cm H2O
100
Pabd
–26
64^
cm H2O
0
Pdet @ Qmax = 28cm H2O
100
Pdet
1
28^
cm H2O
0
600
EMG
0
128
1253^
none
–600
1000
VH2O
0
588^
ml
0
(b)
Bladder neck
urethra
(c)
Preop void: 4/265/55
Post-op void: 26/467/0/3(7/29/09)

**Figure 140.9** A 55-year-old man with severe lower urinary tract symptoms and detrusor underactivity without diagnosable bladder outlet obstruction who underwent transurethral resection of prostate with successful outcome. (a) Urodynamic tracing. At a bladder volume of 588 ml, he had a voluntary detrusor contraction. Maximum flow ($Q_{max}$) = 0.5 ml/s; $P_{det}$ at $Q_{max}$ = 28 cmH$_2$O; voided volume = 10 ml; BOO index = 27; bladder contractility index = 30; postvoid residual volume = 578 ml. (b) X-ray obtained at $Q_{max}$ shows no contrast in the prostatic urethra and a barely visible anterior urethra. (c) Pre and post transurethral resection of prostate uroflow tracings.

## Urinary incontinence

Urinary incontinence occurs in 5–10% of men with clinical BPH. Most of these patients have urgency incontinence. Sphincteric incontinence in men with BPH generally does not occur, unless the patient has a neurologic condition or has undergone prior surgery or radiation. By far the most common cause of sphincteric incontinence is radical prostatectomy for prostate cancer, followed by transurethral prostatectomy, particularly after radiotherapy for prostate cancer [49]. Less common causes are neurologic, including thoracolumbar neurologic lesions, such as spina bifida and multisystem atrophy (Shy–Drager syndrome), and iatrogenic, such as after abdomino-perineal resection of the rectum.

In the vast majority of patients after radical prostatectomy, incontinence is transitory and usually spontaneously subsides in a matter of months; however, it may take as long as 1 year for full recovery. Sphincteric incontinence that occurs in men who have undergone radiation (external beam or brachytherapy), on the other hand, often does not spontaneously remit. Rather, if incontinence improves, it is usually because of the development of a urethral stricture that begins a vicious cycle.

Treatment of the stricture usually results in recurrent incontinence, and treatment of the incontinence (sphincter prosthesis or male sling) is often complicated by the development of recurrent stricture [50, 51].

From a diagnostic standpoint, most patients who complain of a constant, dribbling, gravitational or stress-induced incontinence have sphincteric malfunction, and most who complain of urinary frequency, urgency, and urgency incontinence have an overactive bladder/detrusor overactivity. Despite this, there may be considerable overlap between these two conditions and both may coexist in the same patient. Sphincteric malfunction is the commonest cause of postprostatectomy incontinence (PPI), accounting for 95% of cases, but it may be accompanied by detrusor overactivity and/or low bladder compliance. As an isolated cause, detrusor overactivity causes about 5% of PPI [52–54].

On fluoroscopy, the classic appearance of postradical prostatectomy stress incontinence is the funnel of bladder–urethral anastomosis at rest, with contrast seen in the bulbar or distal urethra during increases in abdominal pressure (Figure 140.10). The presence of and size of the

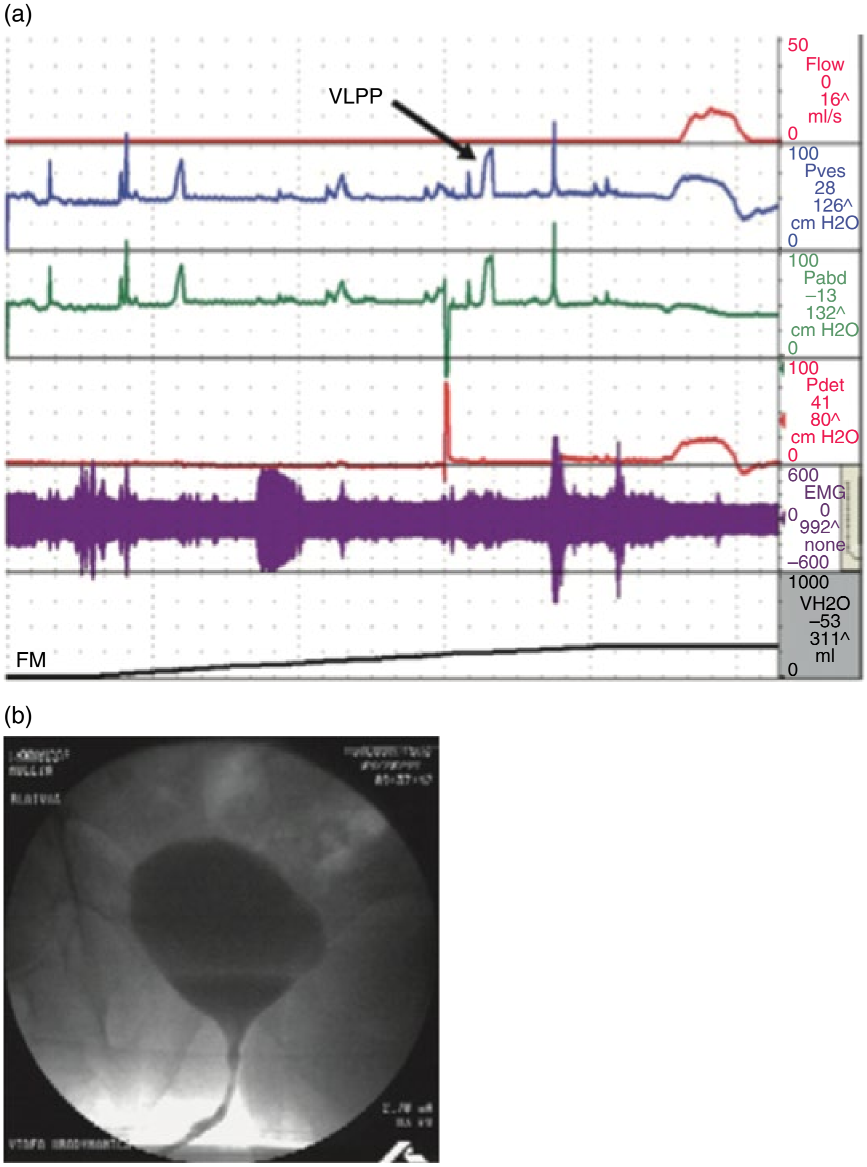

**Figure 140.10** (a) Urodynamic tracing of a 72-year-old man 7 years post radical prostatectomy. His only prior treatment for incontinence was a collagen injection. He wears absorbent pads daily and he changes them three times per day. First sensation of filling (FSF) = 211 ml; first urge = 299 ml; severe urge = 305 ml; bladder capacity = 311 ml; Valsalva leak point pressure (VLPP) = 84 cm$H_2O$; maximum flow ($Q_{max}$) = 16 ml/s; detrusor pressure at maximum flow ($P_{det}$ at $Q_{max}$) = 23 cm$H_2O$; maximum detrusor pressure ($P_{detmax}$) = 23 cm$H_2O$; voided volume = 317 ml; postvoid residual volume (PVR) = 0 ml. (b) X-ray obtained at VLPP shows contrast throughout the entire urethra.

urodynamic catheter used to measure leak point pressure may itself impact the recording and may mask sphincteric incontinence or suggest urethral obstruction when it is not clinically relevant.

In the majority of patients, the etiology of incontinence will be apparent after a careful history, physical examination, voiding diary, and pad test; however, detrusor overactivity and low bladder compliance can only be diagnosed with urodynamic studies.

## Conclusions

Indications for urodynamics in men with LUTS depend upon the threshold of the clinician for obtaining the most accurate diagnostic information. The underlying pathophysiology of LUTS in men with BPH consists of urethral obstruction, impaired detrusor contractility, detrusor overactivity, low bladder compliance, and increased bladder sensation. An accurate diagnosis of the underlying etiology can only be made with urodynamics, but most authorities agree that urodynamics is only necessary when surgical treatment is being considered. Pressure–flow evaluation has been and remains the only "absolute way of diagnosing BOO" [1]. Although PFS has not been shown to predict responses to medical therapy, numerous studies have demonstrated that those patients with proven obstruction benefit more from prostatectomy than those who are not obstructed [10, 26]. The efficacy of surgical treatment in patients with impaired detrusor contractility has not been resolved, but we believe that the majority of patients are, indeed, obstructed, and benefit significantly from outlet-reducing surgery. Regardless, from a clinical viewpoint, video-urodynamics serves no purpose unless the clinician bases therapy on the results of the study.

Notwithstanding these theoretical considerations, PFS is essential and video-urodynamics preferable for men who have failed conservative and surgical therapies, particularly in those considering more invasive treatment. Furthermore, video-urodynamics is recommended for men with known or suspected neurologic disease, including those with a history of spina bifida, diabetes mellitus, cerebral vascular accident, spinal cord injury, multiple sclerosis, Parkinson's disease, and multisystem atrophy. Men with a history of major pelvic surgery or prior pelvic radiation and LUTS should also undergo urodynamic evaluation.

Finally, even if video-urodynamics were found to have no clinical importance, it is still the best method of defining normal and abnormal physiology. Understanding physiology is the means by which new hypotheses are developed, leading to new research, new diagnostic methodologies, and, ultimately, newer and more effective therapies.

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# 141

# Office-based Cystoscopy: Continued Advances

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## Introduction

Cystourethroscopic examination of the bladder and urethra remains the gold standard for the diagnosis of lower urinary tract disorders. It offers direct visualization of the bladder urothelium and provides initial access to the ureteral orifices for assessment and treatment of the upper urinary tracts. It is a cornerstone in the evaluation of gross and microscopic hematuria, and is useful in the investigation of lower urinary tract symptoms. Instruments passed through the cystoscope or specially designed resectoscopes allow minimally invasive diagnosis and treatment of identified pathology. This chapter summarizes the role of cystoscopy (both rigid and flexible) as well as recent innovations in office cystoscopy.

Cystourethroscopy is performed using either rigid or flexible endoscopes. Endoscopes are measured with the French scale and are available in sizes to accommodate both pediatric (8–12 Fr) and adult patients (16–25 Fr). The French scale is equal to the diameter of the cylinder in millimeters multiplied by 3, not the circumference as is sometimes thought. Increasing French units correspond to larger diameter endoscopes.

## Rigid cystoscopy

Rigid cystoscopes are multicomponent instruments that consist of a sheath, an obturator, a bridge, and a telescope (Figure 141.1). The sheath provides a connection to the irrigation system. An obturator is placed through the sheath that aids entry into the bladder through the urethra. Most are hinged to allow a better angled approach past the male bulbar and prostatic urethra. Once inside the bladder, the obturator can be exchanged for a telescope with a bridge that allows for the passage of a variety of treatment implements (i.e. wires, stents, ureteral catheters, laser fibers). The light source connects directly to the telescope, which uses fiber-optic illumination and a rod–lens imaging system to transmit the light and image to the eyepiece. Various lens angles enable the endoscopist to evaluate adequately the entire urethra and bladder. The 0° lens allows the best view of the urethra, providing a straight image. This degree lens is many times the most useful in patients with urethral stricture disease. A 30° lens is used to visualize the trigone, posterior wall of the bladder, as well as the lateral side walls. It is the most commonly used lens in rigid cystoscopy. A 70–90° lens is often used to assess the dome and anterior bladder neck.

Spring-loaded resectoscopes are typically used for the resection of bladder lesions and prostatic hyperplasia. These implements are best used in conjunction with a 30° lens–rod system and require the use of a large-bore sheath (24–26 Fr). Continuous-flow irrigation, which utilizes an outer sheath with both inflow and outflow ports, prevents the bladder from compressing on itself during the procedure. This allows the area of interest (e.g. a bladder tumor) to remain fixed in space to facilitate resection. Continuous irrigation provides for more efficient resection and enhanced visualization, especially in the setting of transurethral resection of the prostate (TURP).

Rigid cystoscopes provide a relatively large working port to accommodate a variety of accessory instruments. This is a major advantage; however, the large size of the rigid cystoscope decreases its applicability in males unless general or regional anesthesia is utilized. In addition, patients must be placed in the dorsal lithotomy position to facilitate an adequate examination. Rigid cystoscopy, therefore, is difficult to perform in the male patient outside of the modern operating room.

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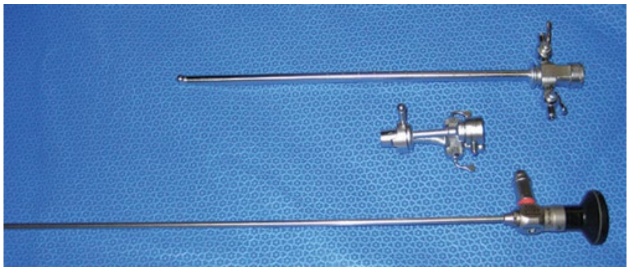

**Figure 141.1** Basics of the rigid cystoscope (from top to bottom): metal sheath with inflow and outflow ports, bridge, and rod–lens system to which the light source it attached.

### Procedures

Rigid cystoscopy is utilized to assess the bladder and upper urinary tracts for diagnostic evaluation of multiple clinical entities, such as hematuria, voiding complaints, and urothelial carcinoma. Retrograde imaging of the ureter and renal pelvis can be accomplished with the use of contrast injected through small catheters passed into the ureteral orifice under cystoscopic guidance. Ureteral stents are commonly inserted via the rigid cystoscope. Upper tract access for ureteroscopy may also be established with the use of wires and open-ended catheters. After wire passage has been confirmed with the use of fluoroscopy, the rigid cystoscope may be exchanged for a ureteroscope. Other uses are possible but have been largely supplanted with flexible cystoscopy.

### Technique

After obtaining informed consent and verifying proper instrument sterilization and availability, the patient should be prepped and draped in a standard sterile fashion. In both male and female patients, lubricant jelly should be instilled into the urethra before the procedure. If the meatus or urethra is unable to comfortably accommodate the cystoscope, dilation should be performed. This can be accomplished with the use of urethral sounds in a serial fashion. The urethra should be dilated to a diameter of at least 2 Fr units greater than the instrument (e.g. dilate to 26 Fr if utilizing a 24 Fr cystoscope).

In the male, the penis should be grasped and straightened as the endoscope is introduced to allow for inspection of the fossa navicularis and the anterior urethra. As the scope traverses the anterior urethra, the examiner's hand should be depressed to bring the penis parallel with the floor. This allows for examination of the membranous urethra and prepares the examiner to view the prostatic urethra. The verumontanum is noted when the examiner reaches the prostatic urethra. The prostatic lobes are seen laterally at this point in the examination. When the bladder neck is in view, it is often necessary for the examiner to depress the endoscope by dropping their hand toward the floor so as to account for the gentle upward angulation encountered before entering the bladder [1].

Once the endoscope is inside the bladder, a systematic evaluation of the entire bladder surface is performed in a routine and reproducible fashion. The trigone is the first landmark encountered when visualizing the bladder with a 30° lens. The examiner should follow the trigone laterally to identify the ureteral orifices effluxing clear urine. Next, attention should turn toward examination of the bladder floor beyond the trigone and the posterior wall. The lateral walls are then carefully inspected by rotating the lens side to side. The dome and anterior bladder wall are best viewed with the 70° lens. The scope should be rotated 180° to facilitate this part of the procedure, paying close attention to keeping the camera head level (if one is being utilized). The air bubble serves as the landmark for the dome. It is often necessary to apply pressure just superior to the pubic bone when visualizing the anterior bladder neck.

## Flexible cystoscopy

Flexible cystoscopy of the urinary tract is a fairly recent phenomenon. In 1973, Tsuchida and Sugawara reported utilizing a flexible "fibercystoscope" for examination of the bladder neck [2]. Since the development of the first purpose-built flexible cystoscope in 1984, flexible fiberoptic cystoscopy has become an accepted diagnostic and therapeutic modality, and today is the most commonly performed in-office procedure by the practicing urologist. The development of working ports, smaller cystoscope diameter with preserved image quality, active deflection, and most recently digital cystoscopes, have greatly enhanced the ability of the user to apply flexible cystoscopy for a variety of diagnostic and therapeutic applications. When compared to rigid cystoscopy, flexible cystoscopy is more comfortable for patients and can be performed with only local anesthesia. The deflection capabilities of the flexible cystoscope allow for easier passage through the bladder neck, as well as superior visualization of the anterior bladder wall (Figure 141.2).

However, there are disadvantages to flexible cystoscopy. Flexible endoscopes are costly and require more delicate care when compared to rigid cystoscopes. These instruments have smaller irrigating ports and lack a separate working sheath. As a result, changing lenses, assessing residual urine and repeat evacuation of irrigant and/or urine cannot be completed without entirely removing the endoscope or actually withdrawing gradually contents via the single, small-caliber channel of the irrigation port.

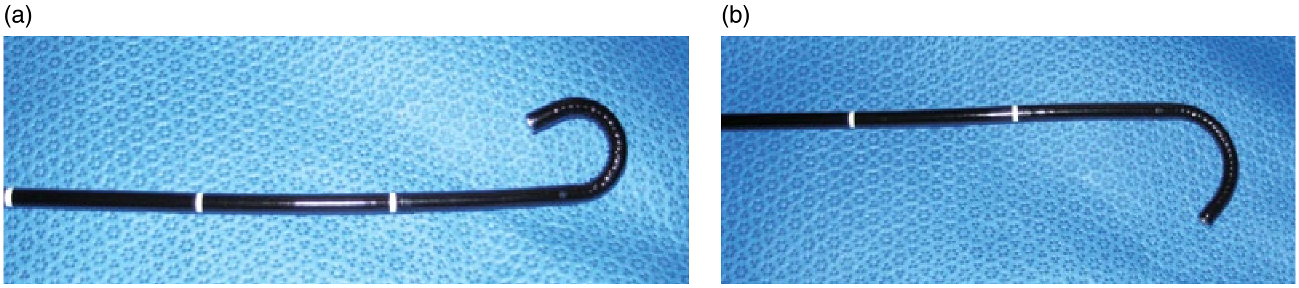

**Figure 141.2** (a, b) Tip of the flexible endoscope can be deflected 180–220° to allow visualization at nearly any angle.

Simply by its nature, the image obtained from a flexible fiber-optic cystoscope is inferior when compared to the rod–lens system employed in rigid cystoscopy. Fiber-optic technology has distinct imaging limitations owing to the finite diameter of the image-carrying glass fibers that make the pixelated "screen door" effect insurmountable [3]. There are generally three fiber-optic bundles within the shaft — two for light and one for the image. The image obtained by the fiber-optic bundle is a composite matrix of each individual fiber in that bundle, analogous to a newspaper photograph in which multiple dots merge into a single reconstructed image. Digital endoscopy, as discussed below, is able to overcome the limitations of fiber-optic endoscopy.

## Procedures

The single most common indication for flexible cystoscopy is evaluation for hematuria, whether gross or microscopic. Visualization of the entire urethra and bladder can be accomplished efficiently and without significant discomfort. Other diagnostic applications include its use in the evaluation of male or female voiding dysfunction. Flexible cystoscopy, however, is not indicated in the routine evaluation of male voiding dysfunction thought to be attributed to outlet obstruction from benign prostatic hyperplasia (BPH), as the endoscopic appearance of the prostatic urethra and bladder does not predict the response to BPH therapy [4]. However, endoscopic assessment is appropriate and often necessary in men being considered for surgical therapy of outlet obstruction to rule out the presence of urethral stricture or bladder neck contracture, especially in those individuals who have undergone prior transurethral surgery. It is essential as well to evaluate any suspected anatomic abnormalities.

In addition to diagnostics, there are many therapeutic office-based applications. These include the injection of urethral bulking agents for stress urinary incontinence and intravesical injection of botulinum toxin for voiding dysfunction. Removal of ureteral stents or of foreign bodies is another commonly employed procedure that is made safe, efficient, and reliable with the use of modern flexible cystoscopy. This can be done with grasping forceps, a retractable lasso device, or four-pronged grasping forceps with a retractable sheath. Once the cystoscope is introduced into the bladder and the object is identified, the grasping device is passed down the working channel and into the field of view. The object is then firmly grasped and the endoscope and graspers are removed as a unit under direct visualization.

Suspicious lesions in the bladder may be sampled in the office setting with the use of flexible biopsy forceps and electrocautery. When biopsies are to be obtained, a topical anesthetic agent (lidocaine 1% solution) is instilled into the bladder and left in place for 10 minutes prior to the procedure. An electrocautery unit and probe must be readily available in this situation. A nonconductive solution such as water or glycine must be the irrigant when electrocautery is used. Laser fulguration of small lesions is possible and is becoming increasingly used. This option is especially useful in patients with known rapidly recurring, low-grade, papillary tumors of the lower urinary tract.

## Technique

The patient should be prepared in a fashion analogous to that for rigid cystoscopy. In both male and female patients, lubricant–anesthetic gel should be instilled into the urethra before the procedure. A recent meta-analysis has demonstrated that subjects who received anesthetic-impregnated gel were 1.7 times more likely not to experience moderate-to-severe pain than subjects who had no intraurethral anesthetic instillation [5].

Examination of the urethra and bladder with the flexible cystoscope is performed in a slightly different manner from rigid cystoscopy. The anterior urethra can be viewed in a retrograde manner. The prostatic urethra should not be examined during retrograde passage of the endoscope as it will often appear obstructed. Instead, the prostatic urethra should be examined antegrade as the endoscope is being withdrawn from the bladder [6].

As with rigid cystoscopy, the bladder should be examined in a predetermined systematic fashion that the examiner can reliably duplicate to ensure adequate examination of its full contour. A standardized approach also aids in reliable documentation. The bladder should be cleared of turbid urine, clot, and debris prior to examination. The bladder is then filled with a sufficient volume to allow distention of mucosal folds. The bladder does not have to be distended as much as in rigid cystoscopy for adequate visibility. The first landmark in the bladder that is often seen is the air bubble at the dome. One systematic approach then is to evaluate the bladder by starting along the 12 o'clock position by pulling the endoscope toward the bladder neck and along the midline until the bladder neck is just entered. The endoscope is then returned to the dome and rotated from the 12 to the 4 o'clock position, and then from the 12 to the 8 o'clock position in a counterclockwise fashion. Next the scope is returned to a neutral position. The scope is then deflected to the six o'clock position to view the trigone. The 5, 6, and 7 o'clock positions are examined as previously described.

## Advances in office cystoscopy

The use of video cameras in endoscopy was introduced in 1956 by French researchers [3]. This development enhanced ergonomics, safety, and success rate for pathologic findings. This approach has many advantages, including the avoidance of contact with body fluids, patient education, and documentation through the use of digital camera technology [1].

Videoendoscopy with flexible scopes allows patients to visualize normal and abnormal anatomy, and thus helps them to understand their pathology. In male patients, videocystoscopy utilizing a monitor has been shown to produce a 40% decrease in the pain and discomfort level compared to those who did not view the procedure on the monitor [7].

Recently, the key advance in office cystoscopy has been the continued improvement and innovation in the visualization mechanism. Digital (distal sensor) endoscopy based on CCD (charge-coupled device) and CMOS (complementary metal oxide semi-conductor) chips has recently been introduced into the field of endourology. Digital sensors are composed of millions of photodiodes which convert photons into electric current that is later transformed into voltage, amplified, and converted to a digital form [3]. On both types of chips, the information is transferred to a controller box for image presentation or storage (i.e. the box that is connected to the cystoscope).

Distal sensor cystoscopes based on these technologies were introduced in an effort to provide urologists with better optical resolution, contrast, color differentiation, and improved durability. Digital image capturing allows for plug-and-play capability. Contemporary digital sensor endoscopes are able to meet the size requirements of flexible cystoscopy. They are already superior to flexible fiber-optic endoscopes in terms of weight and are thus easier to handle during procedures. Additionally, distal sensor cystoscopes do not require white balancing and camera focusing. *In vitro* evaluation has demonstrated that distal sensor cystoscopes are superior to fiber-optic cystoscopes in terms of resolution, contrast discrimination, and red color differentiation [8].

The first commercial digital flexible endoscope was the ACMI DCN-2010 introduced in 2005 (ACMI, Southborough, MA, USA). Quayle et al. compared this cystoscope with three contemporary fiber-optic scopes and found the digital scope to provide superior optics [9]. Okhunov et al. conducted a prospective clinical comparison of distal sensor (digital) and fiber-optic cystoscopes in over 1000 patients who underwent office-based cystoscopy. All surgeons found the digital sensor endoscopes to be lighter and easier to handle. Both subjective optical and functional metrics were significantly better with the distal sensor cystoscopes. Substantial differences were found with cystoscope deflection when instruments were placed in the working channel; however, the evaluating surgeons did not believe that this diminished function. Finally, both the fiber-optic and digital cystoscopes proved durable with a 0.2% repair rate during the study period [10]. It remains to be seen if distal sensor technology will ultimately prove cost-effective.

Narrow-band imaging (NBI) is a high-resolution endoscopic technique that improves detection of bladder tumors without the use of exogenous dye. The technology is available for both flexible and rigid cystoscopes. This enhanced visualization of mucosal and submucosal vasculature is made possible by the CCD chips. This narrow bandwidth of light (415 and 540 nm) is strongly absorbed by hemoglobin and penetrates only the surface of tissue. By narrowing the bandwidth of light from the flexible cystoscope, NBI improves the definition of the epithelial surface and emphasizes the mucosal microvessels. NBI has demonstrated superior sensitivity for identifying recurrent flat and papillary superficial bladder tumors in a surveillance setting when compared with standard white light cystoscopy. Early studies of this technology did not evaluate its benefit for the more difficult to detect lesions, such as carcinoma *in situ* [11]. More recent studies have demonstrated that NBI does improve carcinoma *in situ* (CIS) detection. Herr and Donat evaluated 427 patients for recurrent bladder tumors by white light cystoscopy followed by NBI cystoscopy during the same procedure. 103 patients (24%) had tumor recurrences of which 13% were detected only by NBI cystoscopy. NBI detected extrapapillary tumors or more extensive CIS in 58 patients [12].

Chen et al. compared white light imaging cystoscopy and NBI cystoscopy in the detection of urothelial carcinoma of the bladder in 143 patients [13]. NBI detected a total of 59 additional tumors (34 pTa, 17 pT1, 3 pT2, and 5 pTis) in 44 of 143 patients. The mean ± SD number of identified tumors per patient was 1.97 ± 0.67 for NBI and 1.78 ± 0.53 for while light imaging ($P = 0.01$). Tatsugami et al. evaluated the use of NBI cystoscopy for the detection of bladder cancer and analyzed its diagnostic efficacy in cases of CIS. A total of 313 biopsies were taken from 104 patients, including 161 from sites identified as potentially abnormal by NBI and/or white light imaging cystoscopy. In 26.9% of patients, bladder tumors were detected only by NBI [14]. The authors concluded that NBI was a simple and effective method for identifying bladder tumors because of its high sensitivity and high negative predictive value. Cauberg et al. also studied whether NBI improves detection of nonmuscle-invasive bladder cancer over white light imaging cystoscopy. This prospective trial was a within-patient comparison on 103 consecutive procedures on 95 patients. White light and NBI cystoscopy were performed by different surgeons who independently indicated all tumors and suspect areas on a bladder diagram. A total of 78 patients had a confirmed urothelial carcinoma; in 28 (35.9%) of these patients, a total of 39 additional tumors (26 pTa, 6 pT1, 1 pT2, 6 pTis) were detected by NBI, whereas 4 additional tumors (1.8%) (1 pTa, 1 pT1, 2 pTis) were detected by white light imaging. The detection rate of NBI was 94.7% versus 79.2% for white light imaging ($P < 0.001$) [15]. Shen et al. sought to evaluate if the improved detection of bladder tumors attributed to NBI could result from the second look inspection of the bladder. Investigators evaluated NBI and white light cystoscopy in 78 patients with suspected nonmuscle-invasive bladder cancer. The bladder was mapped with white light cystoscopy then NBI or vice versa within the same observation time. NBI identified significantly more additional tumors than white light imaging, with 36 (17.1%) tumors in 13 patients being detected by NBI only. The sensitivity of NBI versus white light imaging for detecting CIS was 87.8% versus 68.3% ($P < 0.05$) [16].

## Conclusions

As technology continues to evolve, office-based cystoscopic procedures continue to improve and expand. The ability to utilize flexible cystoscopy in an increasing number of clinical situations has benefitted both physicians and patients. At the same time, it continues to be the standard diagnostic evaluation tool for the practicing physician.

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# 142

# Equipment Setup and Patient Handouts

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## Operating room setup and design

Before the patient enters the operating room (OR) all necessary equipment should be assembled and confirmed to be working properly. The OR setup should accommodate at least one table setup, the endoscopic video cart (Figure 142.1), the anesthesia equipment, the laser unit, the electrosurgical unit, the computer station, and the C-arm fluoroscopy.

Easy access to the electronic medical records (EMR) and hospital communication systems is necessary. Modern ORs are equipped with ceiling-mounted boom-arms for housing various surgical and anesthesiology equipment. Boom-arms provide an ergonomic advantage in arranging the OR, reducing the number of cables and trolleys occupying floor space, and making the positioning of cart-based equipment easier. Multiple arms are typically needed for housing all necessary equipment, with additional arms for surgical lights and video monitors. Video monitors mounted on boom-arms can be more easily positioned to accommodate the surgeon's and assistant's' preferences and to minimize neck strain. ORs equipped with boom-arm systems have decreased turnover, anesthesia and surgical preparation times, especially in laparoscopic surgery [1–3]. Before each case, staff should assess the current placement of the boom-arms and make any necessary changes prior to positioning both cart-borne equipment and the patient.

Dedicated space for C-arm X-ray is preferable, since the endoscopic OR is often used for various fluoroscopic procedures (e.g. ureteral stenting, ureteroscopy, percutaneous renal interventions). As many centers do not employ dedicated C-arms in their endoscopic ORs, the C-arm and radiology technician are often mobile, moving from room to room and employing cart-based monitors. This makes the relative placement of necessary equipment crucial as the C-arm and monitors may need to be positioned after the patient is in the room or removed from the room prior to the conclusion of the case. This poses a special challenge in small ORs. Ideally, there will be adequate room to move about freely, to assist the anesthesiologist, and to perform documentation (Figure 142.2).

We recommend a 7 × 7 m (23 × 23 ft) room for endourological ORs. A 3.5 m (12 ft) high false ceiling with a 60 cm (2 ft) gap is used to accommodate cables, wires, piping and air conditioning vents. A powerful active suction device should be available for suction of fluids directly from the patient drapes (Neptune Waste management system, Stryker®, Kalamazoo, MI, USA). If such a system is unavailable, the floor of the endourological OR must be sloped towards a centrally placed drain to allow efficient, hygienic drainage of fluids [4].

If a dedicated cystoscopy suite is used for lower tract endoscopy, a sterile supply area should be dedicated nearby for equipment storage and commonly used supplies may be stored in the OR itself. If a dedicated suite is not employed, the sterile supply store should be organized such that necessary kits and supplies are stored nearest to the rooms used for cystoscopy.

### Lighting

It is important to have adequate lighting during endoscopic procedures. Often, lighting must be changed during the case to accommodate easy visualization of video monitors. We recommend a minimum of 1500 lux for the sterile field and 500 lux for the remainder of the room. We recommend using twin-dome lights that provide a shadowless white light as high as $3 \times 10^5$ lux 1 m

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from the field. In the past, OR lights employed halogen bulbs. At present, LED bulbs are favored as they provide high-quality cold white light and are considerably more durable than halogen bulbs. Control of the light placement and levels should be available to the surgeon in sterile field as well as on a conveniently placed OR control panel to allow easy manipulation by all team members.

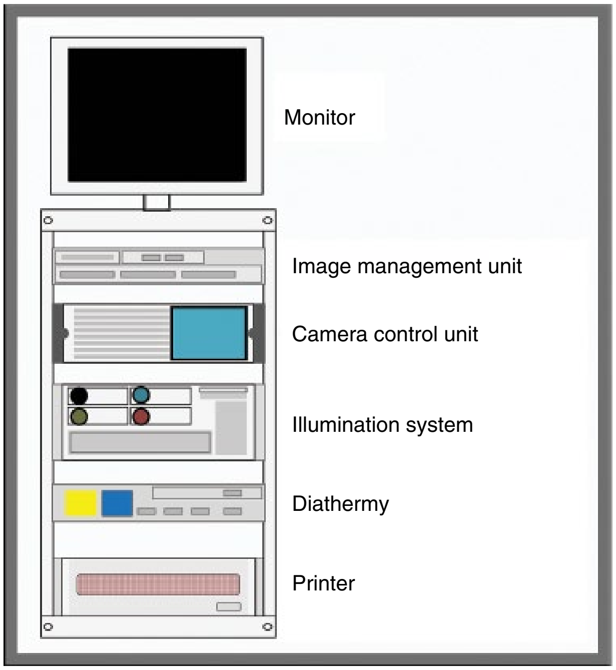
Monitor
Image management unit
Camera control unit
Illumination system
Diathermy
Printer

**Figure 142.1** Schematic of a typical endoscopy tower.

## Table

The operating table for endoscopic procedures should be able to support the patient in lithotomy and supine positions without injury or instability. We recommend the use of a specialized cystoscopy table if a dedicated cystoscopy suite is available. These tables lack some of the functionality of the operating tables described below but are adequate for lower tract endoscopy performed in low lithotomy position. Typically, cystoscopy tables are wide to allow comfortable patient positioning without armboards and have lightweight, easily detachable leg sections to allow for easy removal once the patient's legs are placed in the stirrups. These tables also have eccentrically placed bases to allow for free movement of the C-arm.

Many centers perform lower tract endoscopy in general ORs. Tables in these rooms should be constructed using rust-proof stainless steel. Construction materials should be radiolucent and the table base should be eccentrically placed to allow for C-arm use. With modern tables the table top can be moved relative to the base to allow for proper C-arm positioning. Occasionally, patients must be placed backwards on the table, with their legs over the head section to allow for lithotomy

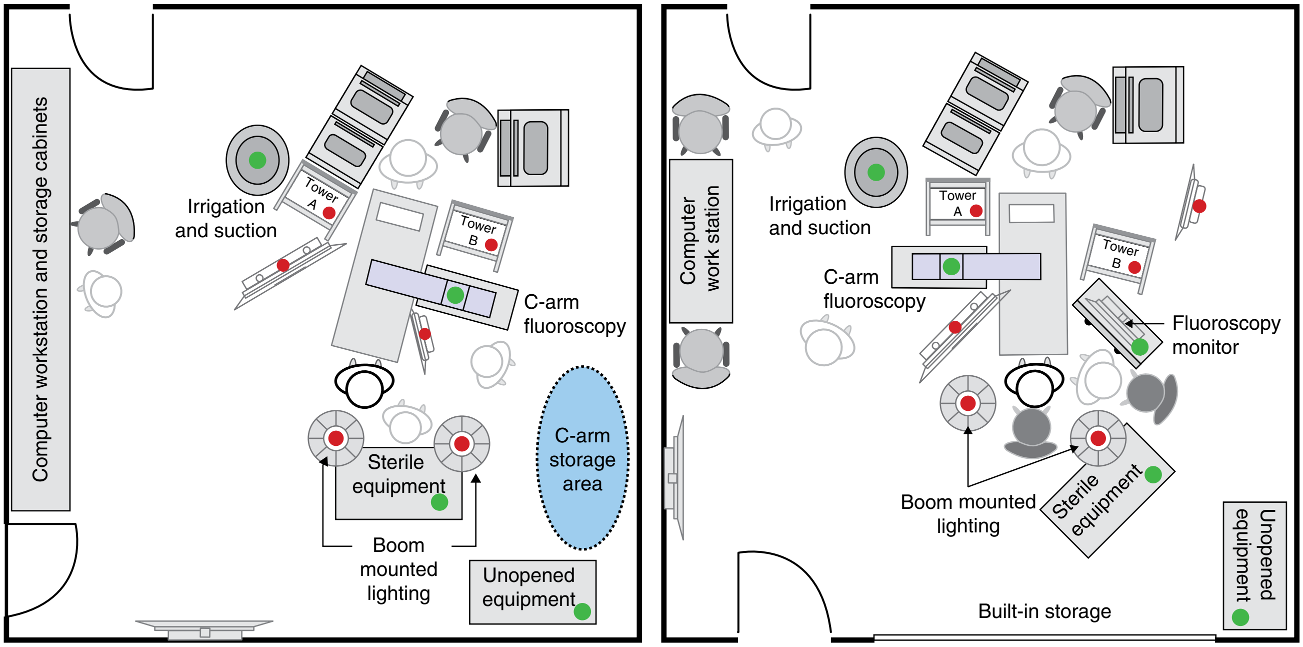
Computer workstation and storage cabinets
Irrigation and suction
Tower A
Tower B
C-arm fluoroscopy
C-arm storage area
Sterile equipment
Boom mounted lighting
Unopened equipment
Computer work station
Irrigation and suction
Tower A
C-arm fluoroscopy
Tower B
Fluoroscopy monitor
Boom mounted lighting
Sterile equipment
Unopened equipment
Built-in storage

**Figure 142.2** Example floor plans for the endourologic operating room. Left: Dedicated C-arm fluoroscopy. Right: Mobile C-arm fluoroscopy and monitor cart. Items marked with red dots are boom-arm mounted. Items marked with green dots are cart-borne.

positioning and C-arm use. The table should be easily movable on built-in wheels with central locking. The head and leg sections should be separable with a gynecological cut-out at the end of the body section. Attachment points for stirrups and fluid collection devices are necessary to allow for an anatomically correct lithotomy position. The table should also be capable of moving relative to the locked base, increasing or decreasing table height, and tilting to allow Trendelenburg, reverse Trendelenburg, and laterally rotated positioning. Ideally, bed positioning should be controlled via remote control available within the sterile field. However, management of bed position often falls to the anesthesia team, as control of the patient's airway can be compromised by repositioning.

### Obesity

Given the rise in morbid obesity, the weight of the patient should be considered in selecting the OR table, lithotomy stirrups, and any other weight-bearing equipment. With the increased utilization of weight loss surgery, robust operating tables have been developed to ensure patient safety and may be considered if a patient is especially obese. Adequate equipment for patient transfer should also be available as traditional roller-boards or drag sheets may be inadequately sized.

## Documentation and operating room integration

Archival of patient-related data for later reference and follow-up is important for clinical management, teaching, research, and satisfying medicolegal requirements. Such archiving is performed via paper documents, electronically, or both. Electronic record-keeping is virtually ubiquitous and modern EMR provide convenient access to the whole medical record, including imaging, financial records, and administrative information. The EMR software should adhere to the Health Level Seven standards to allow for seamless handoff between different software applications. In medical imaging, electronic picture archiving and communication systems (PACS) have been developed in an attempt to provide economic storage, rapid retrieval of images, access to images acquired with multiple modalities, and simultaneous access at multiple sites. The universal format for PACS image storage and transfer is DICOM (Digital Imaging and Communications in Medicine). Non-image data, such as scanned documents, may be incorporated using consumer industry-standard formats such as PDF (portable document format), once encapsulated in DICOM. A PACS consists of four major components: the imaging modalities such as CT and MRI, a secured network for the transmission of patient information, workstations for interpreting and reviewing images, and archives for the storage and retrieval of images and reports.

In the modern OR, integration of audio-visual (AV) signals and control of the data streams from endoscopic instruments, cameras, and fluoroscopy is vital. Through a central control, it should be possible to route any AV signal to any monitor in the OR. Ideally this control system would be available in the sterile field, but quite often it is located at the nursing computer station. The ability to record or transmit this information to separate locations is especially useful for education, and most surgical meetings devote major sessions to live operative workshops. Installation of such systems presents a large upfront expense, but is much cheaper than erecting temporary facilities for similar purposes and should be seriously considered during planned renovations.

## Universal protocol

The Universal Protocol (UP) for preventing wrong site, wrong procedure surgery was developed by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), and has been in effect since July 1, 2004 for all accredited hospitals, ambulatory care, and office-based surgery facilities (goo.gl/wJZWbO). The UP consists of three distinct parts: preprocedure verification, site marking, and a time-out performed immediately prior to the procedure. The UP is applicable to any setting where invasive procedures are performed, not just the OR setting. The Joint Commission International is a branch of the JCAHO that sets and enforces accreditation standards, including the UP, in more than 81 countries.

In accordance with the above regulation, before starting any intervention on the patient, all personnel in the OR follow "time-out" to identify (a) correct patient, procedure, site, side, position, equipment, implants, images, medicines (labeled); (b) allergies, antibiotics; (c) whether all labels from previous case are out of room. It is crucial that all OR staff are present and attentive during the time-out, and that any concerns are raised before the procedure is started.

## Room preparation

Operating room setup for transurethral, vaginal, and lower tract prosthetic surgery is discussed here. Transurethral procedures include cystoscopy, transurethral resection of bladder tumor, transurethral resection of the prostate, and direct visual internal urethrotomy. Increasingly, lasers are being employed in place of diathermy, which requires OR staff to familiarize themselves with the unique safety concerns that accompany high-energy light sources. Endourologic instrumentation and equipment will vary depending on the operative procedure. Vaginal procedures include urethral slings, anterior, posterior and apical repairs of pelvic organ prolapse. These surgeries may use native grafts or synthetic mesh for the repair.

With the current advancements in the understanding of pathophysiology of urinary incontinence and pelvic organ prolapse, most of these can be managed through a vaginal approach with or without usage of graft material. Similarly, prostheses are increasingly being placed for urinary incontinence (artificial urinary sphincter) and for erectile dysfunction (inflatable or malleable penile prosthesis). The OR should be equipped to handle all these procedures.

In general, two nurses are required for setup. The scrub nurse is responsible for setting up the instrument table, ensuring that the instruments are properly sterilized, functioning properly, and neatly arranged for easy availability. Each medical center should develop checklists for each procedure to prevent delays caused by missing equipment. Nurses and surgeons should collaborate to ensure checklists are complete without being excessive, and should specify which instruments will *always* be used and which instruments *may* be used. The former should be opened and arranged prior to the start of the case, while the latter should be retrieved from central supply but kept unopened until they are needed.

## Patient preparation

While the scrub nurse is preparing the sterile setup, the circulating nurse reviews the patient's chart. The circulator acts as the patient's advocate, reviewing the OR sequence with the patient, identifying the correct operative site and laterality, addressing any concerns the patient may have, and communicating with the patient's family. Indications for antibiotics and prophylaxis against deep vein thrombosis are reviewed and the necessary medications and equipment are retrieved if necessary. The patient's anticoagulation status should be reviewed. If withholding anticoagulation is indicated the circulator should confirm that the patient has not taken this medication. The availability of blood products for possible transfusion should be checked before the circulating nurse brings the patient into the OR.

After anesthesia is induced, the patient is positioned appropriately based on the procedure. Lower tract endoscopy, vaginal surgery, and placement of artificial urinary sphincters is performed in the lithotomy position, whereas penile prostheses can be placed while supine.

For lithotomy, patients must be positioned such that when the leg portion of the table is removed, the buttocks are at the table's edge, over the gynecologic cut-out. After placing antiembolic compression stockings or sequential compression devices, *two* team members should raise the patient's legs slowly and simultaneously. Care must be taken to support the knees as the feet are positioned in gel-padded footrest stirrups (Figure 142.3). Padded patient supports and foam sheeting should be used to prevent pressure on the nerves and soft tissues of the upper and lower extremity. Improper positioning can result in nerve damage, venous thrombosis, compartment syndrome, and hip-joint dislocation. Both arms should be secured on padded armboards to prevent injury to the patient's fingers or hands when the table is raised or lowered. There are a number of positioning techniques to prevent injury (Table 142.1).

If monopolar diathermy is being used, a dispersive electrode is fixed distant to bony prominence. No such lead is necessary with bipolar instruments. Any visible contamination of the surgical site should be removed and clipping of hair may be performed. There is level I evidence that there is no difference in surgical site infections between shaved and unshaven incision sites [5]. However, if hair is to be removed, electric clippers are associated with lower infection rates than shaving with a razor. A recent Cochrane review found no difference between day-before and day-of-procedure hair removal but current Association of periOperative Registered Nurses (AORN) guidelines recommend hair clipping the day of the surgery and only if necessary for the procedure [5]. Next, skin preparation is done using an antiseptic solution. A large randomized controlled trial (RTC) of clean-contaminated surgeries and a smaller RTC examining urologic procedures shows lower rates of surgical site infections with chlorhexidine gluconate and isopropyl alcohol as compared to povidine iodine when used for at least 5 minutes [6–8]. We typically use the former (Chloraprep®, CareFusion, El Paso, TX, USA). Because of apprehension of infection associated with prosthetics, surgical site preparation varies significantly between surgeons. While a 10-minute manual scrub of the surgical site is common practice, there is no evidence supporting any specific time requirement to reduce infection rates for penile implant procedures [8]. There is no urology-specific study examining surgeon hand-cleansing method and infection rates, but a large multidisciplinary prospective RTC showed no difference between traditional hand-scrubbing and alcohol-based solutions.

Once the surgical site is properly cleaned, surgical drapes should be appropriately placed to minimize the risk of the prosthesis contacting the patient's skin. Adoption of a no-touch insertion technique has been

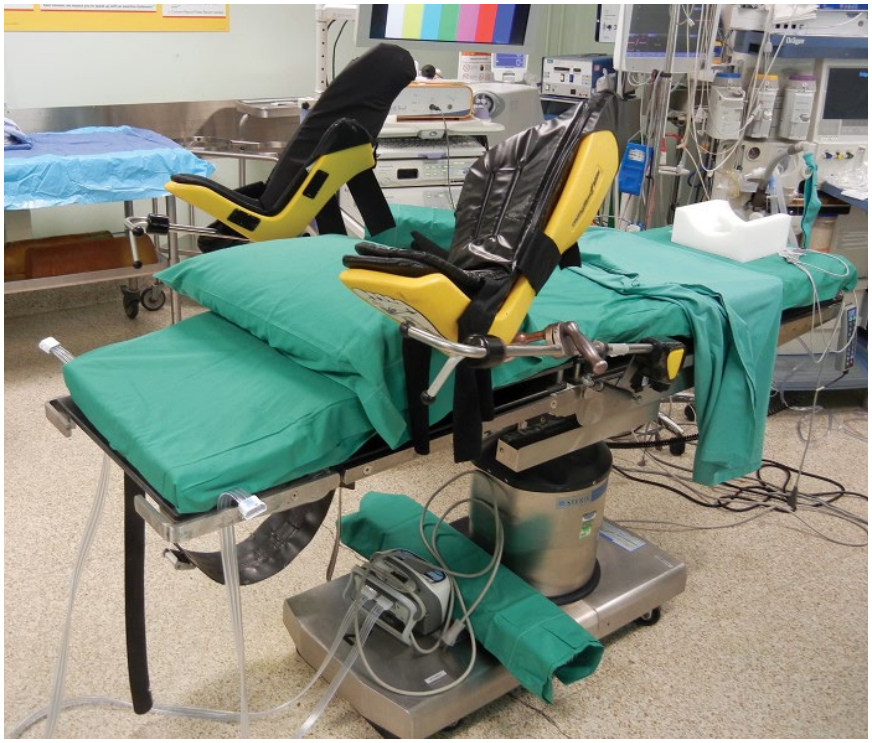

**Figure 142.3** Operating table with Yellofins® stirrups.

**Table 142.1** Complications related to poor patient positioning.

| Complication | Consequence | Positioning technique |
|---|---|---|
| Common peroneal nerve injury | Inability to dorsiflex the foot. "Foot drop" | Ensure the lower leg does not rest dependently on the stirrup. Avoid excessive hip flexion and knee extension |
| Femoral nerve injury | Inability to flex the hip or extend the knee | Avoid hip flexion >90°, minimize internal and external hip rotation |
| Obturator nerve injury | Inability to adduct the leg, hip instability | Avoid leg abduction greater than 30–45°, combine abduction with hip flexion |
| Brachial plexus injury | Varies, weakness and loss of sensation in the upper extremity | Shoulder abduction should be less than 90° or shoulder braces should be used |
| Ulnar nerve injury | Numbness, of the ring and little finger, weak grip | The arm should be pronated and properly padded |
| Compartment syndrome | Ischemia and necrosis of the leg, potential need for fasciotomy | Traction pads to prevent slipping when in Trendelenburg, minimize procedure time and time in Trendelenburg |

shown to significantly decrease infection rates [7]. Ioban™ or similar adhesive barriers can be used to secure the drapes and minimize the amount of exposed skin [9].

## Equipment preparation

### Transurethral surgery

Transurethral surgery is performed through a rigid cystoscope. The outermost piece of the cystoscope is the sheath, and all lenses, resection tools, and fluids must pass through it. The lens is connected to the sheath by the bridge, which has one or two channels through which wires and laser fibers can be passed. The bridge is typically labeled with its outside diameter and the diameter of its working channels(s). Typical cystoscope and resectoscope kits include 0, 30, and 70 lenses, outer and inner sheaths in 19 Fr or 21 Fr, Timberlake, blind and visual obturators, a trumpet valve working element, one and two channel bridges, detachable stopcock for irrigation tubing, flexible grasping forceps, and rigid biopsy forceps. Other kits with 12 (Olympus) and 120 (Olympus and Storz) lenses as well as 15 and 17 Fr sheaths are available on request. If a patient

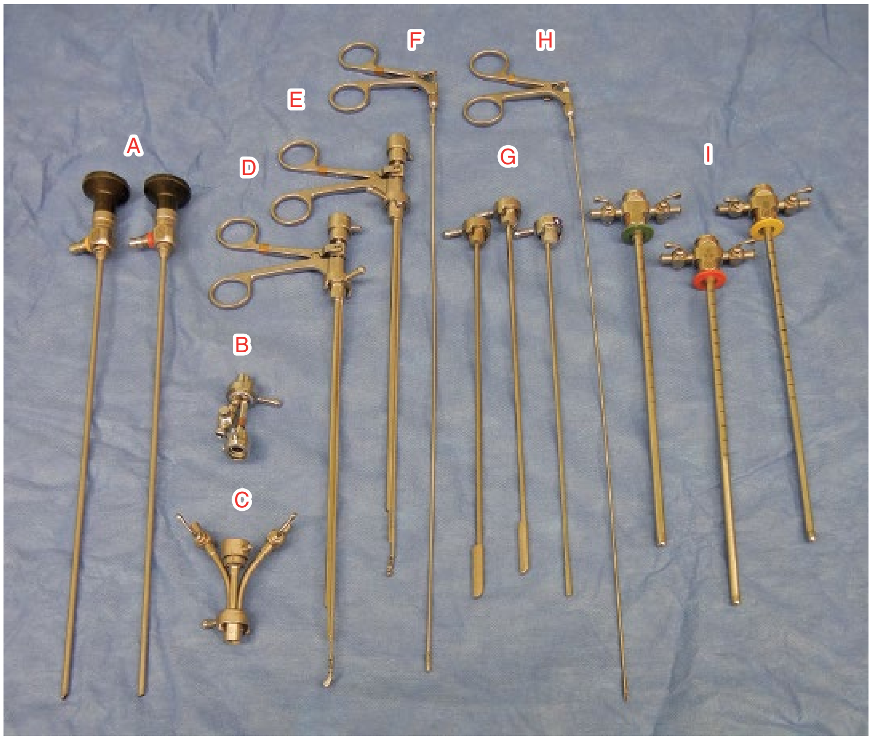

**Figure 142.4** Cystoscopy set. A, Telescopes; B, single channel bridge; C, -channel bridge; D, rigid biopsy forceps; E, rigid foreign body forceps; F, flexible foreign body forceps; G, visual obturator; H, flexible biopsy forceps; I, sheath.

has a high bladder neck, a large prostatic median lobe, or other difficulty anatomy, the use of an Albarran bridge may help to direct any wires, fibers, or catheters that would otherwise be difficult to place.

Cystoscopes are assembled in a stepwise fashion with each subsequent piece fitting over and attaching to its predecessor. A typical initial setup is obturator (visual or nonvisual obturator), bridge, sheath. Visual obturators allow a telescope to be placed inside so the urethra can be traversed under direct visualization. The light source attaches to the lens, while the irrigant tubing attaches to the sheath. Once the cystoscope is in the bladder, the obturator is removed and replaced with the resectoscope (Figure 142.4).

From inside to outside, a resectoscope consists of a lens, working element with loop, outer sheath, and inner sheath. The working element typically has a trumpet valve style articulator. Fluid inflow and outflow are attached to the sheaths. Resectoscopes produced by Storz have fluid inflow through the inner sheath and outflow through the outer sheath, while Olympus resectoscopes have both on the outer sheath. This allows inflow and outflow to function with only the outer sheath inserted, leaving a larger working channel. A special attachment is available for the Storz that allows inflow and outflow through the outer sheath.

UroLift® is a novel device that places implants made of nitinol, stainless steel, and PET suture to lift and compress the lateral lobes of the prostate to treat benign prostatic hyperplasia (BPH)-related urinary symptoms. The UroLift kit includes its own specialized cystoscope, designed for application of the implants. Each implant device is placed by a single-use UroLift delivery device under direct visualization. Because these devices are not reusable, several devices should be available but unopened before the procedure begins. Typically 4–6 implants are needed.

After patient positioning, the leg portion of the surgical table should be removed and the appropriate fluid collection device should be placed and connected to suction. Various proprietary drapes are available with inbuilt collection system (Kimberly-Clarke®, Reigate, Surrey, UK; Microtek Medical, Columbus, MS, USA; G Surgiwear, Shahjahanpur, UP, India).

A typical setup for transurethral resection procedures is described below:

### Back table

Cystoscopy pack with back table drape, patient drapes, irrigation "Y" tubing, transurethral resection (TUR) set, k-y jelly, a marking pen, and labels for labeling fluids, a 10 and 20 ml syringe, a Telfa pad (Kendall, Covidien, Mansfield, MA, USA) for specimens, a disposable graduated cylinder and two small basins and three disposable towels. Gowns and gloves should also be opened and available. These should be arranged with attention to when each piece of equipment will be needed.

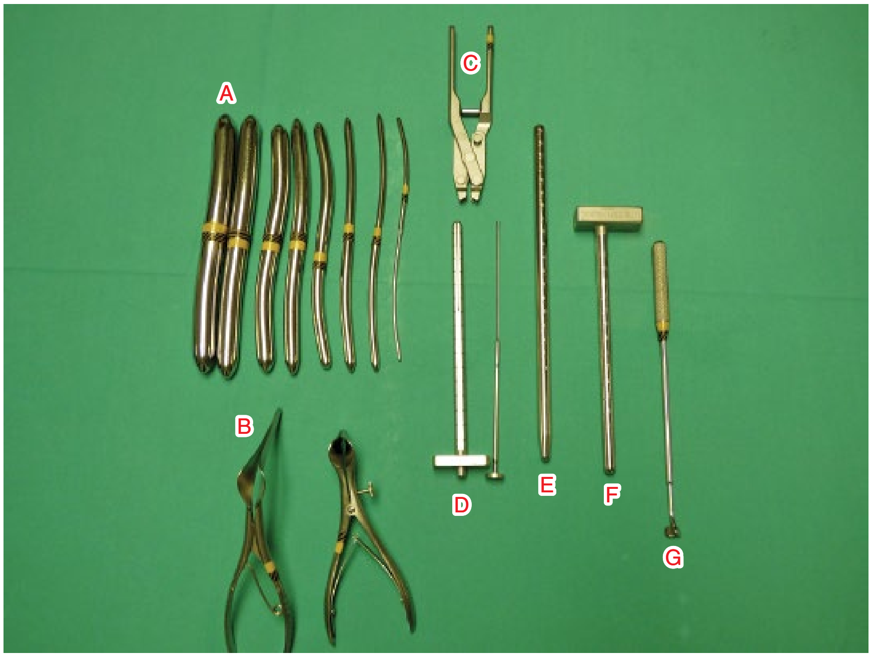

**Figure 142.5** A, Hegar dilators; B, nasal speculum; C, crimper; D, Furlow introducer; E, measuring rod; F, dialmezinsert device; G, insertion tool.

Patient drapes are placed in the left lower corner of the back table. All cords to be passed off are placed in the left upper corner of the back table (camera, light cord, cysto "Y" tubing, bovie or bipolar cord). A towel with k-y jelly is placed beside the drapes. The Van Buren sounds should be placed in sequential order from smallest to largest. The double channel bridge should be attached to the 30° telescope and the 70° bridge should be attached to the single channel bridge. A nipple should be placed on each channel and all stopcocks placed in the OFF position to control the fluid channel. These should be arranged between the 22 ft cystoscope sheath with obturator and the resectoscope (Figure 142.5).

### Prep table

For female patients, a prep set is opened that contains basins to hold the appropriate antiseptic solution according to surgeon preference and patient allergies. Of the 10 sponges in the preparation pack, 5 should be used for patient preparation. The additional 5 sponges in the tray should be placed on the back table. For male patients a 26 ml Chloraprep applicator stick is used.

### Resection kits

Monopolar, bipolar and laser resection kits have different components.

- *Monopolar*: Continuous flow resectoscope set 26 Fr/28 Fr; outer sheath, inner sheath, visual obturator with single channel, Timberlake deflecting tip obturator, passive or active type working element for the resectoscope, a disposable loop, and a Toomey syringe or Ellik's evacuator. Adequate 1.5% glycine and 0.9% normal saline should be available for intraoperative and postoperative irrigation respectively.
- *Bipolar*: Gyrus-ACMI (now an Olympus company), Olympus and Karl Storz manufacture bipolar resection systems. Of these the Gyrus PK® Superpulse® is the most extensively studied and widely used. Each set is specific to the manufacturer and typically includes a 25.6 Fr /27.6 Fr inner and outer sheath, visual sheath, Timberlake obturator, Iglesias working element and disposable loop. The irrigant of choice for this procedure is 0.9% normal saline.
- *Laser*: Holmium:YAG and KTP and thulium are commonly used lasers for prostatic diseases. The resectoscopes/cystoscopes for these are separate from the above as well as from each other. Each basic set has similar components (i.e. outer sheath, inner sheath, obturator, working element), but the working elements have specially designed channels to accommodate the laser fiber.

## Prosthetic surgery

The use of prosthetics in urology has become commonplace in recent years. Advancements in device design and infection prevention strategies have encouraged patients and surgeons alike in choosing inflatable penile prostheses and artificial urinary sphincters.

Before the procedure it is vital that the circulator nurse confirm the patient has received the necessary antibiotics and that the antibiotics for irrigation are in the room. The scrub nurse should confirm the availability of all the

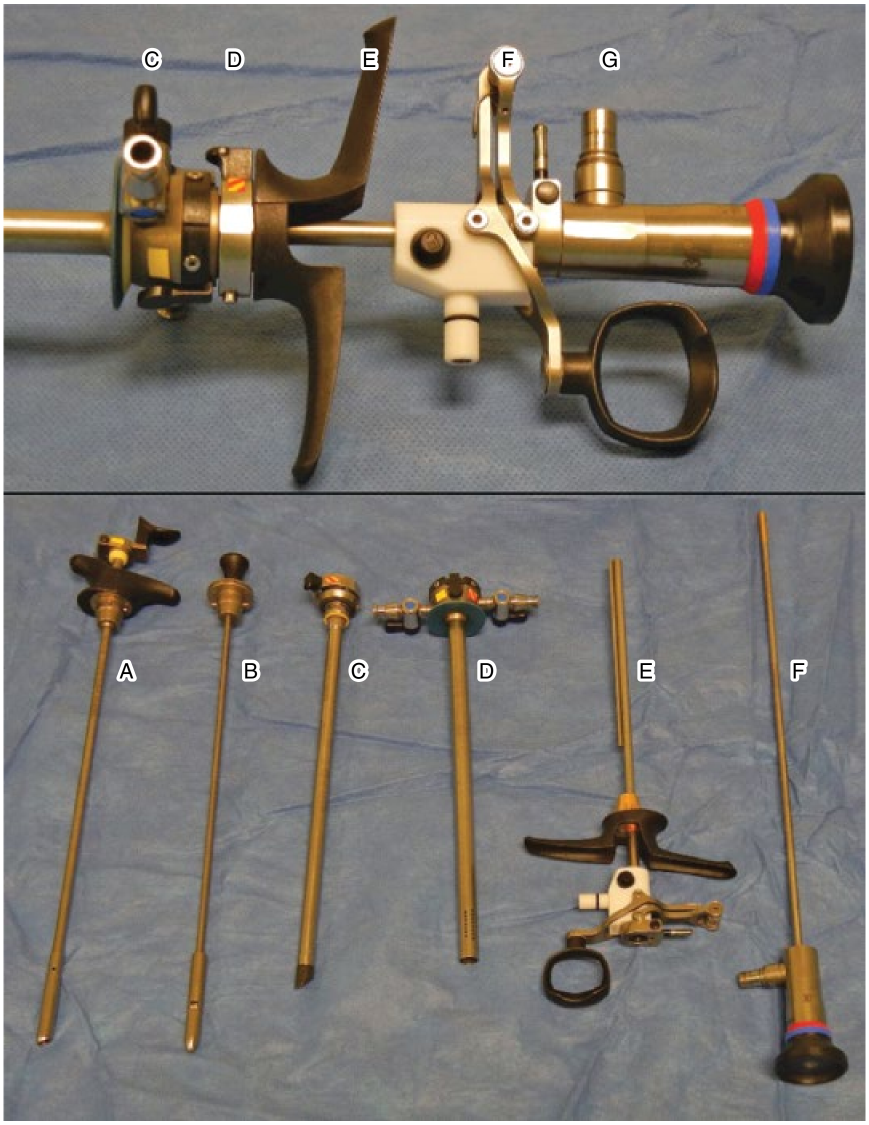

**Figure 142.6** Resectoscope, left: disassembled right: assembled. A, Visual obturator; B, Timberlake (blind) obturator; C, inner sheath; D, outer sheath; E, working element with trumpet valve control; F, telescope; G, light source connector.

various sizes of the prosthetic and the special instruments needed to place it (Figure 142.6).

A typical setup for insertion of a penile prosthesis is described below.

### Back table

Major prep pack: table cover, 5 half sheets, 2 wetproof drapes, 12 towels, 1 mayo cover, 2 wet proof towels, 4 gowns. Urology minor set, penile prosthesis set, Lone-Star retractor with hooks, dilamezinsert inserter, no. 15 blade with handle, needle protector, marking pen, monopolar pencil, bipolar forceps, suction tubing and tip, 10 ml syringe for the Foley catheter, 20 ml syringe ×2 for flushing the prosthesis tubing, 60 ml syringe ×2 for filling the prosthetic and reservoir, 14 Fr Foley catheter and drainage bag, steridrape, marking pen, labels for medication and fluids, small basins for antibiotic irrigation, tray for prosthesis soaking. Rifampin–gentamicin solution should be available for irrigation and/or device soaking if indicated. At present, the Boston Scientific inflatable prosthesis devices are impregnated with antibiotics and no additional preparation of the device is necessary.

### Mayo stands

One mayo stand should be draped in the typical fashion with an impervious steridrape placed over it. A small round basin, large round basin, rectangular tray, and all syringes are placed on this stand. Rubber-shodded mosquito clamps are kept in the small basin. The large basin and the rectangular tray are filled with 0.9% saline. Hegar dilators, nasal speculum, measuring devices, dilamezinsert, the Furlow tool, and the quick-connect devices should be placed in the rectangular basin. Any instrument placed here should be rinsed in sterile water beforehand.

The second mayo stand should be draped in the normal fashion and have Adson forceps, short Debakey forceps, suture scissors, 4 straight hemostasis, 4 curved hemostats, 1 Allis clamp, and 1 Lahey dissector arranged neatly on it.

#### Double ring stands

Both stands should be draped and large basins appropriately placed. One should be placed on each side of the patient and filled with 0.9% saline for glove washing before the prosthesis is handled.

Setup for placement of an artificial urinary sphincter and placement of a penile prosthesis are very similar. Additional equipment includes a ¼ inch Penrose drain or vessel loop to place around the urethra, Kittners and methylene blue. Hegar dilators, nasal speculum, measuring device, dilamezinsert, Furlow tool, and quick-connect devices may be used.

### Vaginal surgery

Room setup for vaginal surgery is similar to endoscopic surgery, with a specific vaginal surgery kit available at most centers.

#### Prep table

For female patients a prep set is opened that contains basins to hold the appropriate antiseptic solution according to surgeon preference and patient allergies. Of the 10 sponges in the preparation pack, 5 should be used for patient preparation. The additional 5 sponges in the tray should be placed on the back table. Instruments that may be useful in vaginal surgery include weighted vaginal retractor, Lone-Star retractor, Breisky-Navratil vaginal retractor, Sim's speculum, Stamey needles, Heaney curve-tip needle holders, and Mueller S-shaped dissecting scissors.

## Energy sources

### Diathermy

#### Monopolar

Monopolar instruments are the most readily available and commonly used method for electrosurgery. All electrosurgery instruments have two poles (bipolar) and electrical current runs between two poles. Monopolar diathermy employs an active electrode located in the cutting instrument, and a dispersive electrode located in a metal or metalized plastic pad attached to the patient's skin. Because the cutting instrument is small, the concentration of current is highest where it contacts the tissue. In contrast, the dispersive electrode is large, allowing current to flow without damage the tissue. Ideally, the dispersive electrode should be between the site of surgery and any metal implants the patient may have. This avoids current running selectively through the implant and causing tissue damage. If the patient has metal implants on both sides of the body (i.e. bilateral hip replacements) the pad should be placed between the implants where possible.

Monopolar instruments can cause severe burns if contact with the dispersive electrode is insufficient or if there is tissue in contact with other metal objects that can "leak" current. In addition, if current from a monopolar instrument demodulates, as can happen when the current arcs through the air to the tissue, the frequency of the current can drop into the range commonly used by implantable pacemakers and defibrillators. This can lead to malfunction as the device interprets the current as cardiac in origin and can respond inappropriately [10].

It is important to note that a monopolar generator can be used in any setting that requires monopolar diathermy and a single cord can be used with multiple instruments. Monopolar generators and instruments are less expensive and more readily available than bipolar instruments.

In endourology, monopolar instruments *require* the use of nonconductive fluids such as sorbitol, glucose, or glycine to prevent dispersion of current through the irrigant. Because these solutions are hypotonic, prolonged exposure through procedures such as transurethral resection of the prostate (TURP), can cause TUR syndrome. TUR syndrome is characterized by dilutional hypervolemic hyponatremia, which can lead to congestive heart failure, pulmonary edema, seizures, coma, and death. Because of this, procedure time should be limited to 90 minutes when monopolar resection is used.

#### Bipolar

Bipolar instruments function using the same principles as monopolar instruments, with a current running between two poles. Unlike monopolar instruments, which require a large dispersive electrode elsewhere on the body, bipolar instruments have both electrodes located within the instrument. Monopolar instruments send current through the patient's whole body as it flows between the active and dispersive electrode. Bipolar instruments only send current through the target tissue located between the electrodes. Monopolar and bipolar endoscopic instruments come in various configurations (Figure 142.7).

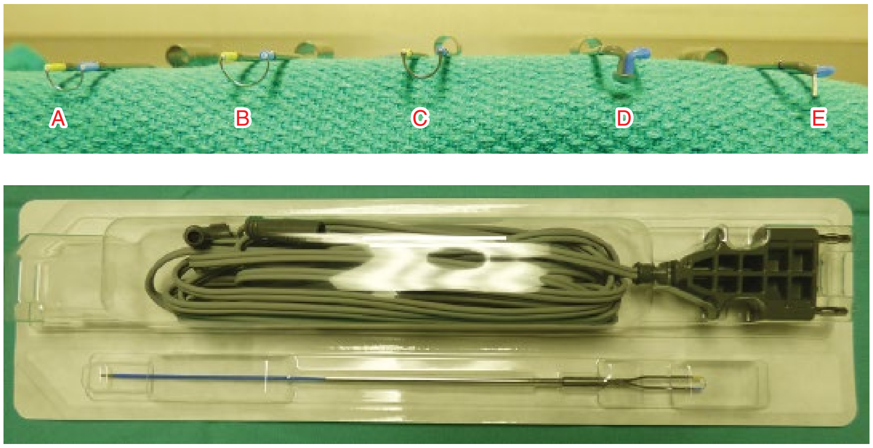

**Figure 142.7** Bipolar implements. Top: A, small loop; B, large loop; C, band electrode; D, button electrode; E, needle electrode. Bottom: Implement in packaging with dedicated cord.

Because current runs so directly between the on-instrument electrodes, bipolar instruments can be used with saline irrigant, allowing longer procedure times without concern for TUR syndrome as described above. This allows for extensive resection of large prostate glands that would have required a staged procedure with monopolar instruments. Resection time, intraoperative blood loss, need for transfusion, hospital stay, and catheterization times are all decreased in bipolar TURP as compared to monopolar TURP, while short- and medium-term outcomes are the same [11–14]. We suggest the use of bipolar resection of the prostate over monopolar resection when possible.

Although bipolar instruments decrease procedure-associated morbidity, they do pose a significant increase in cost. Bipolar generators are more expensive and less common than monopolar generators and cannot be used interchangeably the way monopolar generators can. In addition, if multiple instruments are to be used, monopolar instruments can be attached to the same power cord, while bipolar instruments each require their own.

### Laser

Since their introduction in urologic procedures in the late 1980s, lasers have been used for a variety of urologic procedures, most notably for lithotripsy, vaporization of the prostate, and incision of strictures. Current lasers used in urology are outlined here, and this section focuses on safety and technical considerations for lasers in the endoscopic OR. A thorough description of the mechanisms of laser function and their applications in urologic surgery is available in other chapters.

The three most common lasers used in the United States are holmium (Ho:YAG), thulium, and the green-light laser (KTP). Of these, holmium and KTP are more common. As mentioned above, dedicated laser scopes are available through Storz or Olympus, or the laser fibers can be deployed through regular cystoscopes. Filters can be attached to the scope to protect the camera from laser damage if specialized scopes are not used. Continuous flow sheaths are preferred for use with lasers.

***Technical considerations*** Laser units are typically mobile, mounted on rotating casters, and are moved from room to room as needed. They require a power source and the path of the electrical cable should be considered in room setup. Laser fibers are sterile and should have a dedicated place on the sterile equipment table. Because the laser fiber is long and thin, everyone who handles one should be mindful of controlling its whole length when it is not in use. This is especially true for the holmium laser, as its fiber is especially fine. We recommend the use of a wet sterile towel draped over the fiber to keep it in place. An additional towel may be placed on the lithotomy stirrup where the fiber crosses into the sterile field. This towel can be folded over the fiber to maintain its position while in use.

***Laser safety*** The laser produces an intense, highly directional beam of light. If directed, reflected, or focused upon an object, laser light will be partially absorbed, raising the temperature of the surface and/or the interior of the object, potentially causing an alteration or deformation of the material. A full awareness of the potential hazards and necessary safety standards associated with laser use is necessary, as the application of lasers in urology has increased dramatically in recent years. Laser safety and hazards cannot be completely described in this chapter; nevertheless, important aspects are covered and referenced for a more detailed reading. The reader can refer to http://www.laserinstitute.org/ for a comprehensive understanding of lasers.

***Laser hazards*** Lasers pose the greatest risk to the eyes and skin of OR staff. The precise effect varies with the frequency and intensity of the laser. Eye protection is particularly important when using lasers as all three of the commonly used laser types can damage eye structures. Energy from the holmium laser has a wavelength of 532 nm. Because this wavelength is in the visible spectrum, holmium lasers can cause severe retinal burns. Thulium and holmium lasers have wavelengths of 2013 nm and 2140 nm, respectively, placing them in the infrared portion of the spectrum. These lasers spare the retina but can damage the lens and the cornea. Skin is far less likely to be damaged by lasers because of the layer of dead keratinized cells. However, medical lasers do have the power to cause burns, photosensitivity, and darkening if contact is prolonged. Apart from bodily damage, lasers pose other hazards such as electrocution, fire, and asphyxiation related to damage or malfunction of the laser apparatus.

Staff must understand and comply with the mandatory safety regulations laid out by their health system and the device manufacturers. Because different lasers exploit different wavelengths of light, different eyewear is required for each laser. Glasses meant for protection from the green-light laser are not suitable for holmium, and vice versa. Appropriate warning signs must be placed prior to the procedure. Nursing staff should ensure that there is extra eye protection near the main entrance. This allows other personnel to enter during the procedure without risking injury. The patient's eyes and eyelids should be protected from the laser beam in a method deemed appropriate by the laser safety officer. Any change in the status of the laser must always be announced (e.g. active or stand-by) by the surgeon and repeated by the individual manually changing the laser settings. Prevention of injury is key as there is no first aid for laser eye damage. Any hazardous exposure to laser should be reported to hospital authorities.

Because of the potential hazards of working with medical lasers, various governing bodies have prescribed regulations and safety standards and best practice guidelines for their use. In the United States, Occupational Safety and Health Administration (OSHA) creates and enforces these guidelines. All laser manufacturers must comply with the standards outlined in ANSI Z136.3-1996/2011 of the American National Standards Institute. European equivalent standards are designated EN207/208/60825.

### Radiation

Interventional fluoroscopy is essential in endourology. Advancements in the field have led to more complex and time-consuming procedures, making protection from radiation even more important for the surgeon, staff, and patients. The hazards of radiation to the patient include immediate or delayed skin injury and a small but real delayed risk of cancer. Studies from percutaneous transluminal coronary angioplasty have estimated long-term cancer risk of 0.1% in men older than 60 years with exposure of 80 Gy/cm$^2$ (effective dose 20 mSv) [15]; the risk is estimated to be up to fourfold in children younger than 10 years. The exposure of OR staff during endourological procedures is significantly less than for patients, but because they are at risk for exposure regularly, proper containment is paramount [16, 17].

The recommendations for containment of radiation within the OR is a minimum of 2 mm of lead equivalent in walls. This requires 15 cm thick concrete or 25 cm thick brick or cinder block walls if lead is not used [16]. Personal protection equipment including articulated shielding, lead aprons, gloves, thyroid shields, and glasses must always be available in adequate numbers and sizes. The minimum recommendation in lead garments is 0.25 mm lead thickness for protection against scattered radiation, and 0.50 mm lead thickness for protection against direct radiation. There should be an easily visible indicator outside of the OR whenever fluoro is in use. We advise use of dosimeters by all staff for periodic monitoring of radiation exposure and many centers provide dosimeters on request. The principles of proper shielding, minimizing time and radiation, and maintaining proper distance from source are known by the acronym ALARA (as low as reasonably achievable). Guidelines and recommendations have been published by the National Cancer Society and the International Atomic Energy Agency (http://goo.gl/VfKmgZ).

## Patient handouts

In the age of shared decision-making, it is important for patients to have an adequate understanding of their disease, its treatment, and how to care for themselves after surgery. Verbal teaching with time for questions should be integrated into the patient visit at the time of diagnosis, but is not typically sufficient to ensure patient understanding. The use of diagrams or models alongside printed literature can fill the gaps left after consultation. Having an easily understood handout written in plain language encourages patients to develop a greater understanding of their condition and allows them to absorb information at their own pace. This aids in truly informed consent and creates opportunity for patients to ask more insightful questions about their disease. Patients may be directed to https://www.urologyhealth.org/educational-materials for peer-reviewed literature, frequently asked questions, and perioperative care information.

At the time of the initial consultation, the appropriate procedure is explained to the patient and any questions and concerns are addressed. Most often, patients want to know the length of the procedure and hospitalization, the amount of pain and its treatment, and how long the recuperation period will be. The literature provided to the patient at this encounter should describe their condition, explain the options for treatment including surgery, outline the necessary preoperative workup, and cover the basics of what to expect before and after the operation. Patient literature should also include a list of instructions that the patient must follow before surgery. This includes withholding food prior to the procedure, any site preparation that may be necessary, medications that should be withheld before the surgery, and any remaining preoperative workup. Important preoperative tests to perform for endoscopic lower tract procedures include a complete blood count, electrolyte panel, coagulation studies, urinalysis, and urine culture. If the urine culture is positive the patient should be treated preoperatively with appropriate antibiotics. Electrocardiogram and chest radiography are sometimes performed based on the patient's age and medical history. All of these tests should be reviewed the day of surgery. Preoperative handouts should also include day-of-surgery information, including the location of the medical center, the location of surgical check-in, maps for parking and navigation through the hospital, and relevant addresses and contact information.

Additional literature should be provided to the patient and their family or social support on the day of the procedure. Undergoing surgery is a stressful experience for patients and family, and any information provided in the perioperative period is quickly and easily forgotten. Because of this, handouts provided after surgery should complement the previously provided literature and include a brief explanation of the condition that required surgery.

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# 143

# Local Anesthesia for Minimally Invasive Treatment of the Prostate in the Office Setting

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## Introduction

Despite a wealth of information regarding outcomes for most minimally invasive surgical treatments (MIST) options for lower urinary tract symptoms caused by benign prostatic hyperplasia (BPH), there are limited studies regarding the best method of local anesthesia for prostate procedures. No "standard" exists with respect to the office-based anesthetic protocol.

During the past decade, as minimally invasive techniques have continued to proliferate and reimbursements for hospital-based procedures have diminished, reimbursements for office-based procedures have remained favorable. Physicians in private practice have increasingly sought to perform procedures in the office. Microwave procedures could be performed without intravenous analgesia [1]. Urologists also found transurethral needle ablation (TUNA) using radiofrequency energy and interstitial laser coagulation could be performed with local anesthesia in the office [2–4]. Similarly, prostatic urethral lift procedures (e.g. UroLift®) can be performed under spinal and local anesthesia in the office setting [5], and currently, urologists are performing and developing techniques for safe and comfortable laser ablation of the prostate in the office setting. Such a trend may change as reimbursement changes; nevertheless, an in-office procedure has a potential to be safer (in that only local anesthesia is used), more convenient and efficient for the patient. Such procedures are also less costly overall, saving on hospital/surgery center fees and professional anesthesia charges. Whether urologists continue to develop and advance in-office MIST remains to be seen. Urologic outcomes should be similar to procedures performed in the hospital or surgery center with full anesthesia or intravenous sedation. True evidence-based conclusions comparing procedures performed with anesthesia and anesthetic monitoring to those performed under local anesthesia in the office do not exist.

This chapter discusses the common pharmacologic agents that can be used as local anesthetics, and the application and techniques used to deliver local and regional anesthesia. The techniques used to anesthetize the prostate for MIST continue to evolve. It is hoped that the information presented will stimulate proper study for the development of improved local anesthetic protocols and techniques. Any local anesthetic protocol for the performance of MIST of the prostate in the office setting should have the following goals: (i) to provide satisfactory anesthesia such that the patient and surgeon feel comfortable with the performance of the procedure in the office setting; (ii) to safely administer the anesthetic so that proper patient monitoring requires nothing more than vital signs and observation; (iii) to minimize the risk of complications or bleeding that might interfere with proper performance of the procedure; (iv) to carry out the MIST in a fashion that is complete and not compromised by the use of local anesthesia instead of regional (i.e. spinal) or general anesthesia.

## Patient selection and preparation

In order to enhance the likelihood of patient acceptance and comfort, preoperative counseling is paramount. The experienced urologist should also develop the skill of patient selection, much like that in selecting patients for in-office vasectomy and cystoscopy. Patient size, prostate size, and patient comfort level with the office physical examination and preoperative counseling need to be taken into account. Patients should be counseled on the

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Companion website: www.wiley.com/go/smith/textbookofendourology

likelihood that they will not be fully anesthetized such that they will not be numb to all feeling. Some discomfort should be expected but this should be mild and generally well tolerated. Time should be spent explaining the delivery technique of the local anesthetic so that patients know what to expect.

## Pelvic neuroanatomy

The following is a brief discussion of the relevant prostatic and urethral neuroanatomy. With a basic knowledge of genitourinary innervation, it is easier to understand which nerves can be appropriately targeted for prostatic and posterior urethral anesthesia.

The inferior hypogastric (pelvic) plexus receives both sympathetic (hypogastric nerve) and parasympathetic (pelvic splanchnic nerve) innervation. The plexus is a 4–5 cm long rectangle and its midpoint reaches to the tip of the seminal vesicles [6]. It runs on either side of the rectum, communicating behind the rectum and sending branches to encompass the vesical neck (Figure 143.1). The distal end of the pelvic plexus gives off branches to the posterior lateral aspect of the prostate, running in close association to the arterial and venous supply (neurovascular bundle) [7]. The nerves lie in the lateral endopelvic fascia near its junction with Denonvilliers' fascia [8]. The nerves then coalesce at the apex of the prostate at the 5 and 7 o'clock positions [9, 10]. Superficial branches innervate the urethral sphincter at the 3 and 9 o'clock positions, while deep branches are sent to the bulbourethral glands. As the cavernous nerves reach the penis, branches innervate the urethra at the 1 and 11 o'clock positions, while small branching fibers join the dorsal nerves of the penis [4, 6].

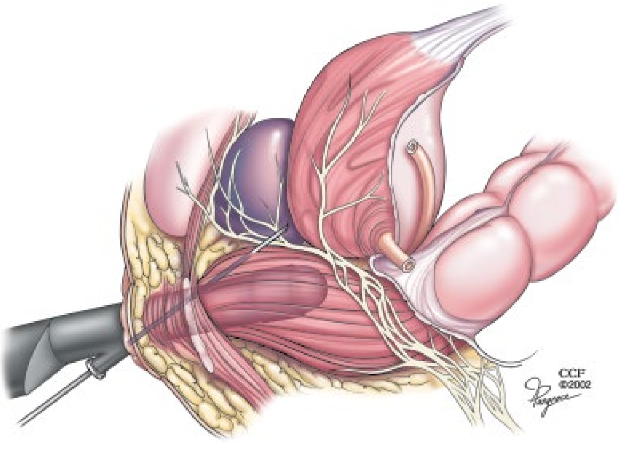

**Figure 143.1** Prostatic neuroanatomy. The inferior hypogastric (pelvic) plexus lies on either side of the rectum and its midpoint stretches to the tip of the seminal vesicles. *Source:* Cleveland Clinic, Ohio, USA. Reproduced with permission of Cleveland Clinic Center for Medical Art and Photography © 2015–2017.

The pudendal nerve originates from Onuf's nucleus in the sacral spinal cord (S2–S4), leaves the pelvis between the piriformis and coccygeus muscles, and enters the greater sciatic foramen [11]. It then re-enters the pelvis through the lesser sciatic foramen and passes through the pudendal canal. Branches are sent off to the rectum (inferior rectal nerves), perineum (perineal nerve), and penis (dorsal nerve of the penis) [12]. The urethral sphincter has both autonomic and somatic innervations. Hollabaugh et al. performed a study of 12 fresh cadaveric dissections and confirmed the presence of an autonomic (pelvic nerve) and dual somatic (intrapelvic pudendal and perineal nerve) innervations of the rhabdosphincter [13]. From these descriptions it can be reasoned that a local anesthetic delivered anywhere from the seminal vesicles to the apex of the prostate should have some effect on sensory input from the prostate. Likewise, the rhabdosphincter could also be affected by nearby local anesthetics.

## Local anesthetic pharmacology

Local anesthetics act by inhibiting voltage-gated sodium channels that allow sodium ion influx into the nerve. This results in membrane stabilization and inhibition of neuronal action potential [14]. Amide local anesthetics are the most common class of anesthetics used by urologists. Allergic reactions are class specific, meaning that a person may have a hypersensitivity to multiple anesthetics in the same class [14].

The addition of epinephrine (1:200 000) can provide vasoconstriction. This will decrease blood flow to the injected area, decrease intraoperative bleeding [15], and causes a slower reabsorption/extended effect. Epinephrine should not be injected into areas that are supplied by end-arteries (fingers/toes, glans penis, nose, etc.).

Amides are common local anesthetics used in urology and include lidocaine, bupivacaine, and mepivacaine (Table 143.1). Lidocaine is the most commonly used local anesthetic and it is well known to urologists. It can be given as a 0.5% or 1% solution at a maximum dose of 3–5 mg/kg. The onset of action is 2–5 minutes and it has duration of action of 30 minutes to 2 hours [16]. A 0.5% solution provides 5 mg/ml, so an 80 kg person can receive up to 80 ml of a 0.5% lidocaine solution or 40 ml of a 1.0% solution. Lidocaine, when used without vasocontricting agents, shortens its own duration by dilating local vasodilation; this is contrast to bupivacaine and mepivicaine [17]. Bupivacaine has more than twice the duration of action of lidocaine, up to 8 hours. A full dose of bupivacaine is 1–2 mg/kg, or 3 mg/kg in combination with

**Table 143.1** Common local anesthetics used in urology.

| | Concentration (%) | Dose (mg/kg) | Onset (min) | Duration (h) |
|---|---|---|---|---|
| Lidocaine | 0.5–1.0 | 3–5 | 2–5 | 0.5–1 |
| Mepivacaine | 0.5–1.0 | 4 | 3–5 | 1–1.5 |
| Bupivacaine | 0.25–0.5 | 1–2 | 2–10 | 2–4 |

*Source:* From Berde and Strichartz [14], with permission.

epinephrine. A 0.25% solution provides 2.5 mg/ml of bupivacaine, so an 80 kg person can receive up to 64 ml of a 0.25% solution or up to 32 ml of a 0.5% solution. There is a known toxicity of ventricular arrhythmias/cardiac arrest with overdosing [16]. Mepivacaine is dosed at up to 4 mg/kg with a quick onset of action of 3–5 minutes and a duration of action of 45 minutes to 1.5 hours. A 0.5% solution provides 5 mg/ml of mepivacaine, so an 80 kg person can receive up to 64 ml of a 0.5% solution or up to 32 ml of a 1.0% solution. Toxicities include central nervous system (CNS) side-effects/seizures and bradycardia/heart block [16].

In general, toxicities can occur if an overdose of anesthetic is given, or if the anesthetic is mistakenly injected into the vasculature. Proper infiltrative techniques, including a fundamental knowledge of the surrounding anatomy and aspiration prior to injection of the anesthetic, help to avoid these complications. CNS side-effects include a spectrum of symptoms from tinnitus and metallic taste in the mouth to seizure activity. Cardiovascular side-effects range from bradycardia, atrioventicular block, and ventricular arrhythmias to cardiac arrest [16]. Allergic reactions can occur at any dose if there is a hypersensitivity, and can cause anything from hives to overt anaphylactic shock. Amide anesthetics are metabolized by the liver and excreted by the kidneys, so the dosage should be decreased in patients with either liver or kidney failure [14]. For the purpose of local anesthetic for MIST of the prostate, the doses needed for a reasonable block seem to be well below anything close to the maximum dose, making toxicities very unusual. Lidocaine is clearly the most commonly used agent in the office setting.

## Oral supplementation

Many office-based MIST protocols for the prostate involve preoperative oral medications to mitigate pain, anxiety, and bladder symptoms. As such, oral pain medicines, sedatives, and antianxiety medications are often considered along with anticholinergics. These preoperative "cocktails" are developed by word of mouth, with urologists sharing experiences as they bring a MIST into the office.

The use of oral medications, while likely very beneficial to patients, has not been studied in a way that allows "best practices" to be established. It can be safely said that the preoperative medications used are generally very well understood by urologists, who use similar medicines in the day-to-day management of their patients (Table 143.2). Any study of local anesthesia for MIST of the prostate will be hampered by the added effects of these oral medications. If a local anesthetic technique is capable of working alone for a specific MIST, it must be proven as effective without oral supplemental agents. Nevertheless, preoperative oral medications that add to patient comfort and safety are clearly appropriate.

If prescribing oral sedation, urologists should be aware of any state medical board or society regulations for office-based surgical procedures. They should at least be certified in Basic Cardiac Life Support (BCLS) or Advanced Cardiac Life Support (ACLS) with course completion/recertification within 2 years.

## Topical urethral anesthesia

Prior to flexible cystoscopy being available, urologists routinely performed rigid diagnostic cystoscopy in the office with or without an anesthetic gel, such as 2% lidocaine. There is no question that a significant number of patients found the exam very uncomfortable and rarely would any patient suggest there was no discomfort at all. Urologists experienced with rigid cystoscopy understood that most of the discomfort tended to occur as the scope traversed the membranous and prostatic urethra, straightening the bulbous and proximal urethral anatomy. Patients reflexively resist cystoscopy by tightening the perineal musculature and membranous urethra. However, once in the bladder, patients would often relax with the words "the worst part is over." The diagnostic cystoscopy could then be completed in most instances.

Again, patient selection was still very important in enhancing the odds of a successful procedure.

**Table 143.2** Oral medications for minimally invasive prostate therapy.

| | Dose (mg) | Onset (min) | Duration (h) | Toxicities |
|---|---|---|---|---|
| **Benzodiazepines** | | | | |
| Diazepam | 5–10 | 45–90 | 2–24 | Respiratory, seizures, anaphylaxis |
| Lorazepam | 1–2 | 45–90 | 6–12 | Respiratory, seizures, anaphylaxis |
| Alprazolam | 0.25–0.5 | 60 | 6 | Respiratory, seizures, anaphylaxis |
| **NSAIDs** | | | | |
| Napoxen | 220 | 30–60 | 7–12 | Gastrointestinal, bleeding, renal |
| Ketorolac | 10 | 30–60 | 4–6 | Gastrointestinal, bleeding, renal |
| **Narcotics** | | | | |
| Hydrocodone/acetaminophen | 1–2 tabs (5/500) | 10–30 | 4–6 | Respiratory, constipation |
| Oxycodone/acetaminophen | 1–2 tabs (5/325) | 10.30 | 4–6 | Respiratory, constipation |
| **Anticholinergics** | | | | |
| Hyoscyamine | 0.125 | 2–3 | 4 | Gastrointestinal, urinary retention, dry mouth |

Intraurethral lidocaine was first described in 1949 by Haines and Grabstald in 250 patients undergoing cystoscopy. Lidocaine acts on suburothelial nerves to inhibit impulse transmission [18]. Although lidocaine gel has been used for decades for cystoscopy in males, the proof that it works well as a local anesthetic is lacking. Stein et al. showed no benefit of lidocaine gel compared to a water-based lubricant for rigid cystoscopy in males in a prospective randomized controlled double-blind study [19]. Dwell time for the lidocaine was 5–10 minutes. In an effort to see if dwell time was insufficient, Goldfischer et al. performed a similar study using 30 ml of 2% lidocaine gel with a dwell time of 20 minutes before cystoscopy, comparing this to water-soluble lubricant. They found a slightly significant difference in patient-perceived pain scores [20]. Both lidocaine gel and lubricant-only groups had discomfort and perhaps the difference was not clinically significant, as urologists could not differentiate who received lidocaine and who did not. Another study by Eggersmann et al. demonstrated in a randomized, double-blind placebo-controlled study that pain –relieving effects of lidocaine required an exposure time of greater than 10 minutes. Further studies showed no added utility in dwell time greater than 15 minutes [21]. This being said, there are numerous modern studies suggesting that 2% lidocaine works no better than water-soluble lubricant for flexible cystoscopy in the male [22–27]. This is likely secondary to the difficulty to efficiently block afferent pain signals of the entire urethra secondary to the complex innervation of the rhabdosphincter.

It is therefore of interest that virtually every publication of in-office MIST of the prostate discusses some form of topical lidocaine instillation transurethrally. It is likely that very little lidocaine is actually delivered to the prostatic urethra or is able to dwell there. Normal retrograde urethrograms seldom show much contrast in the prostatic urethra. Some urologists add cooled 2% lidocaine solution instilled through a catheter to their MIST protocols. Though intravesical lidocaine has been used as a local anesthetic for bladder procedures, it has not been suggested as a prostatic anesthetic [28, 29]. However, intravesical chilled lidocaine may mitigate discomfort during the bladder distention that is associated with cystoscopy.

Until studies are done comparing procedures performed with topical lidocaine to those performed without, the true value of topical lidocaine is open for discussion in MIST protocols. That said, all catheter-based technologies (i.e. transurethral microwave thermotherapy of the prostate (TUMT)) call for some form of lidocaine gel instillation before placing the catheter. Likewise, most technologies for MIST involving endoscopes call for lidocaine topical gel as an added local anesthetic. In general, 10–30 ml of 2% lidocaine gel is instilled for a 5–20 minutes dwell time prior to the particular procedure. Cooling the gel may aid in the comfort of delivery [30]. There should rarely be any complication from transurethral lidocaine gel and system levels of lidocaine are not seen [31]. If indeed lidocaine gel is nothing more than a placebo, it may be a valuable placebo. Both patients and urologists are comforted by the idea of delivering an anesthetic through a "painless gel" rather than a needle, which is what is required for any of the prostate blocks that are discussed below. The current evidence, however, suggests topical local anesthesia to the urethra and prostate for MIST procedures probably is marginal in its true value, and clearly more expensive than water-soluble lubricant.

## Prostate blocks

MIST options for the prostate that involve high-powered TUMT or rigid cystoscopy with either TUNA, interstitial laser energy, or laser evaporative/ablative techniques require more than simple topical lidocaine to the urethra. These endoscopic procedures must be performed with clear visualization of the prostatic urethra for optimal performance. Any sudden motion of the patient can jeopardize the procedure because of bleeding or patient discomfort. As such, all procedures were originally developed under general, regional (spinal) or intravenous sedation. Urologists experienced with prostate blocks for prostate biopsy and transurethral needle injection technique began to develop techniques to block the posterior urethra and prostate in such a way that these procedures could be performed in the office setting. They were motivated to develop their own in-office protocols in the hope of saving overall costs without diminishing physician reimbursement. Standard techniques developed after evidence-based studies have not been established. Local anesthesia involving prostate blocks for MIST are still evolving. There are no studies comparing different in-office local anesthetic techniques for MIST. There are, however, articles on local prostate block for prostate procedures and much has been written on local anesthesia for prostate biopsy.

With regard to prostate biopsy, preprocedure anxiety is associated with exaggerated pain perception throughout the procedure. Similarly, pain during probe insertion has a positive correlation with pain during biopsy. Unsurprisingly, younger patients are more susceptible pain due to low anorectal compliance, higher pretest anxiety, and higher sphincter tone. The apex of the prostate is most painful site of biopsy secondary to rich somatic nerve innervation to the mucosa below the dentate line [32]. Moffat injected 10 ml of 1% lidocaine with epinephrine into each lobe of the prostate of 18 patients via a digitally guided transperineal route using a 20G spinal needle [33]. Then, using nothing more than topical lidocaine per urethra, he was able to dilate the urethra to 30 Fr using sounds, and he then performed transurethral resection of the prostate (TURP) using a 28 Fr resectoscope sheath. All procedures were performed in the operating room with anesthesia monitoring. Supplemental sedation was required in 10 of 18 patients. Remarkably, 8 of the 18 patients had no intravenous sedation and no preoperative medications were given. Although this technique was seldom used, the fact remained that injection of lidocaine directly into the prostatic parenchyma must have anesthetic value if it allowed for a full TURP.

Orandi followed up on this in 1984, describing multiple endoscopic procedures, including TURP, performed using transurethral lidocaine injected into the prostate and bladder neck via a specially devised endoscopic needle [34]. Supplemental oral and parenteral medications were used in his cases. The publication was presented as a “cost reducing idea.” The technique similarly did not catch on. In 1993, Hugosson et al. published their results with transurethral incision of the prostate under local anesthesia [35]. Mepivacaine was injected transurethrally under direct vision into the bladder neck and posterior prostate to allow performance of a 6 o’clock incision of the prostate to treat men with lower urinary tract symptoms. The patients apparently received no supplemental preoperative or intraoperative medications. Twenty-eight of 30 patients claimed they would agree to the same procedure if another were needed. These examples suggest that local prostate block can allow for major endoscopic prostate procedures and that the block itself is responsible for pain control rather than oral or parenteral supplements.

Pain from prostate biopsy generally originates from the prostatic capsule. The prostatic plexus surrounds the capsule and has extensive autonomic innervation [32]. Prostate blocks did not become common place, however, until the development of transrectal ultrasound-guided biopsy and ultrasound-guided periprostatic and intraprostatic blocks. Prior to transrectal prostate ultrasound, digitally guided transrectal biopsy of the prostate was routinely performed with acceptable patient tolerance using no anesthetic. As template biopsies were developed in the prostate specific antigen (PSA) era, along with saturation biopsy, local anesthetic techniques developed and showed that transrectal ultrasound-guided lidocaine for periprostatic block at the prostatic base could mitigate the discomfort of the biopsy [36–38]. Subsequent studies suggested that ultrasound-guided transrectal lidocaine at the apex worked just as well or better [39–42]. Transrectal intraprostatic injection of the prostate has been suggested as better than a periprostatic block for pain control [43]. Finally, a periprostatic and intraprostatic combination block may work best of all for transrectal ultrasound-guided biopsies [44–46].

Armed with the knowledge that prostatic block could work in the operating room for transurethral resection procedures and that transrectal block worked well for prostate biopsies, urologists are adapting these technologies for office-based MIST of the prostate.

## Transrectal block for office-based minimally invasive treatment

Although most urologists are aware of and familiar with transrectal ultrasound-guided periprostatic and intraprostatic blocks for prostate biopsy, it should not be assumed that this will be optimal for transurethral MIST of the prostate. While it is traditionally thought to be well tolerated by most patients, some literature suggests between 65% and 90% of patients report discomfort during the procedure [47]. The largest criticism of transrectal periprostatic block is its inability to relieve pain from probe insertion. In addition, the incidence of febrile episodes after transrectal prostate biopsy may be increasing. Nam et al. found hospital admission rates after transrectal ultrasound-guided biopsy of the prostate increased fourfold from 1996 to 2005; 72% of these were admissions for infection [48]. Efforts should be made to ensure the rectal vault is empty of stool prior to biopsy. Urologists should administer prophylactic antibiotics, such as those recommended by the American Urological Association better practice guidelines for antimicrobial prophylaxis.

The standard technique calls for ultrasound-guided injection of at least 5 ml of 1% lidocaine into the fat plane seen laterally at the base of the prostate, between the seminal vesical and rectum. On sagittal view, this appears as a “triangle,” referred to by Jones as the “Mount Everest sign” [36]. Each side must be injected. Alternatively, or at the same time, 5 ml of 1% lidocaine can be injected into the periapical fat, deep and lateral to the apex, between the prostate and rectum. On sagittal view, infiltration of anesthetic can be seen to separate a tissue plane that courses towards the base [39, 42]. The article by Berland and Jones in e-medicine fully describes transrectal periprostatic blocks and is a useful website (http://emedicine.medscape.com/article/459599-overview). When local anesthetic injections are administered too laterally (i.e. lateral to the tip of the seminal vesicles), pain relief is ineffective secondary to distance from neurovascular bundle. Using the same ultrasound-guided technique, intraprostatic anesthesia can be delivered by injecting 10 ml of lidocaine in increments in 2–3 sites within each lobe of the prostate from apex to base [43]. In addition, the use of combined intrarectal local anesthesia with periprostatic nerve block helps to improve pain control during prostatic biopsy and should generally be performed in conjunction with periprostatic anesthesia delivery [44].

Although none of the transrectal local lidocaine blocks were developed for procedures other than biopsy, urologists have adapted them for MIST. Kedia used a digitally guided transrectal lidocaine block to perform interstitial laser coagulation of the prostate [49]. Other than transurethral lidocaine (a liquid and gel), patients received no oral or parenteral medications other than antibiotics. Turk has performed Evolve™ diode laser transurethral resection procedures in the office without any intravenous sedation, assisted in part by transrectal ultrasound-guided periprostatic block [50]. However, it should be noted that he now favors a transurethral prostatic block. Meyer has performed many Prostiva™ radiofrequency procedure TUNA in the office using a transrectal periprostatic block with lidocaine from apex to base on each side, although oral analgesics and sedatives were also used. He claims not to have terminated or abbreviated any procedures in over 300 cases (personal communication).

With more contemporary TUNA treatments that use radiofrequency-produced convective steam (i.e. Rezum), it is important to not violate the prostate capsule with a needle. During TUNA with Rezum, this steam penetrates the interstices and is confined in the prostatic capsule; a perforation of the capsule with a transurethral prostate injection or posterior prostate capsule may theoretically affect heat confinement. Transrectal block should be done with ultrasound guidance and near the tips of the seminal vesicles [51]. TUMT procedures were also done with a transrectal block; transrectal ultrasound (which is needed to position the treatment catheter) is used to guide the lidocaine for a prostate block prior to the placement of the treatment catheter. Alcohol ablation or transurethral ethanol ablation of the prostate (TEAP) has been described in the literature utilizing a periprostatic block with oral or intravenous sedation. Similarly, the Rezum radiofrequency system for BPH has been described as having the advantage of being capable of being performed as an outpatient under local anesthesia [52]. Many TUMT procedures can be performed without a formal prostatic block. Members of our groups are performing laser procedures (Evolve and GreenLight) using transrectal ultrasound-guided periprostatic and intraprostatic blocks with lidocaine. Good functional outcomes were presented at our State Urological Society Meeting [53].

## Transperineal block

Transperineal block, although likely least utilized today to provide local anesthesia to the prostate, has the potential for resurgence if in-office MIST procedures continue to develop. Over the last decade or so, there has been an increased incidence of infection and quinolone-resistant flora with a concomitant increase in sepsis rate as high as 5%, thereby renewing the debate of optimal anesthetic delivery, especially in the context of prostate biopsy [54]. Unlike the transrectal technique, the risk of infection should be lessened by allowing for a proper skin preparation and directing the needle to avoid contamination from the rectal mucosa.

A modern technique has been nicely described by Issa et al. [3] and Cohen and Steiner [55]. The patient is placed in the dorsolithotomy position with the perineum prepped and draped. A 27G needle may be used to anesthetize the entry site in the perineum above the perineal body. A 22G spinal needle (3.5 inches long) is attached to a 20 ml Luer Lock syringe containing the anesthetic (i.e. 1% lidocaine). The needle is directed into the midline, deep to the apex of the prostate under transrectal digital guidance. The anesthetic solution is infiltrated, defining a plane between rectum and prostate that may be palpated as the rectum is elevated from the prostate. At least 10 ml of the anesthetic solution is injected deep to the prostate on the right and then the left, from apex to base. This should deliver anesthetic levels similar to transrectal anesthetic technique. The needle need not be removed from its insertion site as injections occur, as aspirating periodically ensures that the injection is not into venous spaces. Interstitial laser coagulation (ILC) therapy has been successfully performed without the need for intravenous sedation using the transperineal periprostatic block [3].

A simple technique for transperineal digitally guided block of the urethrosphincteric region has been recently described by Al-Hunayan et al. [56]. They injected 5–10 ml of lidocaine into the region just caudad to the apex of the prostate, above the rectum on each side of the midline. Their technique showed improved comfort with rigid cystoscopy over lidocaine per urethra (Figure 143.2). Likewise, TUNA of the prostate has been similarly performed [57].

As mentioned earlier, TURP has been performed using a transperineal intraprostatic block without the need for intravenous sedation [33]. The transperineal route could also be very easily used to perform intraprostatic injection of anesthesia for MIST. Using an anesthetic agent that contains epinephrine could potentially mitigate bleeding for transurethral procedures. Bolat et al. examined periprostatic block against transperineal prostatic block in a prospective randomized trial and found lower visual analog scores (VAS) in those patients receiving 10 ml 2% prilocaine in a transperineal block compared with intrarectal lidocaine gel followed by 10 ml 2% prilocaine periprostatic block [58]. Though not studied specifically for MIST, this route also would have an added advantage over the transurethral intraprostatic injections in that the prostatic lumen could be avoided by targeting the needle laterally, thus minimizing potential bleeding from the needle entrance site in the prostatic urethral lumen. Clearly, if the procedure is planned in the office, the MIST modality itself should already be proven to minimize the risk of bleeding.

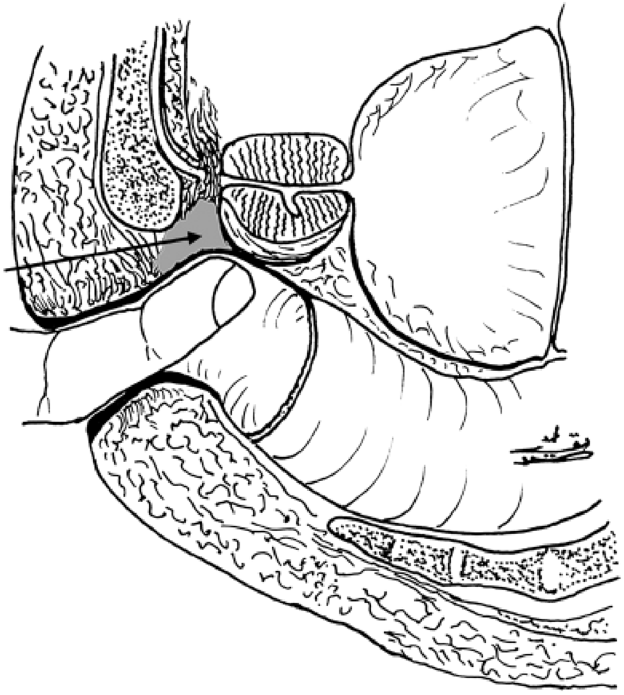

**Figure 143.2** Digital guidance for transperineal prostatic block. This depicts the infiltration of lidocaine (gray area indicated by arrow) in a location bounded by the rectum posteriorly, the rhabdosphincter anteromedially, and the apex of the prostate superiorly. *Source:* Al-Hunayan A, Kehinde EO, Shihab-Eldeen A et al. An assessment of the clinical utility of transperineal urethrosphincteric block (TUSB) in outpatient rigid cystoscopy: a single-blind, randomized study. *Int Urol Nephrol* 2009;41:47–53. Reproduced with permission Springer Science Business Media.

## Transurethral prostate blocks

Since originally described by Orandi, transurethral prostate blocks have been reinvented by urologists in order to perform local MIST of the prostate in the office setting. The technique can easily be performed by any urologist using a flexible injection catheter passed via the cystoscope. The patient is prepared for rigid cystoscopy in the lithotomy position. Oral agents, both analgesics and sedatives, can be helpful. The cystoscope is passed and the prostatic lumen and bladder are examined. An injection catheter (Bard Contigen, Cook Urologic, Storz reusable, etc.) can then be used to inject 3–5 ml of an anesthetic solution (e.g. lidocaine) into the bladder neck at the 5 and 7 o'clock positions. The cystoscope is then moved distally to view the prostatic lobes, which are then anesthetized by injecting at the 3 and 9 o'clock positions with additional lidocaine. Injections can be repeated in different areas if needed for longer or larger glands. Patient selection is important. The transurethral block also avoids the rectum and its potential for infection. Using this technique, urologists have performed ILC, TUNA, and laser prostatectomies, including GreenLight and diode laser prostatectomies. TUMT time can be diminished by transurethral mepivacaine with epinephrine, with improved comfort [15]. These procedures have been performed in the office without the need for an intravenous line or special monitoring, other than close observation and periodic measurement of vital signs.

Published studies regarding outcomes are lacking. Though members of our group have used this technique, they have found bleeding occasionally problematic for laser ablation procedures and now prefer the transrectal technique previously mentioned.

## Pudendal nerve block

Pudendal nerve block is mentioned as it may have endourologic application for the lower urinary tract, and it is an anesthetic that can be delivered by the urologist. Mahmood Hai (Dearborn, MI, USA) probably has the world's greatest urological experience with pudendal nerve block in men, a technique he developed from his knowledge of pudendal blocks in women. In his surgery center he has performed outpatient photoselective vaporization of the prostate on over 1000 patients. His technique involves a transperineal approach. Two 20G 12 cm disposable spinal needles are attached to 20 ml syringes loaded with a 0.5% lidocaine solution. For right-handed urologists, the left index finger is inserted rectally to identify the landmarks; the ischial tuberosity, ischial spine, and sacral spinous ligaments. The needle is inserted perpendicular to the skin about 2.5 cm posteromedial to the ischial tuberosity. The needle is slowly advanced through the ischial rectal fossa towards the ischial spine, guided by the rectal finger. As the needle hits the spine, it is pushed posterior to it by the guiding finger. This places the bevel of the needle at the beginning of Alcock's canal. After attempted aspiration in two planes to make sure the needle is not in a blood vessel, 5 ml of the solution is injected. In most instances, the wheel produced can be palpated by the rectal finger. The needle is advanced about 0.5 cm and the remaining 5 ml are injected. The needle is withdrawn and firm pressure is applied over the area by the rectal finger for 1–2 minutes. A similar procedure is done on the opposite side. The anesthetic should be effective within 5 minutes and photoselective vaporization of the prostate can be started.

This form of anesthesia is not one that should be considered in the office setting without an intravenous line and proper monitoring. There is a potential for bleeding and nerve damage, as can rarely occur with any regional nerve block. Dr. Hai does have an intravenous line for sedation, monitored by an anesthesiologist. Nevertheless, it is worthwhile being aware of this technique as it represents a locoregional anesthetic which urologists can and are being trained to perform. Specifically, when discussing prostate biopsy, when combined with periprostatic nerve block, it has demonstrated statistically better pain control throughout probe insertion, biopsy punctures, and up to 1 hour after biopsy [59]. In one prospective study, unilateral pudendal block is as efficacious as intrarectal lidocaine with periprostatic blockade in pain reduction for both probe insertion and biopsy punctures [60]. More study will be needed before we know the true risk-to-benefit ratio compared to other anesthetic techniques.

## Conclusions

This may be a new era in urologic practice; treating more patients in the office with MIST of the prostate. As technologies evolve, so will the consensus of "best practice" regarding office-based local anesthesia. Studies that compare one anesthetic technique to another are sorely lacking. The potential for tremendous cost savings still exists if hospital and anesthesiology charges can be avoided by office-based therapy. Office-based therapies, however, must be proven to be just as effective with comparable long-term result. Urologists interested in pursuing office-based procedures under local anesthesia should realize that the information presented in this chapter will hopefully be dated in 5 years, as more outcome and comparative studies are done so that evidence-based recommendations can be made on the "best practice" of office-based anesthesia for the MIST of the prostate. It is likely that combining the techniques described in this chapter will result in improved local anesthesia for MIST of the prostate. Finally, without question, new technologies and techniques will continue to arise to treat lower urinary tract symptoms due to BPH. Office-based therapy has a great potential to provide for major cost savings as long as the urologist finds it economically viable to pursue such care in the office. Regardless, all urologists should be aware of the importance of minimizing anesthetic risks and cost for MIST of the prostate. Local anesthetic techniques may diminish anesthesia needs, time of recovery, and costs.

These cost savings may also be realized in the hospital or ambulatory surgery center setting. Such techniques might be applicable to more invasive hospital-based procedures, such as TURP in high-risk individuals or the very elderly, where close anesthetic monitoring is always required. The anesthetic risks may possibly be diminished by the use of local anesthetics. Similarly, though MIST of the prostate may be easy to perform in the office, caution and proper monitoring are always needed in high-risk or very elderly patients. Judgment is always required in selecting candidates for office-based MIST of the prostate using local anesthesia.

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# 144

# Laser in Benign Prostatic Hyperplasia Treatment: Basic Principles

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## Introduction to lasers

In his publication on quantum theory in 1917, Albert Einstein postulated the existence of extremely focused light beams [1], but it was another 43 years before the first commercially available laser became available, as published by Maiman [2]. The acronym LASER was created by Gould in 1957; it stands for laser amplification by stimulated emission of radiation [3]. In simple terms, a laser is a parallel light of a specific wavelength and direction [4]. Immediately after its first description, manifold lasers were developed and were widely used in many fields of medicine. Most of them did not stand the test of time, however, and the unsuccessful clinical application of laser devices led to a general decline in their use during the 1980s.

Ten years later, an improved understanding of laser principles provided better knowledge that led to the selection of appropriate lasers for specific medical applications [3–7]. With the development of lasers with many different wavelengths and qualities, various laser systems that could be used to treat urological conditions were developed. This chapter reflects the cumulative understanding of several different urological surgeons on the most widely used laser systems at this time.

An important facet of the clinical application of lasers is the optimization of the absorption process of light energy in tissue, with the knowledge that laser radiation is a directed light of a narrow bandwidth with specific effects. Each laser is synonymous with a single color or electromagnetic wavelength, and each laser can be derived from many wavelengths of the invisible and visible electromagnetic spectrum [8].

## Generation of a laser beam

Laser light is created by a quantum mechanical principle of "stimulated emission" of radiation in an excited state (active media: gas, crystal, glass, dye). Excitation of the laser medium can be achieved in various ways (e.g., excitation by photons from a flashlamp). Some of the excitation photons are absorbed by the active medium, leading to an excited state [4]. According to the theory of spontaneous emission, these excited states return to the ground state, statistically releasing a photon at a characteristic wavelength. If these spontaneously emitted photons hit another excited state of the same excitation energy, it stimulates the excited ion to return to the ground state by emitting a further photon with the same wavelength and the same direction of propagation and the same phase. This is called stimulated emission of radiation (Figure 144.1) [4–7]. The emitted wavelength is characteristic for the optically active components of the laser medium [4].

To achieve controlled excitation of the laser medium, it is embedded into an optical resonator, a set of mirrors within the optical axis of the laser medium that redirect emerging photons into the laser medium for further amplification. One of the resonator mirrors has a reflectivity at the laser wavelength of nearly 100% (high reflector) and the other one is partially transparent to allow laser radiation to exit from the resonator (output coupler). Laser radiation is emitted from the resonator in a continuous wave or pulsed manner depending on the construction of the laser device (e.g. excitation source, characteristics of the laser medium) or the presence of additional optical elements, such as a Q-switch [4].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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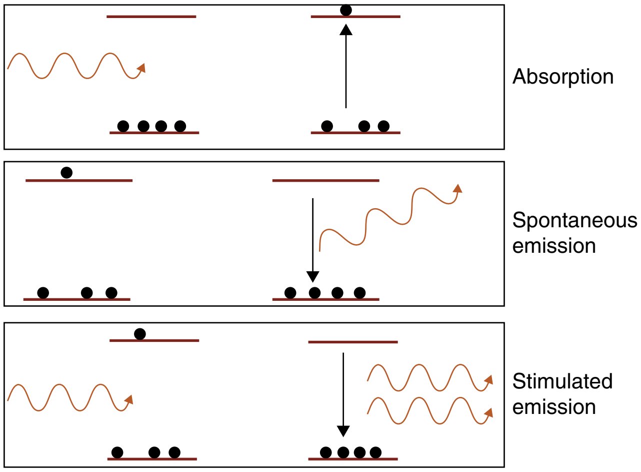

**Figure 144.1** Spontaneous and stimulated emissions of radiation. *Source:* Bach T, Muschter R, Sroka R et al. Laser treatment of benign prostatic obstruction: basics and physical differences. *Eur Urol* 2012;61:317–325. Reproduced with permission of Elsevier.

Q (or Quality)-switching is a technique to generate short, high-peak, powerful laser pulses by modulating the cavity Q-factor (cavity loss) of the laser resonator. This comprises an optoelectronic shutter that is embedded within the laser resonator, which is periodically opened and closed. When it is closed (low cavity Q-factor), stimulation of emission is suppressed, but the population inversion reaches a large value due to the ongoing excitation process. When the shutter opens (high cavity Q-factor), spontaneously emitted photons start oscillating within the resonator, leading to an avalanche of stimulated emission. The larger the population inversion, the higher the Q-switch pulse peak power. The Q-switch pulse terminates with depletion of the population inversion [4].

Second harmonic generation (SHG) is a second-order nonlinear process used to convert a given laser (used in the potassium titanyl phosphate (KTP) laser) to half of its fundamental wavelength (second harmonic). It comprises a nonlinear crystal that needs to be carefully matched with the fundamental laser wavelength. Sufficient power density of the fundamental laser and exact alignment of the nonlinear crystal with the direction of propagation is required to generate second harmonic photons, which are double in frequency and/or half in wavelength [4].

In diode lasers, a semiconductor laser diode is used to generate laser radiation. The semiconductor material defines the wavelength. Electrical current flow is used to stimulate the semiconductor, which emits laser radiation after exceeding the threshold. Diode laser systems achieve a high electrical-to-optical energy conversion efficiency [4].

In contrast to diode lasers, other commonly used laser systems (holmium, thulium, GreenLight) utilize a crystal as the laser medium. In these laser systems the active laser ion is doped into the yttrium–aluminum–garnet (YAG) crystal that serves as a carrier for rare earth material defining laser characteristics. The widespread use of the YAG crystal is rooted in its physical properties. Crystals with garnet structure offer three crystallographic sites of different size and geometry, $\{C_3\}(A_2)[Al_3]O_{12}$, that are suitable for doping with optically active transition metal and rare earth metal ions. YAG is isotropic and has a broad range of spectral transparency. The YAG crystal also offers excellent mechanical and thermal properties. It is easy to grow following the Czochralski technique, which involves growing single crystals from their melt. During the growth process, the molten material is kept in a heated crucible. A seed crystal is lowered from above until it reaches the melt surface. The crystal boule is grown by pulling the seed crystal slowly upwards under continuous rotation [4–7].

For these reasons the YAG crystal is the material of choice for a variety of solid-state laser materials. By replacing a percentage of the yttrium ($Y^{3+}$) ions at the crystallographic C-position (doping) with three valent rare earth ions such as neodymium ($Nd^{3+}$), holmium ($Ho^{3+}$), thulium ($Tm^{3+}$), or erbium ($Er^{3+}$), optically active solid-state laser materials may be created. Under excitation, these crystals have the ability to amplify their own fluorescence light by stimulated emission of radiation [4–7].

## Delivery of laser radiation

### Laser fiber design

Optical fibers deliver laser radiation to the target safely and efficiently, although several issues have to be resolved. Laser radiation has to be coupled from the generator to the fiber and transported within the fiber to the desired point of application [4].

A laser fiber includes a circular fiber core and two or more levels of fiber cladding clasped around this core. Laser radiation is delivered through the circular fiber core, whereas the adjacent layer provides entrapment of laser radiation within the core and the remaining layers conserve fiber integrity [1, 6]. The optical core is made from silica. Standard silica material is used effectively for visible light, but the transmission of 2 μm radiation by flexible silica laser fibers, as in holmium and thulium lasers, requires purified low hydroxide (OH) silica to eliminate power loss during the delivery due to energy absorption in the $OH^-$ ion [6].

To suppress leakage of laser radiation, the core is surrounded by an optical cladding made from a transparent material of a lower refraction index. Fluorine-doped silica cladding is considered the primary choice for high-quality fiber applications. Less flexible fluoroacrylate cladding (TECS) is used for fibers to transmit shorter wavelength and low-power applications [5].

To launch laser radiation into an optical fiber, a focusing lens with a receptacle for the fiber connector is necessary. Connecting the fiber to the laser generator is critical for energy transmission [5]. A slight deviation of the focal point of the fiber coupler lens leads to laser radiation absorption by the connector, which guides the laser fiber to the coupler lens. Thus it will result in heating of the connector. At sufficiently elevated power levels, the focused laser beam will melt and vaporize, resulting in destruction of energy transmission [4].

### Types of fiber endings

Independently of the fiber type, the laser beam is delivered through the optical core of the fiber [4–7].

#### Side-firing fibers

In side-firing fibers, the reflection of the laser beam is achieved by an oblique surface at the fiber tip where the radiation is reflected sideways either by total reflection of the beam on a core–air interface or an additional reflective coating. This deflects the laser beam toward the tissue at an oblique angle of about 70°, which is provided by the physics of total reflection at an internal glass–air surface. By sweeping the beam and changing the distance between fiber tip and tissue surface, coagulation as well as vaporization can be achieved. The pitfalls of side-firing fibers are the limited lifespan due to exposure to heat that is generated by carbonization at the laser beam output [6], leading to fiber damage and consequently to loss of efficacy [5, 9]. However, continuous flushing of the beam exit with cooler irrigation fluid alleviated this effect as designed in the MoXy™ fiber. By increasing the optical core diameter and the introduction of liquid cooling as well as a metal capping of the fiber tip, the lifespan of the side-firing fiber seems to be increased [10]. Although it is generally plausible to manufacture a MoXy-type side-firing fiber for all laser systems, this design is currently applied only with the GreenLight XPS™ system [4].

#### End- or front-firing fibers

Laser radiation discharges from the tip into the tissue by rapid heating of the tissue in a very small tissue volume. Tissue effects such as vaporization and disruption can be achieved.

#### Twister fibers

Another approach called twister fiber is used for contact laser vaporization, as introduced by Biolitec for its laser system. The Biolitec laser uses a wavelength at which water is included as a chromophore. As a result, in front of the fiber tip a steam bubble is created, within which vaporization is achieved; vaporization is also created by the secondary heated button-shaped fiber tip [4]. A near-contact technique is required.

## Pulsed and continuous wave lasers

Laser radiation is emitted from the resonator in a continuous wave (cw) or pulsed mode depending on:

- the laser device (excitation source, characteristics of the laser medium) and
- the presence of additional optical elements, such as a Q-switch.

Holmium lasers are normally excited by flashlamps, which restricts the repetition rate due to heat accumulation in the laser crystal. In contrast, Tm:YAG lasers may operate in a cw-mode if excited by a laser diode. Pulsed holmium lasers create large pulsating steam bubbles in the irrigant surrounding the tip of the laser fiber, whereas the bubbles are much smaller for cw-mode lasers (Figure 144.2a,b). For the holmium laser, the lifetime of the steam bubble corresponds to the duration of the laser pulse (~500 μs) which is too short to be visible in video transmission during endoscopic procedures [8].

The expanding steam bubble is used in holmium laser enucleation of the prostate (HoLEP) for the separation of the adenoma from the peripheral zone. Coagulation is achieved by the heat within the steam bubble. In contrast, thulium lasers constantly support a steam bubble between the fiber tip and tissue. This bubble provides the optical contact for the laser radiation into the tissue. The constant steam bubble follows the fiber movement and the cw-mode thulium lasers allow smoother incisions in soft tissue, which is considered to be advantageous in urologic surgery. Accuracy, power efficiency, and minimal collateral damage are reported with the cw mode rather than the pulsed mode of the holmium lasers [8].

However, the cw mode is disadvantageous for the thulium laser's applicability for lithotripsy, since the required pulse peak mode for lithotripsy is not available in the cw mode of this laser [8, 11].

## Light–tissue interactions

The principal light–tissue interactions comprise reflection, scattering, re-emission, and absorption by tissue chromophores. Light distribution and absorption affect the optical penetration in a wavelength-dependent manner.

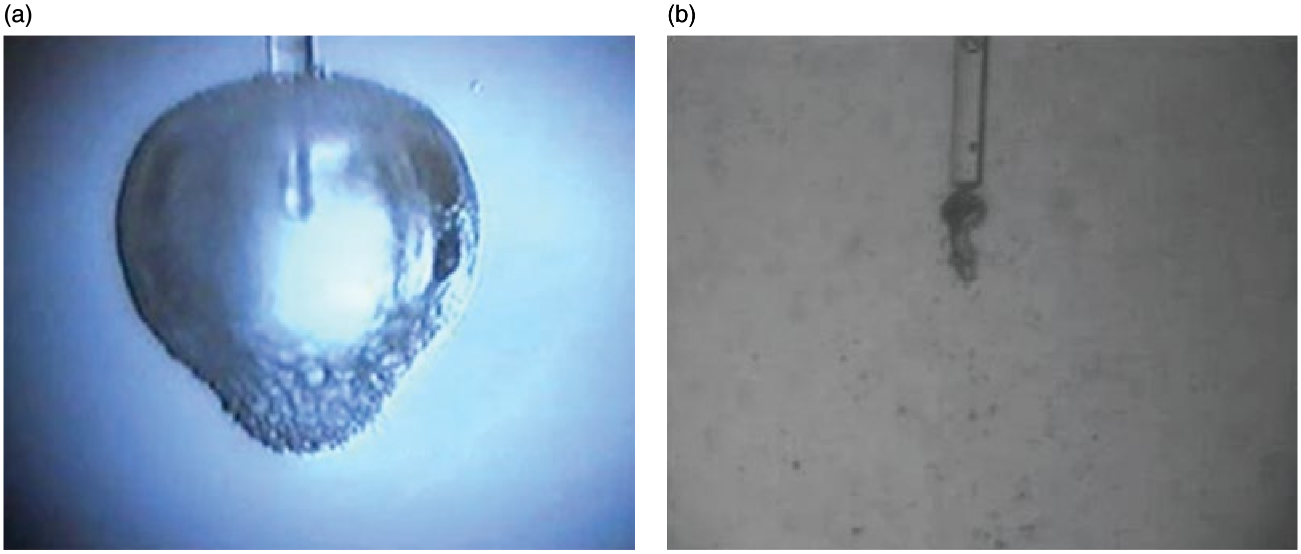

**Figure 144.2** (a) A large steam bubble forms at the end of a 550 μm laser fiber when using a Ho:YAG laser. (b) A small, relatively constant steam bubble forms at the end of a 550 μm laser fiber when using a Tm:YAG laser.

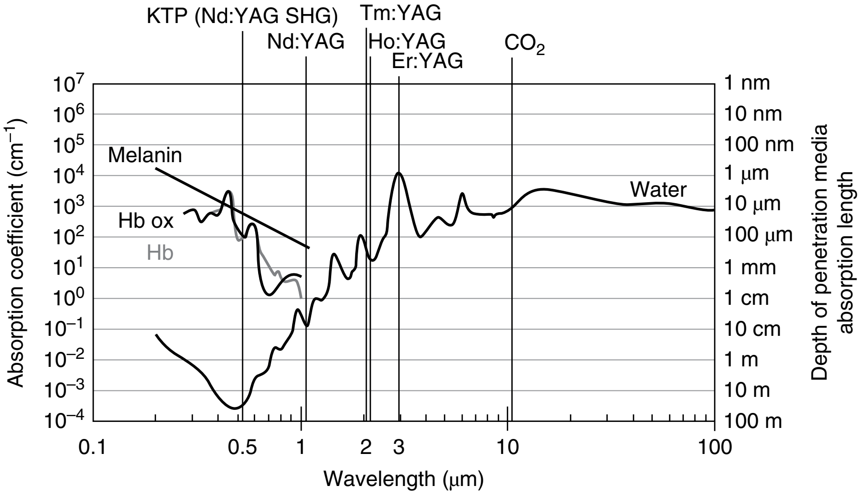

**Figure 144.3** Absorption spectra of prevailing body chromophores and wavelengths of different lasers. *Source:* Teichmann HO, Herrmann TR, Bach T. Technical aspects of lasers in urology. *World J Urol* 2007;25:221–225. Reproduced with permission of Elsevier.

For surgical applications, the most important process in the interaction of light and tissue is absorption [6]. When the laser beam hits tissue, a certain percentage is reflected by the boundary layer. This reflected radiation not only is lost for its surgical purpose but also becomes, in the form of heat, a potential risk to surrounding tissue. Reflection depends on the optical properties of the tissue and the irrigant surrounding it, but is not very dependent on wavelength and therefore may be neglected when evaluating a laser wavelength for surgical purposes. Since tissue is not homogeneous, part of the incident laser beam is scattered, taking the applied laser beam out of its intended direction. The degree of scattering depends on the size of the particles that the laser beam encounters and on the wavelength of the laser. Shorter wavelengths are scattered to a much higher degree than longer wavelengths. Blue laser radiation is scattered more than green, green more than red, and red more than infrared. This scattered fraction of laser energy is not only lost for the intended purpose but may also cause unintended side-effects [6, 8].

In order to achieve absorption, a chromophore is required. Useful body chromophores for surgical procedures are melanin, blood, and water, although melanin has no use in urologic applications [4–7, 12]. The wavelength dependencies of their absorption lengths are shown in Figure 144.3. The absorption length defines the optical pathway along which 63% of the incident laser energy is absorbed. Another concept, the extinction length, defines the depth at which 90% of the incident laser beam will have been absorbed and converted into heat [6].

A knowledge of the absorption process makes it easier to understand the laser–tissue interaction, both intended and unintended. When entering into an absorbing medium, the intensity of any laser beam decreases exponentially (Lambert–Beer's law). Absorbed laser energy is converted into heat and causes an increase in temperature. Depending on the density of absorbed heat, the impact on the tissue may vary between coagulation and vaporization. The temperature in tissue increases with the density of heat per volume of tissue. This offers the opportunity for various surgical procedures, such as vaporization, vaporesection (in continuous lasers), or vapoenucleation when used for the treatment of benign prostatic hyperplasia (BPH) [4, 6].

The tissue effect is determined by the power density of the absorbed laser power. The more complete the absorption by a tissue, the lower the absorbed laser power available to generate heat in the deeper layers. An understanding of this principle is important for any surgical laser application. At the same power level, a wavelength with a long absorption length may create a deep necrosis due to more laser power being available to be absorbed at the deeper levels, whereas with a laser wavelength with a much shorter absorption length, the absorbed laser power will be confined to a smaller volume. Effective delivery of high power to a small volume can lead to an effective increase of temperature above boiling point and to immediate confined vaporization of tissue [4, 6, 8].

## Lasers used for treatment of BPH

### Holmium lasers

Holmium lasers have been available for clinical use since the 1980s and multiple surgical transurethral laser prostatectomy techniques have been introduced.

#### Active (laser) medium

The YAG crystal is the material of choice for a variety of solid-state laser materials. As described earlier, a percentage of the $Y^{3+}$ ions at the crystallographic C-position (doping) are replaced with three valent rare earth ions, such as $Nd^{3+}$, $Ho^{3+}$, $Tm^{3+}$, or $Er^{3+}$, creating optically active solid-state laser materials. Under excitation, these crystals have the ability to amplify their own fluorescence light by stimulated emission of radiation [4, 13].

#### Excitation source

A flashlamp is the source of photons required for excitation of the laser medium emitting holmium laser radiation.

#### Wavelength

The holmium laser wavelength (2123 nm, nonvisible/infrared) is absorbed by water. The depth of penetration is 0.4 mm [4, 6].

#### Mode of operation

Energy is released in a pulsed mode [4].

#### Tissue chromophore and clinical translation of laser–prostate interaction

Holmium laser radiation is primarily absorbed by water as the main active chromophore. Energy absorption by the irrigant forms a steam bubble around the laser fiber tip and this result in a microexplosion, causing a jackhammer effect that can cut tissues. Due to the wavelength and the short high-peak power laser pulses, high-energy concentration can be achieved with each pulse, resulting in vigorous expanding and collapsing steam bubbles within the duration of the laser pulse [8].

These steam bubbles are used for surgical effects, such as coagulation and ablation. Coagulation occurs if the tissue is heated to temperatures greater than 70°C but less than 100°C and, either through decreasing the energy pulse or by pulling the fiber tip away from the tissue (defocused beam), the tissue temperature is lowered and ablation does not occur. Because the heat is absorbed into the tissue coagulation occurs. For ablation or cutting, the energy is absorbed by water in the prostate cells and the tissue is heated to more than 100°C.

Based on its physical properties, the holmium laser deemed versatile for different techniques of transurethral BPH treatment, such as holmium laser transurethral incision of the prostate (HoL-TUIP), holmium laser ablation of the prostate (HoLAP), holmium laser resection of the prostate (HoLRP), and holmium laser enucleation of the prostate (HoLEP) [4].

#### Laser fibers and evolution of holmium laser generators

More than one holmium laser generator has been developed for the treatment of BPH. Different levels of power range from 50 to 120 W. In the early days the tendency was to use high power for prostate ablation, starting from 60 to 80 and finally 100 W. Recently, the newly launched 120 W with its renovated XPEEDA fiber was introduced for prostate ablation. Higher power holmium lasers have also been used (80–100 W) for prostate enucleation, but Rassweiler et al., reported in 2008 on the feasibility of using low power for safe and effective HoLEP. They used a 40 W holmium laser machine to accomplish the enucleation procedure with reasonable efficacy [14]. Nevertheless, there are no randomized trials available to date assessing safety, efficacy, and cost saving associated with low-power HoLEP versus high-power HoLEP.

Laser generators are available from different manufacturers and the following fibers are available as laser delivery systems:

- End-firing fibers (single-use/reusable): larger fiber diameters have been used for prostate treatment (550–1000 µm).
- Side-firing fibers (single-use): DuoTome™ SideLite is a single-use, 550 µm fiber designed for a fluid environment that directs laser beam at 70°, useful for HoLAP. The maximum power output is 100 W and 4 J. Xpeeda™ D/S/L fiber is a single-use side-firing fiber that can deliver more energy to the tissue while in direct contact with it as proposed by the manufacturer for use with 120 W laser system [15].

## Thulium lasers

There are two different kinds of thulium lasers available: Tm:YAG (wavelength 2013 nm) lasers and Tm-fiber lasers (wavelength 1940 nm), which matches the water absorption peak in tissue at $\lambda = 1.94\,\mu m$ [16] (Figure 144.4).

### Active (laser) medium

The Tm:YAG is the optically active solid-state laser material. In contrast to the Tm:YAG laser, the active gain medium of the Tm-fiber laser is an optical fiber doped with thulium ions. A fiber laser utilizes the fiber itself as the amplification medium, and is pumped by a diode laser [7].

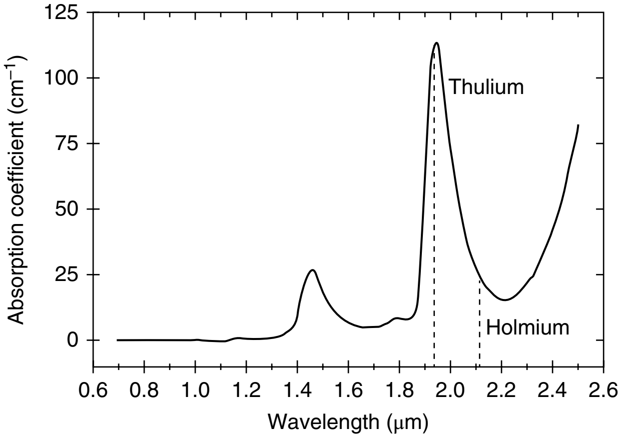

**Figure 144.4** Mid-infrared water absorption curve near 1.94 µm peak. Absorption coefficient for water is 114 $cm^{-1}$ at thulium wavelength of 1.94 µm and 36 $cm^{-1}$ at holmium wavelength of 2.12 µm. *Source:* Fried NM and Murray KE. High-power thulium fiber laser ablation of urinary tissues at 1.94 microm. *J Endourol* 2005;19:25–31. Reproduced with permission of Mary Anne Liebert, Inc.

### Excitation source

In contrast to the flashlamp excitation of the holmium laser, thulium ions are directly excited by high-power laser diodes. The narrow band excitation by laser diodes avoids excessive heat generation inside the crystal (or the fiber) as in the case of broadband excitation of the chromium ion by flashlamps in the holmium:YAG laser. This technical improvement increases the power efficiency of the laser by a factor of about 5 and eliminates the need for special electrical installation [4, 6, 16].

### Wavelength

The thulium laser wavelength (1940 nm (Tm-fiber laser), 2013 nm (Tm:YAG laser), nonvisible/infrared) is absorbed by water as the chromophore. The depth of penetration is 0.2 mm (Figure 144.2) [6, 12].

### Mode of operation

The Tm:YAG/thulium fiber laser is diode pumped, which allows it to be operated in either cw mode for applications requiring maximum hemostasis and coagulation, or in pulsed mode for applications requiring precision cutting [4, 16].

### Tissue chromophore and clinical translation of laser–prostate interaction

Thulium lasers operate at a wavelength close to the peak absorption of water, therefore using water as the chromophore. Although the absorption characteristics in tissue are similar to those of the holmium laser, the properties of the cw output in soft tissue surgery is superior. Because of the slightly shorter wavelength, the depth of penetration is decreased to 0.25 mm. Instead of the tearing action on tissue which is caused by the pulsed operation of the holmium laser, the cw output allows smooth incision and vaporization of tissue with excellent hemostasis due to a relatively constant steam bubble between the fiber tip and tissue, compared with the expanding steam bubble of the holmium laser (Figure 144.2a,b) [4].

A major technical advantage arises out of the temperature stability of the water molecule, which is the target body chromophore for the 2 µm wavelength. Water retains its absorption properties when heated by the laser beam up to its boiling point, which is the onset of tissue vaporization. The tissue left behind after each laser pass is covered by a coagulated seam of tissue which provides hemostasis. It still contains sufficient water for efficient absorption of the following laser pass. Thus the laser tissue effect remains unchanged and effective throughout the entire surgical procedure [6].

Because of the high proportion of vaporization during thulium laser treatment of the prostate, four different techniques have been defined: Tm:YAG vaporization of the prostate (ThuVaP), Tm:YAG vaporesection of the prostate (ThuVaRP) Tm:YAG vapoenucleation of the prostate (ThuVEP), and Tm:YAG laser enucleation of the prostate, a transurethral blunt enucleation of the prostate with Tm:YAG laser-assist [17].

#### Laser fibers and evolution of thulium laser generators

Thulium laser generators have been produced with wavelengths of 1940 nm (Tm-fiber laser), 2010 nm (Tm:YAG laser), and 2013 nm (Tm:YAG laser) and different levels of power, ranging between 50 and 200 W. High-powered thulium lasers (120–200 W) have mainly been used for ThuVAP or ThuVaRP, while 70–90 W thulium lasers are sufficient for ThuVEP or ThuLEP. Laser generators are available by different manufacturers and the following fibers are available as laser delivery systems:

- End-firing fibers (single-use/reusable): larger fiber diameters have been used for prostate treatment (optical core: 550–1000 μm).
- Side-firing fibers (single-use): SideFib™ is a single-use, optical core, 600 μm fiber with side-fire deflection of 78°, which is useful for ThuVAP.

### High-power 532 wavelength laser (characterized by its green light color)

Four generations of 532 wavelength or “GreenLight” lasers have been made: the 60 W KTP laser, the 80 W KTP laser, the 120 W lithium triborate (LBO) HPS laser, and the 180 W LBO XPS laser (all wavelength 532 nm) [18].

#### Active (laser) medium

The KTP laser is a derivative of the Nd:YAG laser. The additional KTP crystal (frequency doubling crystal) in the laser resonator converts the fundamental Nd:YAG wavelength (1064 nm) by SHG into 532 nm radiation [6].

#### Excitation source

An arc lamp is the source of photons required for excitation of the Nd:YAG crystal in first-generation GreenLight lasers. In second-generation GreenLight lasers, the Nd:YAG laser is diode pumped.

#### Wavelength

The green light wavelength (532 nm) is strongly absorbed by hemoglobin [6]. The depth of penetration is 0.8 mm in prostate tissue [4]. The 532 nm wavelength laser operates at a wavelength where the absorption in water is at a minimum (Figure 144.3). Without the presence of the hemoglobin molecule the extinction length for the KTP laser increases dramatically and the beam transmits through the irrigant with minimal power loss until it reaches its main tissue target, with effective penetration into tissue containing the active main chromophore for power absorption. Although absorption of light energy is shallow, it is deeper than the superficial effects of a holmium and thulium procedure, and can remove tissue via a true tissue vaporization effect. The challenge with this technique is to limit the heat effects to the target tissue. For effective volume reduction vaporization and minimal tissue coagulation effect, local thermal conduction is needed from the area of primary vaporization [6].

#### Mode of operation

Energy is delivered in a cw or quasi-cw mode [6, 18].

#### Tissue chromophore and clinical translation of laser–prostate interaction

The high-power 532 nm or KTP/LBO wavelength penetrates vascular tissue only a few micrometers (0.8 mm). In red, well-perfused tissue the density of absorbed power is high and results in an immediate increase of tissue temperature above the boiling point. Heat then diffuses deeper into the tissue layers via continuous irradiation at a single point. The longer the area is heated the deeper the effect. This phenomenon does not produce enough energy for vaporization, but results in coagulation due to local convection thermal energy that is high enough to denature protein. The unique characteristic of the 532 nm wavelength with melanin and hemoglobin as the active selective chromophores as well as its nonabsorption in an aqueous medium lead to the technique being given the name “photoselective vaporization of the prostate” (PVP) [18, 19].

The PVP technique results in a large amount of tissue being vaporized with a coagulated seam that provides hemostasis. This coagulated seam is produced by the local increase in temperature that is not enough for vaporization but enough for coagulation. Although subsequent laser passes travel through the coagulated seam, increasing the laser beam scattering, the effective use of high power and quick passes can limit the effects of scattering. Although lack of absorption in coagulated tissue can impair efficient removal because of the scattering of the green wavelength, this effect is easily overcome by the applications of higher power and power density as conferred with the more powerful 180 W 532 nm laser systems or GreenLight XPS laser system [6].

Side-firing fibers are used exclusively for PVP to ensure better visual control on the point of impact of the laser beam on the prostatic lobes [6].

### Laser fibers and the evolution of KTP laser generators

Four generations of GreenLight lasers with 60, 80, 120, and 180 W power have been produced. The 60 W KTP was a very effective and safe laser, but its lower power resulted in a less-than-ideal vaporization effect and speed with higher levels of coagulation necrosis effects. The 80 W was therefore created in order to increase vaporization speed. The 120 W system has the same properties as the 80 W laser but uses a different SHG crystal [20]. A LBO crystal is used and a Nd:YAG laser beam is passed through this medium in order to create the 532 nm wavelength. This LBO system is better collimated in comparison to the KTP beam.

The 180 W laser utilizes a control power feedback mechanism that exits the system and has a high-power fiber. The fiber has a thicker inner core (MoXy Fiber, American Medical Systems, San Jose, CA, USA) [18, 21]. Further modifications made were to the coagulation power mode. This coagulation mode is delivered across a variety of intermittent pulses [21], which copy that of the power in electrocautery coagulation used for hemostasis. This fiber has been adapted to be used with arterial bleeders. In addition, intermittent pulses and continuous flow of room temperature irrigant over the tip of fiber help to limit the laser coagulation heat on the contact tissue [21]. The overall power of the 180 W system improved the rate of vaporization efficiency [21]. In order to have maximum output of 180 W, a new fiber was necessary. This new fiber has a wider diameter (750 µm vs. 600 µm), which provides a wider and more efficient zone for vaporization. This increases the beam area by 50% [18].

The following side-firing single-use fibers are available as laser delivery systems:

- 1.75 mm OD, 600 µm CCD, 70° deflecting, silica fiber ADD Stat™ delivery device but by an 88% more collimated beam and smaller spot size, resulting in much higher irradiance or power density in W/cm$^2$ than its two predecessors with a beam divergence of 8° vs. 15° [18, 22] (120 W LBO PVP).
- 2.10 mm OD, thicker 750 µm CCD, continuously cleaned/cooled, metal-capped, silica, MoXy™ fiber. This has the same 8° beam divergence but due to its larger 750 µm CCD the new fiber emits a larger diameter laser beam. Consequently, it creates a 50% larger spot size. However, since it also emits 50% more power, it achieves the same irradiance or power density in W/cm$^2$ as the existing ADD Stat™ fiber (50% less power and 50% smaller spot size) [18] (180 W LBO PVP).

### Others

**Diode lasers**

There is no unique diode laser. The term diode laser defines a group of lasers using a semiconductor excited by an electrical current as the excitation source to generate laser radiation. By using different semiconductor elements (GaAlAs (750–870 nm), InGaAs (900–1000 nm), InGaAsP (1300–1550 nm)) and layer structures, the generation of various wavelengths is possible (Figure 144.3), providing laser systems emitting at 940, 980, 1318, and 1470 nm [5]. Reviewing the basics of laser–tissue interaction and Figure 144.3, it becomes clear that different wavelengths must be judged independently [5]. The target chromophore differs depending on wavelength. Compared with the GreenLight LBO laser, different diode laser systems showed comparable or superior tissue ablation rates and lower bleeding rates. However, tissue necrosis and penetration depth were significantly higher [23–25].

## Dedication

This chapter is dedicated to Professor Mostafa Elhilali (1937–2017) who passed away on April 29, 2017. Professor Elhilali made a huge scientific contribution to different areas of urology. Specializing in endourology, he was involved in developing and establishing the holmium laser enucleation of the prostate technique for the treatment of benign prostatic obstruction.

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# 145

# Holmium Laser Therapy of the Prostate

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## Introduction

Transurethral resection of the prostate (TURP) has been the reference standard for the treatment of benign prostatic hyperplasia (BPH) for decades. It was reported that TURP was associated with significant perioperative morbidity (13–24%) [1], but with significant technical advancements over years its perioperative morbidity has been significantly reduced (11.1%) [2]. However, it still has limitations that increase the perioperative morbidity, particularly when treating large prostates and patients with coagulopathy. Reich et al. showed that with resected prostate weight more than 60 g, blood transfusion rate was 9.5%, transurethral resection syndrome was 3%, surgical revision rate was 9.8%, and perioperative mortality was 0.71% [2]. Furthermore, data showed that coagulopathy independently impacted TURP outcome in terms of more bleeding complications [3].

Laser prostatectomy was introduced as a less invasive modality for treatment of BPH, because it overcomes the disadvantages and limitations of the standard TURP and open prostatectomy. It is much less invasive than the open procedure [4], and, because it uses physiological saline as an irrigant, the incidence of transurethral resection syndrome is reduced and a higher safety profile is achieved in patients with comorbidity who are on anticoagulants or antiplatelets during surgery [5]. Laser prostatectomy also can be used to tackle large prostate glands beyond the limits of TURP. It is often done as day surgery with a shortened catheterization time. These considerations result in it being more cost effective [6].

## History and evolution

The holmium (Ho) laser has been associated with strong clinical evidence for its effectiveness in many applications in urology, such as incision of ureteral stricture [7], lithotripsy of urinary calculi [8], ablating superficial urothelial tumors [9], bladder neck incision (BNI) [10], and surgical management of BPH.

The combination of the Nd:YAG laser with the Ho:YAG laser was used early on to vaporize and coagulate tissue using a technique known as combination endoscopic laser ablation of the prostate (CELAP). The initial experience of this technique was first reported by Gilling et al., who found the use of the Nd:YAG laser led to a longer catheterization time, delayed symptom improvement, and high recatheterization rate (26%) [11]. These side-effects limit the usefulness of this technique, and CELAP has been replaced by the holmium-only technique. Since its first use in 1994, various techniques using the holmium laser wavelength have been used in the surgical management of BPH: holmium laser ablation (HoLAP), resection (HoLRP), and enucleation of the prostate (HoLEP) [12].

## Physics

Every new laser technology has specific advantages; however, its physics may result in significantly different outcomes. The holmium:yttrium–aluminum–garnet (Ho:YAG) laser emits a pulsed, invisible infrared beam with a wavelength of 2140 nm, which is absorbed strongly by water (which constitutes 60–70% of the prostate).

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

The depth of penetration is 0.4 mm, which predominantly causes vaporization without a deep coagulation zone when used with a side-firing fiber. It provides a precise incision and enucleation while maintaining hemostasis when used with an end-firing fiber. Energy absorption by the irrigant forms a vapor bubble around the laser fiber tip and this result in a microexplosion, causing a jackhammer effect that can cut tissues or disintegrate stones when in close contact to the target tissue. If direct contact is not adequately maintained, laser efficiency will be reduced due to consumption of energy in the formation of vapor bubbles [12, 13].

## Equipment and instruments required for holmium laser management of BPH

- Laser capital equipment: High-power holmium laser system is essentially required for management of BPH. As low as 50 W laser power has been used for holmium laser-based transurethral prostate procedures, but 80–100 W systems are the most frequently used [14]. Recently a 120 W system has been introduced with significant enthusiasm, particularly for prostate vaporization.
- Endoscopy set: Continuous-flow 26 Fr resectoscope (inner, outer sheath, and an obturator system), 30° optical lens and laser guide probe (used for stabilization of laser fiber), working element (thumb controlled for the laser guide probe), and saline for irrigation (Figure 145.1).
- Video monitoring system.

## Holmium laser transurethral incision of the prostate

### Technique (see Video 145.1)

Holmium laser transurethral incision of the prostate (HoL-TUIP) is performed using a 100 W Ho:YAG laser and a 550 μm end-firing fiber. The bladder neck is deeply incised at 5 and/or 7 o'clock, just distal to each ureteral orifice, using laser energy to create a trough down to the true capsule to either side of the verumontanum (laser energy of 2 kJ and rate of 50 Hz). Usually a single incision is sufficient as the bladder neck splits open wide. Rarely a second incision is necessary on the other side. A two-way 22 Fr Foley catheter is inserted and connected to straight drainage [10] to be removed before discharge the same day if the urine is clear.

### Safety

HoL-TUIP can be performed safely as a catheter-free outpatient procedure [15].

### Efficacy

Cornford et al. confirmed the efficacy of this technique at 2-year follow-up. The mean maximum urinary flow rate ($Q_{\text{max}}$) increased from 9.7 to 18.2 ml/s [15].

### Durability

The long-term outcome could be improved and the reoperation rate minimized with appropriate selection of cases. Elkoushy et al. reported on 82 patients who underwent HoL-TUIP; 9 (11%) patients were reoperated for recurrent symptoms of bladder outlet obstruction. Only prostate size independently predicted reoperation after HoL-TUIP (adjusted odds ratio [aOR] 7.12, 95% confidence interval [CI] 2.92–9.14, $P = 0.01$) with cut-off value of prostate volume of 29 ml to characterize long-term reoperation, with area under the curve (AUC) of 0.96, sensitivity of 89.7, and specificity of 88.9 [16].

### Cost efficacy

Comparing cost efficacy for HoL-TUIP and GreenLight (532 nm) laser photoselective vaporization of the prostate (PVP) for treatment of small prostates including high-risk patients, the mean estimated cost per HoL-TUIP procedure was significantly lower than that per PVP procedure. The higher cost of PVP was mainly due to the cost of a single-use laser fiber and a significant difference in hospital admission time [10].

## Holmium laser ablation of the prostate

### Technique

Using a 550 μm side-firing laser fiber with laser settings ranging from 2 J and 50 Hz to 3.2 J and 30 Hz, without the need for any tissue retrieval instruments. HoLAP is performed with the patient under general or regional anesthesia and normal saline is used as the irrigant. Vaporization of the prostate usually starts at the bladder neck using the side-firing laser fiber to make a bladder neck incision at 5 and 7 o'clock; then the laser fiber is gently moved over the surface of the obstructed lobe toward the apex of the prostate proximal to the verumontanum. The end-point of the laser procedure is a TURP-like cavity lined by capsular fibers [17].

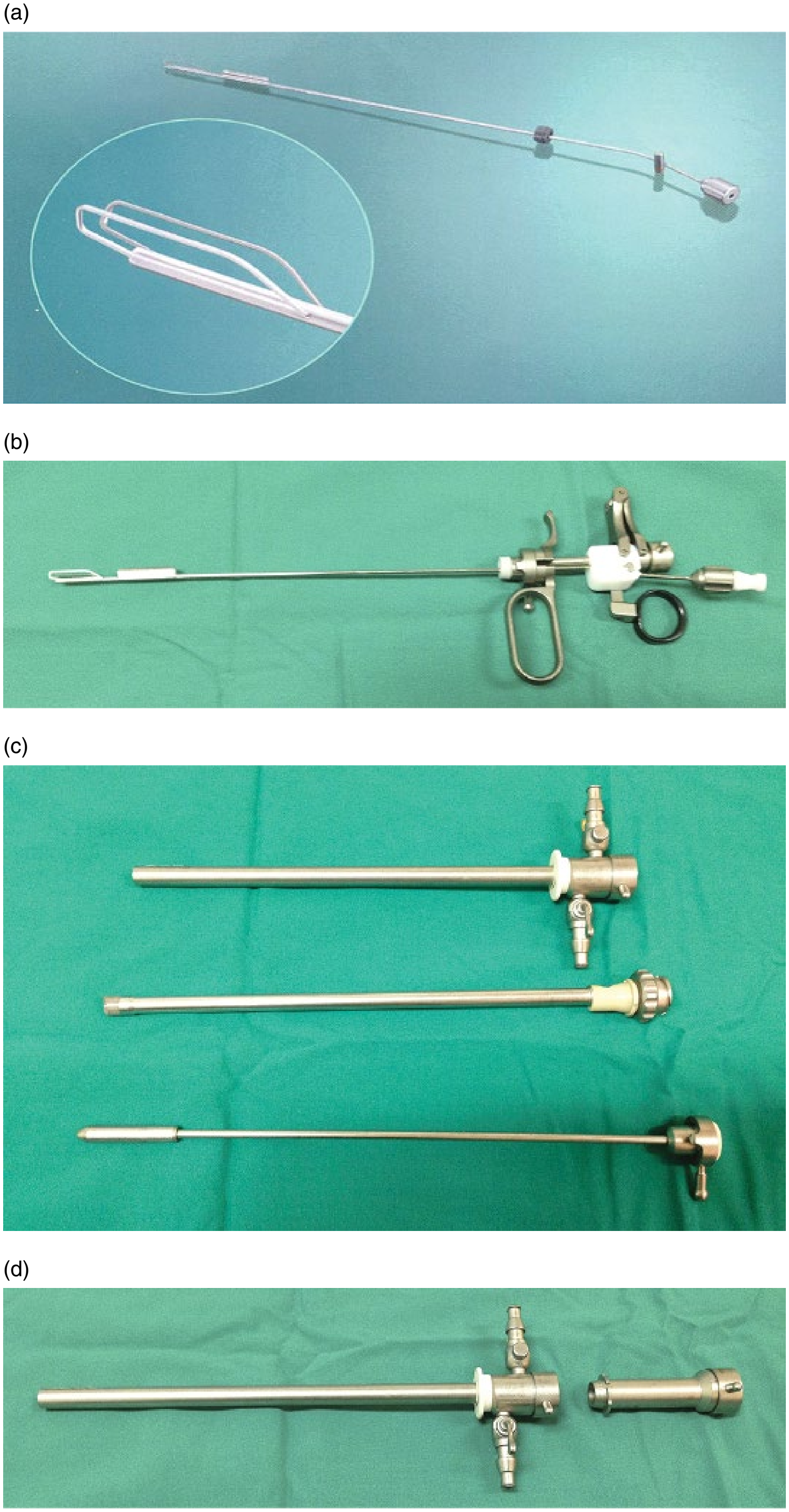

**Figure 145.1** Endoscopy set. (a) Laser guide probe with retracting beaks. (b) Laser guide probe with retracting beaks. (c) Continuous flow 26 Fr resectoscope with inner and outer sheaths and an obturator system. (d) Connecting piece/adaptor for the outer sheath to fit indirect nephroscope for morcellation.

### Safety

A controversial issue related to HoLAP when compared to TURP is the lack of tissue for histopathologic examination, which could lead to diagnoses of prostatic carcinoma being missed. Therefore, it is mandatory to perform a thorough evaluation of patients with an elevated prostate specific antigen (PSA) level or abnormal digital rectal examination (DRE), with transrectal ultrasound (TRUS)-guided biopsies prior to the intervention. Recently, with the increased popularity of using multiparametric MRI we can probably reduce the chance of missing significant cancer. It is also mandatory to continue postoperative PSA and DRE surveillance.

### Efficacy

In a randomized trial comparing HoLAP and TURP in men with prostates smaller than 60 ml, the subjective and objective improvements in both groups were similar at 1 year follow-up. However, the advantages of HoLAP over TURP included less dysuria and bleeding, and shorter hospital stay and catheter time, without need for any postoperative irrigation [17].

### Durability

Elshal et al. reported after a median of 71.3 months in a randomized trial comparing HoLAP versus GreenLight (532 nm) laser PVP. Retreatment for recurrent infravesical obstruction was 19.2% in HoLAP and 25% in PVP ($P > 0.05$). Smaller prostate volume was significantly associated with bladder neck contracture (BNC) after laser ablation, regardless of the type of laser used. BNC and *de novo* urethral stricture seem to be the main causes for an early (first-year) reintervention. Redo treatment for recurring prostate adenoma was associated with less postoperative PSA reduction (less than 20%) suggesting inadequate tissue ablation. At 7 years follow-up of 34 patients who underwent HoLAP, there was an 83% improvement in $Q_{\max}$, a 47% decrease in symptom score, reoperation rate of 15%, and recatheterization rate of 9% [18, 19].

### Cost efficacy

Looking for cost efficacy of both HoLAP and GreenLight (532 nm) laser PVP for treatment of small to moderate size prostate (less than 60 ml), accounting for all clinic visits and readmissions for reoperations, total costs were 200.45 Canadian dollars lower in the HoLAP group [19].

### Future perspectives

Xpeeda™ D/S/L fiber is a single-use, side-firing fiber that can deliver more energy to the tissue while in direct contact with it, as proposed by the manufacturer for use with 120 W laser system. Laser ablation with the new fiber might revive the use of holmium laser in prostate ablation for further clinical studies [20].

## Holmium laser resection of the prostate

### Technique

Before the development of the morcellator for tissue retrieval, Gilling et al. developed a technique that aimed to resect prostatic tissue by the holmium laser, similar to TURP. The resected pieces were small enough to be retrieved by a modified resectoscope loop or Ellik evacuator. HoLRP starts with bilateral incision to define the depth and amount of tissue to be removed. The next step is to join the two incisions just in front of the verumontanum to undermine the median lobe and deposit it into the bladder. Incisions at 1 and 11 o'clock position over the entire length of the prostate are needed to define the upper margin of the excision of the lateral lobes. Dissection occurs precisely in the plane between the adenoma and capsule in a retrograde fashion until only a bridge of tissue remains at the bladder neck [21]. The technique of HoLRP produces a cavity identical in appearance to TURP, but with a relatively bloodless procedure that results in a short catheter time, immediate functional improvement, and minimal postoperative irritative symptoms.

### Safety

HoLRP offers significant improvements over TURP in terms of catheterization time, length of hospital stay, risk of bleeding, and incidence of untoward events [22].

### Efficacy

Fraundorfer et al. reported in their randomized trial comparing HoLRP to TURP that HoLRP offers equivalent outcomes to TURP in terms of rapid relief of symptoms and improved urodynamic parameters [22].

### Durability

The long-term data have shown sustained improvement of flow rate and symptom score for a minimum of 4 years [23].

### Cost efficacy

HoLRP offers a 24.5% cost savings over TURP when in-hospital and postdischarge events were analyzed.

Furthermore, 93 procedures annually for 5 years would achieve total machine payback, including fiber and service costs [22].

## Holmium laser enucleation of the prostate

HoLEP reproduces the removal of the obstructing prostatic tissue with a true anatomic surgical enucleation of the adenoma, identical to using the index finger in open prostatectomy. The advantages of this technique include an almost bloodless field, allowing better vision with simultaneous coagulation of all bleeding vessels. Moreover, the dissection can be sharp or blunt. Three-dimensional awareness and hand–eye coordination are mandatory in this technique. The visibility in HoLEP, compared with standard TURP, is much better because of the bloodless field and the greater image magnification.

### Technique

#### Inspection

Inspection of the prostate anatomy looking for presence or absence of grossly enlarged median lobe and the depth of the grooves at the bladder neck determines the location of the first incision and plan of enucleation.

#### Enucleation

- Three-lobes technique is used for grossly enlarged median lobe and deep grooves at the bladder neck (see Video 145.2.a)
- Two-lobes technique is used whenever there is only a single or no deep groove at the 5 or 7 o'clock positions of the bladder neck (as in the majority of cases).
- In one-lobe technique (en-bloc technique) the whole adenoma is dissected as one unit for delivery into the bladder [24].

Following median lobe enucleation (in case of three-lobes technique) or creation of the initial incision at the deepest groove at the bladder neck (in case of two-lobes technique) (see Video 145.2.b.i), lateral lobe enucleation is achieved.

Enucleation is done using a combination of blunt and sharp dissection in a retrograde fashion. The blunt enucleation is achieved by using the tip of the scope, just like using a finger, to separate the adenoma from the surgical capsule in a technique similar to traditional retropubic prostatectomy but in a retrograde manner.

The operator should always use a rotating movement to follow the contour of the prostate and care must be taken to avoid using excessive force so as not to unnecessarily stretch the external urinary sphincter or go through the surgical capsule. Blunt enucleation should be avoided if the tissues do not separate easily. Instead, the laser should be used to cut any attachments. The proper plane can be identified from its appearance, as well as from the ease with which the tissues separate (see Video 145.2.b.ii). The dissection of the adenoma continues, progressing toward the bladder neck. When the adenoma is separated laterally and the anterior aspect of the prostate is reached, the dissection is extended across the midline in order to facilitate the later separation of the two lobes in the midline anteriorly when the 12 o'clock incision is performed, eliminating any guesswork about the depth needed.

Eventually, the adenoma is attached at the bladder neck, apical mucosal strip at the level of the urinary sphincter, and the anterior commissure to the contralateral adenoma.

The adenoma is sharply dissected from the bladder neck completely then the apical mucosal strip is carefully incised using short energy bursts at settings of 1.5 J at 30 Hz for an energy level of 45 W, to minimize the risk of thermal damage to the sphincter (see Video 145.2.b.iii). The incision is extended through the anterior commissure, separating the two adenomas without the need for guesswork on the depth of incision. The lateral lobes are gently pushed into the bladder.

#### Hemostasis

Special emphasis is placed on achieving excellent hemostasis before starting morcellation because the visibility with the indirect nephroscope is not as good as with the cystoscopic lens. When coagulating a bleeding vessel, the laser fiber is defocused but directed end-on toward the bleeding point. A whitening of the tissue around the vessel can often be used as an indicator of adequate coagulation (see Video 145.2.c).

#### Morcellation

There are two popular commercially available tissue morcellators. The main differences between them are the type of movement of the cutting blades (guillotine vs. oscillation) and shape of the blade (nontoothed vs. toothed) in the VersaCut™ (Lumenis Inc., San Jose, CA, USA) and Piranha (Richard Wolf GmbH, Knittlingen, Germany) morcellators [25], respectively (see Video 145.2.d). Alternatives to tissue morcellators are the mushroom technique and mini-laparotomy suprapubic extraction of the enucleated adenoma [26].

Morcellator is introduced through a long nephroscope and an adaptor is used to fit the nephroscope with outer sheath of the 26 Fr resectoscope.

Morcellation is one of the most critical steps of the procedure and is often considered potentially dangerous. In order to avoid complications, two principles need to be strictly observed. First, the patient's bladder should be adequately distended. This is achieved by ensuring that the patient's abdominal muscles are relaxed and that the irrigation inflow is not interrupted, a second inflow tubing attached to the exit tap adds more security and ensures bladder fullness at all times. Second, the morcellation process should always be performed under direct vision. This is achieved by having adequate hemostasis and by keeping the engaged piece directly in front of the lens of the nephroscope, with the nephroscope tip and cutting blades in the middle of the bladder. Lastly the prostatic fossa is inspected for bleeders or any residual adenomas (see Video 145.2.e).

## Postoperative care

At the end of the procedure, a 20–22 Fr, 30 ml balloon two-way Foley catheter is inserted. Sometimes a stylet is needed to insert the catheter. The catheter is fixed to a Y-connector, which is used to deliver intermittent irrigation to the bladder if needed in the recovery room. Rarely, a three-way catheter and continuous bladder irrigation are used.

The catheter is removed on the next morning unless otherwise indicated and the patient is discharged.

## Safety

### Perioperative

Naspro et al. performed a randomized study comparing HoLEP to open prostatectomy in 80 patients (41 vs. 39 patients, respectively) with a prostate size greater than 70 g [26]. HoLEP was shown to be safer than open prostatectomy in the perioperative period, requiring a lower number of blood transfusions (4% vs. 12.8% $P < 0.001$) in addition to a shorter catheterization time (1.5 vs. 4.1 days, $P < 0.001$) and hospital stay (2.7 vs. 5.4 days, $P < 0.001$) [27]. Furthermore, the safety in elderly people (octogenarians) with high morbidity index [5] and in patients who are on an ongoing anticoagulation/antiplatelet therapy during the procedure have been reported [28].

## Continence

Postoperative transient stress urinary incontinence (SUI) following HoLEP has been reported. Elmansy et al. found that risk of postoperative SUI is associated with prostate volume more than 81 g, postoperative reduction in PSA more than 84%, and in patients with diabetes mellitus [29]. Some reports showed high incidence of postoperative SUI in the first year that significantly improved with time and pelvic floor exercise [30]. Postoperative transient urge urinary incontinence (UUI) is a time-limited event that is related to the time needed for detrusor muscle recovery with or without anticholinergic medications.

Early postoperative SUI occurs as a rare event after HoLEP and is reported in around 2% of cases, which is comparable with results from TURP and open prostatectomy [31, 32].

## Urinary retention

Patients with urinary retention represent a particular challenge to urologists, as they often experience inferior functional outcomes and a higher complication rate when compared to patients without urinary retention. Peterson et al. retrospectively evaluated 164 patients in urinary retention treated by HoLEP [33]. Mean duration of urinary retention was 28.9 days (range 2–365 days). Their results confirmed the safety and reliability of this procedure for treating urinary retention in men with large prostates. All patients were able to void following treatment and remained catheter free. Mean urine flow rate was 26.7 ml/s (range 4.3–54.8 ml/s) and mean postvoid residual (PVR) was 32.5 ml (range 0–150 ml).

The outcome for patients with chronic urinary retention and hypotonic bladder may be less satisfactory. Mitchell et al. reported on 14 patients with detrusor hypocontractility and 19 patients with acontractility and evidence of benign prostatic obstruction (BPO) who underwent HoLEP. Preoperatively, 5 (35.7%) men with hypocontractility and 19 (100%) men with acontractility had catheter-dependent urinary retention for a median of 3 and 9 months, respectively. At a median follow-up of 24.7 months, all 5 (100%) men with hypocontractility and 18 of 19 (94.7%) men with acontractility were voiding spontaneously without the need for intermittent catheterization. Individuals with hypocontratile bladders had statistically significant improvements in the American Urological Association Symptom Index (AUA-SI) (21.5 vs. 3; $P = 0.014$), maximum urine flow ($Q_{\max}$ 10 vs. 21 ml/s; $P = 0.001$), and PVR (250 vs. 53 ml; $P = 0.007$) from baseline to postoperative assessments. In patients with an acontractile bladder, 15 of 19 (78.9%) displayed significant return of detrusor contractility, whereas 4 of 19 (21.1%) were voiding exclusively by Valsalva effort on follow-up urodynamic study. Postoperatively, patient satisfaction, as ascertained by AUA-SI, was high for both groups [34].

## Sexual function

HoLEP had no negative impact on sexual function. Furthermore, sexual satisfaction improved in proportion to the improvement in lower urinary tract symptoms following HoLEP [35]. In a study of 99 HoLEP patients, significant improvement in most of the subdomains of the International Index of Erectile Function (IIEF) was observed, although the orgasmic function domain did not show a significant substantial change, which may be related partially to the high prevalence of retrograde ejaculation/anejaculation [36]. This finding is consistent with what was reported after open enucleation procedure (suprapubic prostatectomy) of significant increase in sexual desire and overall satisfaction despite the high prevalence of retrograde ejaculation (80–90%) and minimal impact on erectile function.

## Efficacy

### Operative efficacy

In a study of matched pairs of open prostatectomy, TURP, and HoLEP, resection speed and operative time for laser enucleation were statistically significantly faster than for TURP (0.61 vs. 0.51 g/min and 62 vs. 73 minutes, $P < 0.01$) and similar to those of open prostatectomy (0.92 vs. 1.0 g/min and 101 vs. 90 minutes, respectively, $P \geq 0.21$). Based on resection speed, HoLEP is faster than TURP and similar to simple open prostatectomy [37].

### Urinary outcome measures

HoLEP produces immediate and sustained improvement of objective and subjective outcomes similar to both open prostatectomy and TURP. The pre- and postoperative urodynamic assessment has confirmed that the relief of obstruction with HoLEP is superior to, or at least equivalent to, TURP and open prostatectomy [38–40]. Wilson et al. compared the functional outcomes of HoLEP to TURP in a randomized study of patients with a prostate size of 40–200 g. At one-month follow-up, functional outcomes in terms of AUA-SI score (8.6 vs. 5.7) and $Q_{\max}$ (22.3 vs. 18.4 ml/s) were observed in the HoLEP and TURP groups, respectively [38]. The improvement in functional outcomes was maintained for up to 24 months.

In 2007, Ahyai et al. published interesting data regarding the efficacy of HoLEP compared to TURP [31]. A total of 200 patients with a prostate volume of less than 100 ml were prospectively randomized to HoLEP or TURP and followed up for up to 3 years. At 2- and 3-year follow-up, HoLEP micturition outcomes compared favorably with those of TURP. The AUA-SI score was significantly better at 2 years postoperatively in the HoLEP group (1.7 vs. 3.9, $P < 0.0001$) and similar at 3 years (2.7 vs. 3.3, $P = 0.17$). PVR was significantly better at 2 years (5.6 vs. 19.9 ml, $P < 0.001$) and 3 years (8.4 vs. 20.2 ml, $P = 0.012$) postoperatively in the HoLEP patients. However, $Q_{\max}$ was similar in the HoLEP and TURP groups at 2 years (28.0 vs. 29.1 ml/s, $P = 0.83$) and at 3 years (29.0 vs. 27.5 ml/s, $P = 0.41$) postoperatively.

In comparing HoLEP to open prostatectomy, Naspro et al. demonstrated equivalence in terms of improvement in obstruction, starting with the three months follow-up and reaching a plateau at the 24 months follow-up [27]. At 24 months, $Q_{\max}$ had improved to clinically normal levels in both the HoLEP and open prostatectomy groups (19.19 vs. 20.11 ml/s, $P < 0.9$, respectively).

Kuntz et al. confirmed the previously reported data on large prostates in a randomized trial in patients with prostates larger than 100 g [39]. Both HoLEP and open prostatectomy resulted in effective and long-lasting postoperative improvements in symptom scores, $Q_{\max}$, and PVR. The differences between HoLEP and open prostatectomy in functional outcomes were not significant at each time point during follow-up.

### Prostate specific antigen and prostate volume reduction

Measurement of PSA may be a useful surrogate tool for the objective assessment of the amount of residual prostatic tissue following different therapies for BPH. It has been reported that serum PSA level is markedly reduced after open prostatectomy or transurethral surgery, as the transition zone is the major source of PSA production. Stamey et al. reported the changes in PSA after open prostatectomy or transurethral procedures for the treatment of BPH [41]. There was a mean decrease in PSA of 95% in the open prostatectomy group and of 84% in the TURP group (73 men). Others have confirmed a mean percentage PSA reduction of 70–75% after TURP [42].

HoLEP produces a significant reduction in PSA that correlates well with the weight of adenoma resected (Figure 145.2). Tinmouth et al. examined PSA data before and after HoLEP from two institutions performing high volumes of this procedure in a retrospective evaluation of 509 patients [43]. The average weight of adenoma resected was 49.8 g (range 5–300 g) in the McGill group and 90.4 g (range 7.9–312 g) in the Methodist Hospital group, and the mean decrease in PSA 81.7% and 86%, respectively. Elmansy et al. evaluated 335 patients treated with HoLEP between 1998 and 2006 in a longitudinal study [44]. They found that the mean PSA dropped from 5.44 to 0.91 ng/ml and the mean PSA reduction was 75.4%, indicating that HoLEP is an effective technique in near complete adenoma resection. Moreover, this percentage reduction in PSA was maintained for up to 7 years follow-up, suggesting that the reduction in gland size after HoLEP is durable and more complete. In addition, they proposed that if the reduction of PSA after HoLEP is less than 50%, closer follow-up with PSA measurements every 3–6 months for the first 2–3 years is indicated to allow earlier detection of prostate cancer.

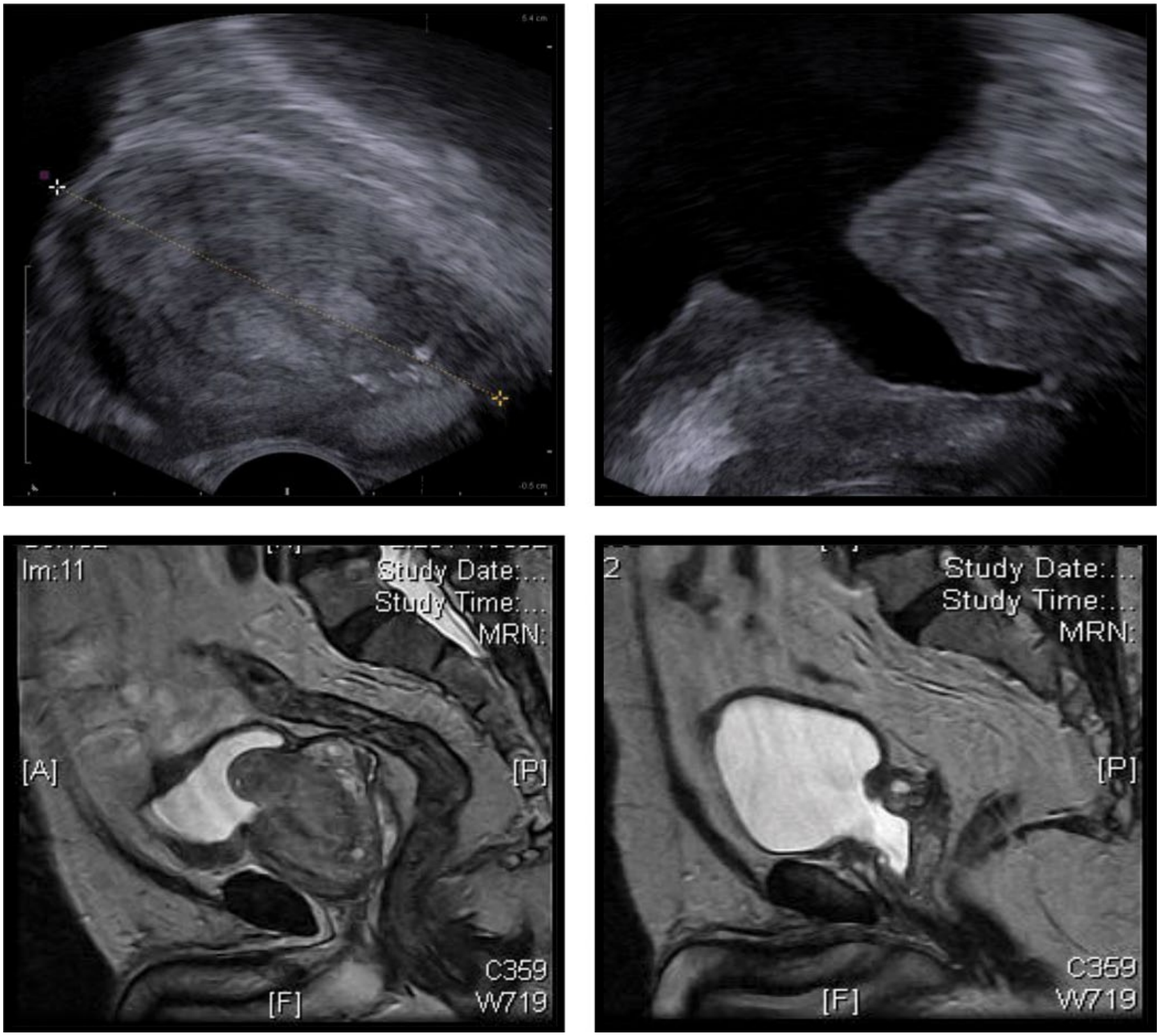

**Figure 145.2** Postoperative 82% and 84% volume reduction following holmium laser enucleation of the prostate (HoLEP) as shown in preoperative and four months postoperative (TRUS and MRI) that correlate well with postoperative PSA reduction of 79% and 83%.

## Durability

Sufficient data prove HoLEP's durability for most prostate sizes at long-term follow-up (Figure 145.3).

In a report on a total of 1216 HoLEP procedures and after a median follow-up of 7.6 years (1–14 years), 52 (4.3%) patients needed reoperation for recurrent lower urinary tract symptoms, including 13 (1.07%) for residual/recurrent adenoma, 14 (1.15%) for BNC, and 25 (2.05%) for *de novo* urethral stricture. In multivariate regression, smaller prostate size (<62 ml), PSA reduction <50%, and history of previous prostate surgery were significantly associated with recurrence of adenoma. BNC was significantly associated with smaller glands (<54 ml), while longer operative time and postoperative catheterization were significantly associated with urethral stricture. Kaplan–Meier curve demonstrates post-HoLEP freedom from reoperation of 96.9% at 5 years and 95.1% at 10 years [45]. Long-term reports on the need of reoperation for recurrent infravesical obstruction following HoLEP are summarized in Table 145.1 [18, 31, 32, 39, 46–49].

## Learning curve

HoLEP has been limited by its steep learning curve, a limitation often stated by the urologists. HoLEP requires longer training than standard TURP.

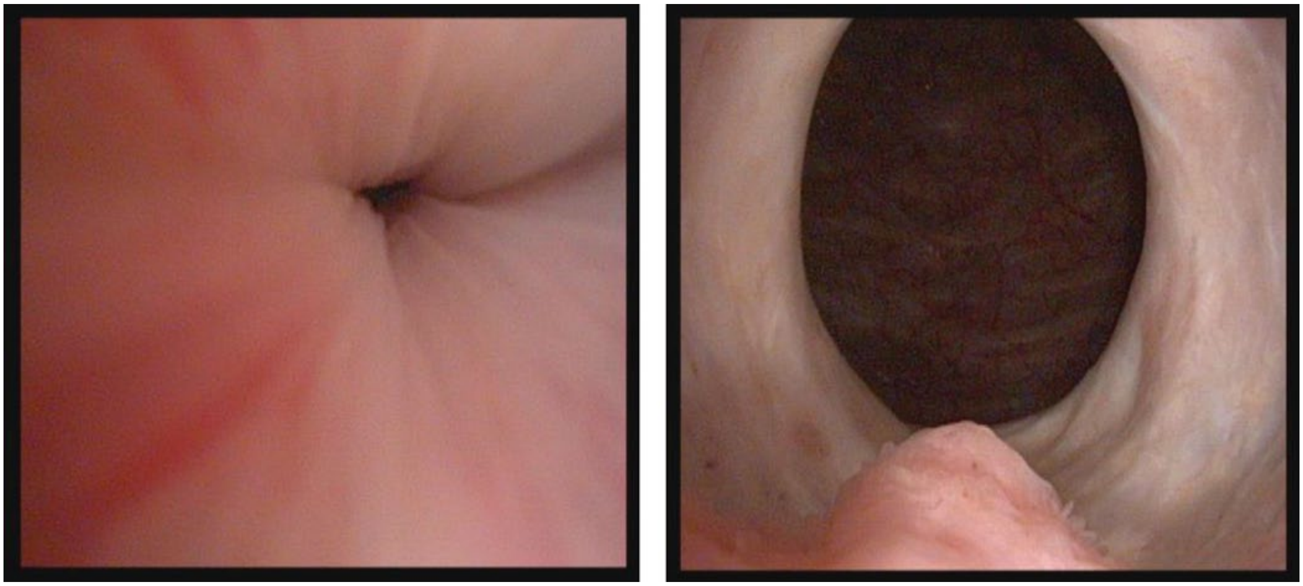

**Figure 145.3** Cystoscopic view 6 years after HoLEP.

**Table 145.1** Short- and long-term follow-up and reoperation rates.

| | Study type | Mean prostate size (ml) | No. of pts | Follow-up duration | Bladder neck contracture (%) | Urethral stricture (%) | Residual/regrown adenoma (%) |
|---|---|---|---|---|---|---|---|
| Tan et al. (2003) [18] | RCT | 77.8 | 25 | 1 yr | – | 4 | – |
| Montorsi et al. (2004) [32] | RCT | 70.3 | 52 | 1 yr | – | 1.7 | – |
| Gupta et al. (2006) [46] | RCT | 57.9 | 50 | 1 yr | – | 2 | – |
| Vavassori et al. (2007) [47] | Cohort | 62 | 262 | 3 yr | 0.6 | 3 | 2.7 |
| Ahyai et al. (2007) [31] | RCT | 55.3 | 75 | 3 yr | 3.1 | 4.1 | 1 |
| Kuntz et al. (2008) [39] | RCT | 114.6 | 42 | 5 yr | 1.7 | 3.3 | – |
| Krambeck et al. (2010) [48] | Cohort | 99.3 | 578 | <6 mo | – | 0.9 | – |
| | | | 425 | 6–12 mo | 0.8 | 1.3 | – |
| | | | 313 | 1–5 yr | 1.3 | 1.3 | – |
| | | | 79 | >5 yr | 6 | – | 0.1 |
| Gilling et al. (2012) [49] | RCT | 77.6 | 14 | 7 yr | – | – | – |

RCT, randomized controlled trial.

Extensive experience with transurethral surgery and the supervision of an experienced urologist are mandatory to master this technique. In particular, the initial apical enucleation and incision of anteroapical mucosal attachments of the lateral lobes are difficult to master.

El-Hakim and Elhilali presented the initial experience of a senior urology resident with HoLEP. He treated 27 patients with a mean prostate size of 54.8 g under the supervision of an experienced urologist. His overall results were comparable with those reported for the supervisor. They found that an average of 15–20 cases was needed for the trainee to feel confident with the technique [50]. However, Shah et al. reported that an endourologist inexperienced with HoLEP could perform the procedure with reasonable efficiency after about 50 cases, with an outcome comparable to that of the experts [51]. A higher incidence of complications, including capsular perforation and stricture urethral stricture, was seen in first 50 cases, with enucleation efficiency reaching a plateau after 50 cases. There was no significant difference in the functional parameters between the first cases and the last 62 cases.

Seki et al. also showed that significant relief of symptoms and urodynamic parameters could be achieved even very early in urologist's experience [52]. However, the authors concluded that enucleation efficiency was likely to be associated with a learning curve of up to 50 cases, as the average enucleation efficiency was 0.29 g/min for the first 10 cases but 0.75 g/min by the 70th case.

Elzayat et al. performed a retrospective study evaluating 118 patients who underwent HoLEP and compared the results for the first 50 patients with a later group of patients [53]. There was no significant difference in the enucleation and morcellation times in both groups. However, the retreatment rate after 5 years follow-up in the earlier group was higher (8% vs. 1.4%).

New practitioners need a high volume of cases to become familiar with this technique. Urologists who do not treat enough cases to maintain a reasonable operative frequency will have a longer learning curve that could be reflected in their complication rate [54]. We feel that it is also important in the learning process for the procedures to be carried out within a short interval, so as to build on experience rather than starting from the beginning each time.

### Cost efficacy

HoLEP for treatment of large BPH seems to be more cost effective than simple open prostatectomy, both in developing and developed countries. Salonia et al. carried out prospective comparison of the inpatient cost of HoLEP versus simple open prostatectomy in 63 patients. They concluded that HoLEP is associated with significant hospital net cost savings compared to open prostatectomy. They found that the hospitalization cost of HoLEP was 9.6% less than that for open prostatectomy. The cost reduction is mostly related to the shorter hospital stay and the significant reduction of blood loss, which eliminates the need for blood transfusion [55].

Elshal et al. carried out matched-pair analysis comparing costs of HoLEP and open prostatectomy for treatment of large prostates in limited healthcare resources systems. Two years after adopting the technique and accounting for the laser capital equipment cost, they found that HoLEP costs for the hospital were equal in the first three months after procedure to those for open prostatectomy. Significant hospitals cost savings are anticipated in subsequent cases [6] once the capital costs are amortized.

The initial high cost investment in the capital equipment when adjusted as a per case cost would be markedly balanced with good flow of cases, particularly with the versatility of Ho:YAG laser as an effective lithotripter.

### Future perspectives

One of the weaknesses remains the efficiency of the morcellation for prostate tissue retrieval following HoLEP, which is still not yet optimized and needs further research and innovation. Different laser power settings could be tested for the process of enucleation, and learning modules are needed for wider adoption of the procedure among urologists.

## Conclusions

Different types of lasers have been used to perform laser prostatectomy and give comparable and durable result similar to TURP with minimal morbidity, short catheterization time, short hospital stay, and low reoperation rate with no significant complications. The holmium laser has been effectively used for many urologic applications. HoLEP seems to offer the most favorable functional outcomes in terms of subjective and objective parameters with no prostate size limitation. Emerging data have confirmed this technique to be durable with an overall low reoperation rate. For other modalities, long-term follow-up and randomized comparative studies are still needed to confirm the effectiveness and durability of each technique.

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# 146

# 532 nm High-power Transurethral Laser Prostatectomy

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## Introduction

Traditionally, the gold standard for treatment of benign prostatic hyperplasia (BPH) has been the electrocautery-based transurethral resection of the prostate (TURP). TURP, however, is associated with several complications and side-effects, including fluid absorption, electrolyte imbalance, intraoperative and postoperative bleeding, and inadequate resection. Laser therapy has several advantages over standard TURP, including technical simplicity and the absence or minimization of complications such as intraoperative fluid absorption and bleeding. Laser therapy has proven to result in shorter hospital stay and recovery for patients. Theoretically, less bleeding and irrigant absorption allows laser prostatectomy to treat larger glands with less physiologic stress, further suggesting a role for laser therapy in patients with a high burden of coexisting medical disease. An increasing number of practicing urologists are performing laser prostatectomies on patients with symptomatic BPH. Furthermore, the techniques and lasers used for laser prostatectomy are constantly evolving. To fully understand the mechanism of laser interaction with prostate tissue, some basic laser principles must first be understood. We will review the mechanisms of laser–tissue interaction and then provide a comprehensive review of the 532 nm laser prostatectomy.

## Laser physics

The word “laser” is derived from an acronym, standing for “light amplification by simulated emission of radiation” (LASER) [1]. An external energy source is used to excite electrons in a medium with an inherently large population of unstable electrons, causing the electrons to reach a higher energy state, called a metastable level. As the electrons return to ground state, they release an amount of energy equal to that initially absorbed, resulting in the spontaneous emission of photons [1–3]. Unlike normal white light, which is made up of the entire visible electromagnetic spectrum, laser energy is monochromatic (i.e. all of its photons originate from the same energy level transition with both spatial and temporal coherence) [1–3]. In addition, laser rays are parallel to each other and hence do not converge or diverge unless reflected or focused by a lens or mirror. However, when transmitted through flexible fibers by internal reflection, the laser beam will become divergent as it exits the fiber.

Laser energy affects tissue by inducing coagulation, vaporization, or even a mechanical tearing of tissue [4]. Power directly influences the temperature level reached and the speed with which a surgical effect is achieved. In general, a temperature of greater than 50°C is required to produce a coagulative effect, while a temperature of greater than 100°C is required to produce a vaporization effect. Medical laser sources can possess a number of power outputs ranging from 20 to 180 W.

Power density, defined as power per unit area ($P/A$), represents the most important parameter that expresses the strength of the laser at a fixed location. Fibers with narrowly divergent beams will have a much higher power density than fibers with widely divergent beams due to the difference in the size of target areas. As a corollary, this also implies that maximum power density arises when the tip of a laser fiber is almost in contact with tissue (i.e. at the distance where divergence is minimized) [1–3, 5, 6].

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## Laser–tissue interaction

Four major interactions occur when laser energy is applied to human tissue: reflection, scattering, penetration, and absorption.

### Reflection

Up to 50% of the incident energy of a laser beam is reflected away. After the initial reflection, the remaining energy is then transmitted through the tissue for a specific distance, depending upon the type of laser used as well as the particular type of tissue being treated. After absorption, the laser energy is then converted to thermal energy, or heat.

### Scattering

As laser energy strikes the irregularities of a tissue surface, diffuse reflection, also known as scattering, occurs. Scattering may occur in either forward or backward directions. The amount of scatter that occurs depends on tissue characteristics such as water content, cell constituents, and pigments. Scattering also depends on the resonant absorption and re-emission of radiation by the atoms of the receiving tissue, as well as the diffraction or radiation of laser energy in directions away from the line of propagation. As a result of scattering, a laser beam does not merely continue to penetrate in a straight line but dissipates its energy within the surrounding area, beginning when it hits the first tissue interface and continuing to create a zone of heat along the path of the beam.

### Penetration

Alternatively, laser energy may penetrate tissue. The depth of penetration depends on its wavelength and the composition of the receiving tissue. Penetration is often described by "extinction length," the depth of penetration of an incident beam beyond which only 10% of the initial beam energy is left (i.e. 90% absorption). Thus, after one extinction length, 10% of the beam will penetrate further, whereas after two extinction lengths, 1% of the beam will penetrate further, and so on.

### Absorption

Finally, laser energy may be absorbed by tissue. Absorption of laser energy is often described by "absorption length," the depth of tissue through which 63% of the incident beam energy is absorbed. It is important to note that the different components of living tissue absorb different laser energy wavelengths in variable fashions. Water, constituting 75–85% of soft tissue, absorbs 532 nm laser energy very poorly, resulting in deep penetration of the laser beam into tissue. Pigments such as hemoglobin, bilirubin, and melanin absorb 532 nm energy very efficiently. Finally, carbon, an abundant constituent of all living tissue, is a final breakdown product of pyrolysis and represents a strong absorber of all wavelengths of laser energy.

## History of the 532 nm laser

The original 532 nm laser was a potassium titanyl phosphate (KTP)-based laser system that contained a KTP crystal through which a 532 nm wavelength was generated. This had a different interaction with prostate tissue from its parent, the neodymium:yttrium–aluminum–garnet (Nd:YAG) [7]. The 532 nm wavelength is selectively absorbed by hemoglobin, which acts as an intracellular chromophore. The 532 nm laser energy can be fully transmitted through aqueous irrigants into the cell, where it is absorbed by hemoglobin, which is then rapidly heated, leading to vaporization of prostate tissue. The short optical penetration associated with this wavelength confines its high-power laser energy to a superficial layer of prostate tissue that is vaporized rapidly and hemostatically, with only a 1–2 mm rim of coagulation. The thin coagulation zone arises as a result of the quasi-continuous emission characteristics of the 532 nm laser. Typically, continual irradiation of a single point causes heat to diffuse into deeper tissue layers, causing coagulation wherever there is enough convection thermal energy for protein denaturation but insufficient energy for vaporization. These selective characteristics led to the use of the 532 nm laser in prostatectomy as "photoselective vaporization of the prostate" (PVP).

### The 60 W laser systems

Some of the first studies designed to test the efficacy of higher power 60 W KTP lasers first began their experimentation with both *in vivo* and cadaveric canine studies [8]. These initial canine studies were capable of providing evidence to support the 60 W laser's ability in not only vaporizing the tissue, but minimizing any simultaneous coagulation effects. Malek et al. described the first human trials in 10 patients using the 60 W KTP laser [9]. Mean operating time for the procedure was approximately 29 minutes. The results demonstrated no postoperative incidences of urinary retention and no transurethral resection syndrome. This study showed all patients were catheter-free within 24 hours of the procedure. After 24 hours, maximum renal flow rate ($Q_{max}$) had significantly improved by 142% (8 ± 1.3 ml/s vs.

19.4 ± 8.4 ml/s, $P = 0.003266$). These initial results suggested promise at three months follow-up.

In 2000, a larger study of 55 patients followed patients using the 60 W KTP laser [10]. Mean operating time was 44 minutes. At 2 years follow-up patients showed statistically significant improvements in postoperative American Urological Association Symptom Index (AUA-SI) scores (mean 14, 82% improvement), $Q_{\max}$ (mean 29.1 ml/s, 278% improvement), and PVR (27 ml, 75% improvement). After the procedure, all patients were catheter-free within 24 hours. Furthermore, no patients required recatheterization, nor did anyone experience transurethral resection syndrome. Although many patients used antiplatelet agents (at least half), hematuria was negligible. Overall, the results showed that PVP with 60 W KTP was as effective as TURP.

### The 80 W laser systems

The use of 60 W KTP was less than ideal due to its low power, which limited the size of the prostate that could be resected. In order to achieve the desired tissue ablation, the 80 W KTP laser system was introduced. It is interesting to note that to preserve a thin coagulation zone while maintaining high vaporization efficiency, laser pulsing was incorporated into the 80 W higher power KTP laser system. A high-frequency modulation of laser light generates a continuous stream of short micropulses with a duration of 4.5 ms and a peak power of 280 W (i.e. 3.5 times the average laser power of the regular 80 W laser). The short duration of the micropulses does not allow time for heat to diffuse from the superficial layer, thus confining energy to a small volume of tissue, a situation referred to as thermal confinement. As each micropulse generates a very fast temperature increase inside tissue, the tissue water is not only rapidly vaporized but the surrounding tissue matrix is torn apart, allowing for efficient removal of prostate tissue. Continuous bladder irrigation is thus required to cool the tissue as well as to provide a clear aqueous medium for laser light to be transmitted to target tissue without energy loss.

Initial experiments utilizing the 80 W KTP laser began with with *ex vivo* animal models [11]. Twenty perfused porcine kidneys were used to model human prostate tissue. The high-power resection was compared to traditional TURP-like resection and it was found that 80 W KTP showed a statistically significant decrease in hemorrhage ($P < 0.0001$). This demonstrated that bloodless ablation of tissue was possible.

Hai and Malek investigated the first human trials using 80 W KTP laser prostatectomy [12]. A total of 10 patients were followed for 1 year postoperatively. Mean operating time was 19.8 minutes. Patients experienced statistically significant improvements in AUA-SI score (23.2–2.6), quality-of-life (QOL) scores (4.3–0.5), $Q_{\max}$ (10.3–30.7 ml/s), and postvoid residual volume (PVR) (137.6–3 ml). Furthermore, there was a 27% reduction in prostate volume. No patients in the study experienced postoperative urinary retention, infection, incontinence, or erectile dysfunction; none subsequently developed bladder neck contractures or urethral stricture. Interestingly, two patients did not require catheterization following the procedure. One patient actively taking anticoagulants did experience mild transient postoperative hematuria, which required recatheterization for 24 hours. De Nunzio et al. showed in 150 patients that 80 W KTP laser was effective in decreasing storage and voiding symptoms of 81.8% and 90.9%, respectively, at 12 months [13]. Consistent with other published series, these studies further support the procedure's safety, efficacy, and durable improvements on International Prostate Symptom Score (IPSS) and QOL [14].

The 80 W KTP/532 nm laser was also tested on large prostates by Sandhu et al. [15]. Sixty-four men with BPH and prostates with volumes of at least 60 ml (mean 101 ml) underwent vaporization with the 80 W KTP laser. The mean operative time was 123 minutes. The IPSS decreased from 18.4 to 6.7 at 12 months; $Q_{\max}$ increased from 7.9 to 18.9 ml/s, while PVR decreased from 189 to 109 ml. No transfusions were required nor was there evidence of postoperative hyponatremia. All 62 patients were discharged within 23 hours.

Pfitzenmaier et al. conducted a comparative study between vaporization of prostates greater than or equal to 80 ml (39 of 173 patients) and those smaller than 80 ml [16]. PVP was discovered to be safe and effective in prostates greater than or equal to 80 ml [16]. One caveat was that reoperation was higher in the larger prostate cohort. Another study by Rajbabu et al. evaluated 54 patients with prostates greater than 100 ml who underwent 80 W KTP laser prostatectomy [14]. The mean operating time was 81.6 minutes. The mean catheterization for patients was 23.0 hours. Mean urinary flow rate improved from 8.0 to 19.3 ml/s from three months to 24 months postoperatively [14]. PVP, IPSS, QOL, prostate specific antigen (PSA), and prostate volume all showed statistically significant improvements. No complications were reported. In one study, 76 patients with a prostate size of greater than 70 ml were randomized to TURP or 80 W laser prostatectomy [17]. Procedure time was shorter for the TURP group. Hospitalization stay and catheterization time were significantly shorter in the laser group. TURP favored prostate volume reduction as well as significant improvements in IPSS, PVR, and $Q_{\max}$. In addition, reoperation rate was higher in the laser group.

Ruszat et al. randomized 396 patients to either 80 W laser prostatectomy or TURP [18]. Interim 24 months follow-up data found the rates of intraoperative bleeding

(3% vs. 11%), blood transfusion (0% vs. 5.5%), capsule perforations (0.4% vs. 6.3%), and early postoperative clot retention (0.4% vs. 3.9%) were significantly lower in the laser group. There was no significant difference in IPSS and PVR. After 12 months, size reduction was greater in the TURP group (66% vs. 44%) and the rate of repeat procedure was greater in the PVP group (6.9% vs. 3.9%, not significant).

Bouchier-Hayes et al. reported data on 120 patients randomized to undergo TURP or 80 W laser PVP [19]. At 12 months equivalent improvements in IPSS and flow rates were demonstrated. Length of hospitalization, length of catheterization, and adverse events were lower in the laser group. In a nonrandomized study, Bachmann et al. studied 101 patients who underwent either TURP or laser prostatectomy. Perioperative morbidity and symptom improvement was equivalent in the groups at six months [20]. An Australian study had similar results when comparing patients randomized to either 80 W laser prostatectomy or TURP [21]. Both groups showed a significant increase in mean urinary flow rate, improvement in IPSS scores, and no difference in sexual function at 1-year follow-up.

Guo et al. conducted a study evaluating 5-year follow-up after the use of 80 W KPT GreenLight laser vaporization of the prostate in comparison to TURP [22]. The purpose of this study was to compare long-term results of both procedures in comparison to safety, efficacy and long-term durability. This was a two-center nonrandomized prospective study. One hundred and twenty patients underwent PVP and 80 underwent TURP. At 60 months follow-up 30 patients from the PVP arm and 31 patients from the TURP arm were available for analysis [22]. There were no statistically significant differences in IPSS, QOL, $Q_{\max}$, and PVR between the two groups [22]. Those receiving 80 W KTP had a higher reoperation rate due to urethral stricture, bladder neck contracture, and persisting and recurrent adenoma [22].

There have been a number of studies evaluating the long-term outcomes of 80 W KTP laser prostatectomy. Te et al. investigated the use of the 80 W KTP laser in laser prostatectomy in the first large multicenter study. A total of 145 patients were included in the study with long-term follow-up [23]. Overall, there were significant and durable improvements in AUASI scores, QOL scores, $Q_{\max}$, and PVR 12 months postoperatively. Mean AUA-SI scores declined from 24 to 1.8 at 12 months; mean QOL scores improved from 4.3 to 0.4, $Q_{\max}$ from 7.7 to 22.8 ml/s, and PVR from 114.2 to 7.2 ml. Mean prostate volume, as determined by ultrasound, decreased from 54.6 to 34.4 ml. The mean operation time was 36 minutes with no patient requiring a blood transfusion. More than 30% of patients were sent home without a catheter; those with postoperative catheters had them removed in a mean of 14 hours. Approximately 8% of patients experienced mild-to-moderate dysuria that lasted more than 10 days, 8% had transient hematuria, and 3% had postoperative retention. Of the 56 men who were potent prior to the procedure, 27% experienced retrograde ejaculation but none of them experienced impotence.

Ruszat et al. published the largest series of 80 W KTP laser prostatectomies. At a single center, 500 patients underwent PVP, including 45% taking oral. Three years postoperatively, 26.2% of patients were included in the analysis. Mean AUA-SI, PVR, and QOL were significantly improved compared to results at baseline. At 60 months, the retreatment rate was 6.8% and reoperation rate was 14.8%. Urethral and bladder neck strictures were observed in 4.4% and 3.6% of patients, respectively, comparable to the rates in TURP [24]. Te et al. reported a multicenter long-term follow-up in 139 patients who underwent 80 W KTP laser prostatectomy. At 3 years, 33.8% of patients were included in the follow-up and improvements in symptom relief and urinary flow rate were durable [25]. The overall retreatment rate for this cohort was 4.3%.

The safety of 80 W KTP laser prostatectomy has been studied in patients at high cardiopulmonary risk, and demonstrated excellent results due to a robust hemostatic profile and perioperative hemodynamic stability of the procedure. Reich et al. performed 80 W laser prostatectomy on 66 patients with an American Society of Anesthesiology Score of 3 or greater [26]. Of these patients, 29 were being treated with ongoing oral anticoagulant or had a severe bleeding disorder. Throughout the study, no patients presented with major complications during or following the procedure and no patients required blood transfusions. Despite this, within 12 months, two patients required reoperation due to recurrent urinary retention. Mean improvements in IPSS (from 20.2 to 6.5) and peak flow (from 6.7 to 21.6 ml/s) were durable at 12 months.

The final safety aspect of the 80 W KTP laser to be studied in detail was its use in anticoagulated patients at high risk for clinically significant bleeding. Twenty-four anticoagulated patients with BPH were treated with laser prostatectomy using the 80 W KTP laser [27]. Eight were on warfarin, 2 on clopidogrel, and 14 on aspirin. Eight (33%) of these patients had had a previous myocardial infarction; 7 (29%) cereberovascular disease, and 7 (29%) peripheral vascular disease. No patients developed clinically significant hematuria postoperatively and none developed clot retention. No patients required blood transfusions, nor were there any thromboembolic events. Follow-up revealed a decrease in IPSS from 18.7 to 9.5, as well as an increase in $Q_{\max}$ from 9.0 to 20.1 ml/s at 12 months.

PVR decreased from 134 to 69 ml at one month but this was not statistically significant beyond that time point. All patients underwent PVP safely without any adverse thromboembolic or bleeding events. However, more energy and time were required for lasing per gland size in these patients [28].

## The 120 W laser systems

The 120 W is similar to the 80 W KTP laser system, but it evolved to a higher power system (HPS) capable of 80–120 W. The laser emits the same 532 nm wavelength, with the same hemostatic properties as the 80 W KTP laser [29], but uses a different crystal. The 532 nm 80 W KTP laser is created by passing a 1064 nm Nd:YAG laser beam through a KTP crystal. In contrast, the 120 W HPS 532 nm wavelength is created by passing a Nd:YAG laser beam through a lithium triborate (LBO) crystal. The 532 nm LBO-based system also has a beam that is better collimated than the KTP beam.

The use of the 120 W 532 nm laser was first evaluated using animal models. Lee et al. first investigated the use of the 120 W laser in five male beagles [30]. PVP was performed in antegrade fashion through a suprapubic cystotomy at 40, 80, and 120 W settings for three distinct firing periods (5, 10, and 20 seconds) at unique locations in the prostate. The 120 W HPS consistently vaporized more tissue per unit time, while the depth of coagulation (1.2–2.5 mm) was decreased compared to the lower powered systems. Kang et al. compared the use of the 120 W HPS laser to the 80 W HPS laser in 96 specimens of bovine prostate tissue [31]. The 120 W HPS laser vaporized bovine prostate tissue more efficiently than the 80 W KTP laser and coagulation was equivalent. Lee et al. advised caution with the higher power setting, especially at 120 W due to the potential higher risk of capsular perforation and bladder wall perforation [30]. In addition, higher power provides more efficient vaporization with less hemostasis, and as a result, utilization of the lower power coagulation setting is important in achieving hemostasis.

Heinrich et al. used blood-perfused porcine kidneys to determine the ablation capacity, hemostatic properties, and coagulation depth of a 120 W 532 nm laser compared to an 80 W laser [32]. The 120 W LBO laser offered a significantly higher tissue ablation capacity compared with the conventional 80 W KTP laser. The increased efficacy of the 120 W laser device was accompanied by a higher bleeding rate and a slightly deeper coagulation zone.

Woo et al. published one of the first studies evaluating the efficacy of 120 W 532 nm laser prostatectomy in humans [33]. In a multicenter prospective study, 305 patients with BPH underwent laser prostatectomy using the 120 W HPS laser. Study results showed an increase in $Q_{\max}$ as well as decreases in PVR, IPSS scores, and prostate volume from baseline to follow-up. All of these parameters were significant ($P < 0.001$) in all patients. A subgroup analysis was done in three groups of patients: those in retention ($n = 63$), on anticoagulation ($n = 67$), and with prostates ≥80 ml ($n = 52$). Complications were comparatively low in all groups.

In another study by Al-Ansari et al. 120 patients with BPH were randomized to either TURP or 120 W 532 nm laser [34]. Baseline characteristics for both groups were comparable. After 36 months of follow-up, a total of 55 patients in TURP and 54 patients in 532 nm laser groups completed the study. The mean operative time was significantly shorter for TURP. Compared to preoperative values, there was significant reduction in hemoglobin and serum sodium levels at the end of TURP only. In the PVP, no major intraoperative complications were recorded and none of the patients required blood transfusion. Of those patients in the TURP group, “12 (20%) required transfusion, 3 (5%) developed transurethral resection syndrome, and capsule perforation was observed in 10 patients” [34]. Significant improvement was observed in $Q_{\max}$, IPSS, and PVP compared with preoperative values. The degree of improvement was comparable in both groups at all time points of follow-up. Storage bladder symptoms were significantly higher in PVP. Reoperation was required in one TURP patient and six PVP patients ($P < 0.05$). Lukacs et al. conducted a similar study using GreenLight HPS 120 W and TURP. A total of 70 men were randomized to receive 120 W and 69 were randomized to receive TURP [35]. IPSS scores could not be demonstrated to be noninferior. The mean length of hospital stay was significantly shorter in those in the PVP group 1 (interquartile range (IQR) 1–2) versus 2.5 (IQR 2–3.5), respectively ($P < 0.0001$) [35]. Other uroflowmetry clinical values were comparable across both groups [35].

Zang et al. conducted 3-year follow-up after 78 patients underwent PVP using a 120 W system [36]. The patient’s urinary characteristics and QOL scores drastically improved following the procedure. “At 36 months, the average percentage of improvements compared with baseline was as follows: IPSS, 60.2%; QOL, 80.9%; $Q_{\max}$, 138.7%, and PVR, 82.6%” [36]. Patients showed a 50.4% reduction in prostate volume when compared to perioperative results. Complication rates were relatively low with only 6.7% needing reoperation [36]. Similarly, Cho et al. evaluated the GreenLight HPS 120 W system in 68 patients and analyzed their results retrospectively for up to 3 years [37]. At 3 years, 58.8% patients maintained improvements in IPSS, $Q_{\max}$, and prostate volume [37].

### The 180 W laser systems

Compared to the 120 W laser systems, the 180 W laser was developed with a thicker inner core fiber, which is a water-cooled redesign high-power fiber (MoXy™ Fiber, American Medical Systems, San Jose, CA, USA) [38]. Another new modification is applied to the coagulation power mode. The new 180 W capable system delivers the lower power coagulation mode laser light in intermittent pulses. This intermittent laser pulse modality mimics the intermittent delivery of power in electrocautery coagulation for hemostasis. However, the more important utility is the ability to better utilize the fiber for contact coagulation of arterial bleeders. With intermittent pulses, laser coagulation heat on tissue contact is limited by the intermittent pulsing and continuous flow of room temperature irrigant over the tip. Finally, to improve the rate of vaporization efficiency, the power of the 180 W capable system was increased. The new system has a maximal power output of 180 W. To allow utilization of the 180 W capable system, while maintaining the power density characteristics of the 120 W system and its fiber, a new fiber design was necessary. This new fiber has a wider diameter (750 μm vs. 600 μm), which provides a wider and more efficient tissue vaporization effect. This increase in fiber diameter of 0.15 mm increases the beam area by 50%.

Malek et al. first described the 180 W system in living canines. A total of eight dogs underwent antegrade PVP. Researchers discovered this system produced a bloodless 76% larger cavity. Furthermore, this laser “vaporized tissue at a 77% higher rate and in 37% less of the time” [38]. Evaluation showed a 33% thicker mean coagulation zone compare to the 120 W laser [38]. In conclusion, the 180 W laser system had a higher vaporization rate and deeper coagulation zone with healing and tissue interactions comparable to those of the 120 W laser [38].

Bachmann et al. conducted the first study evaluating the use of the 180 W XPS laser involving a MoXy fiber in men with lower urinary tract symptoms (LUTS) secondary to BPH [39]. A total of 201 men were included in the study with a mean follow-up time of 5.8 months. All clinical parameters (IPSS, $Q_{max}$, PVR, QOL, prostate volume, and PSA) had statistically significant improvements as early as one month postoperatively ($P < 0.001$) except PVR ($P = 0.001$) [39].

Lee et al. conducted a retrospective analysis on 384 patients who underwent PVP using the 180 W XPS laser [40]. The purpose of this study was to evaluate any intraoperative or postoperative complications in patients with ongoing platelet aggregation inhibition, and oral anticoagulation [40]. Following the procedure all clinical parameters such as IPSS, QOL, $Q_{max}$, and PVR improved in both those on and those off anticoagulation [40]. At 2 years follow-up there were no significant differences between the two groups.

A few studies over the years have evaluated the 180 W laser system in comparison to the 120 W system. One study by Ben-Zvi et al. looked at the comparative effectiveness of these two laser therapies in 200 patients [41]. Eighty patients were treated with GreenLight HPS 120 W and 120 patients with GreenLight XPS 180 W. Mean operating time was shorter for those in the 180 W group (43 vs. 79 minutes). Furthermore, postoperative characteristics such as IPSS, QOL, and PVR were comparable. There were no reported differences between the groups in terms of a 30-day complication rate. Patients receiving the 180 W laser treatment had a statistically significant reduction in PSA (54% vs. 79%, $P < 0.01$) [41]. Both systems proved to be safe and effective in treating BPH obstruction. However, results of the 180 W XPS laser system suggest a more cost-effective treatment and efficient tissue removal due to shorter operating times, fiber use, and the reduction in PSA [41].

Hueber et al. conducted a global, multicenter study to evaluate the use of the 120 W and 180 W laser systems [42]. Across seven international centers, 1187 patients underwent 120 W HPS and 622 patients underwent 180 W XPS. Similarly, the 180 W laser system had a lower operating time (53 vs. 80 minutes $P < 0.01$) [42]. The larger the prostate volume the more increased the use of fiber, operating time, and laser energy. When these results were stratified according to prostate volume, researchers found that the XPS system had significant advantages over the HPS system in all operative parameter regardless of the prostate size ($P < 0.01$) [42].

In a prospective multicenter randomized controlled trial known as the GOLIATH trial, researchers investigated the noninferiority of the 180 W GreenLight XPS to TURP by evaluating patients’ IPSS and maximum flow rate at six months postoperative [43]. A total of 281 patients with benign prostatic obstruction (BPO) from 29 centers across nine European countries were enrolled in the study [43]. After randomization and those lost to follow-up a total of 134 patients received XPS and attended the six months follow-up visit. Similarly, 131 patients were assigned to TURP and attended the six months visit. At baseline, patient demographics and urodynamic characteristics were similar in each treatment group. When evaluating the primary objectives and outcomes, Bachmann et al. found the end points at six months not to be significantly different between those who had received XPS and those who had received TURP. The noninferiority was met at a $P$-value of 0.002 [43]. Furthermore, researchers found both treatment groups were consistent in their ability to make improvement in IPSS over the six-month follow-up period (XPS = 6.8; TURP = 5.6) [43]. The same noninferiority was met for $Q_{max}$ at six months with XPS = 23.3 and TURP = 24.2 ($P = 0.002$), which demonstrated comparable results in both arms [43]. At six months, patients in both treatment arms showed similar complication-free rates with XPS = 87.3% and TURP = 83.2% ($P = 0.019$) [43]. During the follow-up portion of the study, the overall complication-free rate was higher for those who had received XPS.

Although perioperative characteristics were generally comparable across treatments, researchers found patients in the XPS arm had a shorter length of catheterization, shorter hospital length stay, and a shorter time until their health was stable ($P < 0.005$) [43]. Functional results and efficiency parameters demonstrated QOL, IPSS, PVR, and prostate volume were all significantly decreased at the six-month follow-up for both treatment arms. At six months, prostate volume between groups had a $P$-value of 0.079 [43]. Over the course of the trial, 47.8% of XPS patients and 53.4% of TURP patients were free of treatment-related adverse events. A total of 117 adverse events were reported in those receiving XPS and 98 in those who received TURP. Of these adverse events, in each group the most common events documented were bleeding, urinary incontinence, and storage symptoms.

The GOLIATH trial demonstrated the noninferiority of XPS to TURP and short-term efficiency. This large prospective study showed the comparability of XPS in improving IPSS, $Q_{\max}$, and prostate volume reduction in men with LUTS due to BPO. At 2-year follow-up, Thomas et al. found that noninferiority of the procedures in the clinical parameters and complications was sustained, and that 83.6% of patients in the GreenLight XPS group and 78.9% of those in TURP remained complication-free through the 2-year follow-up [44]. Prostate volume reductions were comparable in both arms of the study [44].

Valdivieso et al. discovered in patients undergoing GreenLight XPS 180 W LBO PVP to treat BPH that increasing the energy level of the laser was able to significantly reduce PSA level by >50% [45]. These results were durable at 6, 12, and 24 months postoperative. Despite this reduction, functional outcomes showed no differences at the 2-year follow-up time point.

Altay et al. investigated the safety and efficacy of the 180 W XPS laser in men with prostates larger >80 ml [46]. A total of 68 men underwent the procedure and had follow-up at 3, 6, and 12 months postoperatively. Significant improvement was seen in IPSS, $Q_{\max}$, and PVR at 3, 6, and 12 months ($P < 0.001$) [46]. At 12 months, the average prostate reduction was 40.5%. For men with larger prostates the 180 W laser system proved to be safe and effective in treating BPH.

Since the GOLIATH trial, recent studies have evaluated the outcomes of the PVP procedure in men with large prostates [47]. In another study by Hueber et al., researchers conducted a multicenter trial to evaluate the safety and efficacy of the 180 W system [48]. A total of 1196 patients were treated and follow-up lasted for 24 months. Those patients with a prostate larger than 80 ml had a significantly higher rate of conversion to TURP when compared to those with a prostate size lower than 80 ml (8.4% vs. 0.6%, $P < 0.01$) [48]. All parameters such as IPSS, QOL, $Q_{\max}$, and PVR were significantly improved across both groups. This procedure further proved to be safe and efficacious for men independent of their prostate size.

## Patient preparation

Many patients today are routinely taking aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and other medications that may affect platelet function. Others may be actively receiving chronic anticoagulation with agents such as coumadin. Although these patients may have raised concerns in the era of electrocautery TURP, the hemostasis associated with laser prostatectomy allows select patients to be treated without stopping or changing their medical regimen [27, 49, 50]. However, the risks of treatment on active anticoagulation therapy should be clearly stated to the patient, as the risk of bleeding will always be higher while on anticogulation medication than off it.

Age-appropriate patients should be screened with both digital rectal examination (DRE) and serum PSA levels as per AUA guidelines [51]. Prostatic abnormalities may be evaluated with transrectal ultrasound and biopsy as indicated. Such screening is important in laser prostatectomy since pathology is not adequately sampled for histologic examination [52].

A minority of patients with bladder outlet obstruction due to BPH will present with active urinary tract infection or significant pyuria. This should be treated prior to laser prostatectomy, especially since potential coagulated, nonperfused, necrotic tissue can remain *in situ* postoperatively and may become seeded with bacteria in the presence of active infection. For the typical patient who presents with sterile urine, routine antibiotic prophylaxis is recommended prior to laser resection of the prostate.

The consent for laser prostatectomy is very similar to that obtained for other transurethral operations. Patients are informed that they will require an anesthetic, and of potential complications associated with any invasive urologic procedure, such as bleeding, urinary tract perforation, infection, urinary incontinence, erectile dysfunction, retrograde ejaculation, and urethral stricture or bladder neck contracture. Finally, the patient should be informed that remaining tissue can grow back, causing recurrent voiding symptoms, and that additional prostate surgery may be required.

## Preoperative preparation

Standard patient positioning in the dorsal lithotomy position with sterile draping and cleansing preparation is used, as for routine cystoscopy or any other transurethral operation. A properly functioning laser source and compatible laser delivery fiber are required. Laser safety should be of paramount importance in the operating room. Laser energy can cause significant thermal injury to human tissues, including irreversible retinal damage. All operating room personnel and the patient must wear proper eye protection. Operating room windows should be covered to prevent the inadvertent passage of stray laser light; doors should be appropriately marked to warn outside personnel that laser energy is in use. When the laser is not being actively used, and in particular when the fiber is removed from the cystoscope and the working end lies free on the operative field, the surgeon should remove their foot from over the laser pedal and nursing personnel should close the shutter on the laser machine to prevent accidental firing, which could lead to drapes being ignited and patients burned with the beam.

## Technique

Laser prostatectomy requires local, regional, or systemic anesthesia due to the pain associated with acute laser burns to the prostatic urethra. Leach et al. have in addition described a transperineal injection technique using lidocaine and bupivacaine to achieve local prostatic and pudendal nerve blockade, which when combined with intravenous sedation may also provide adequate anesthesia to perform laser prostatectomy [53]. When using injection anesthetic, it is important to be aware of the maximum dosage as overdosing may result in significant adverse events.

Cystourethroscopy is performed with a standard 21–26 Fr cystoscope. However, laser prostatectomy requires the specialized continuous-flow cystoscopes that have been designed for laser prostatectomy. If continuous-flow irrigation is inadequate to provide a clear field of vision, a suprapubic catheter can be placed to provide continuous intraoperative irrigation flow as well as postoperative urinary drainage. Since clinically negligible fluid absorption occurs during laser prostatectomy, special irrigation solutions are not required; normal saline is relatively inexpensive, is the fluid of choice compared to osmolar solutions, and provides good visualization. Room temperature, rather than warmed, irrigation provides cooling for the laser delivery fiber, limiting thermal damage as well as prolonging the usable lifespan of fibers. The irrigant is hung 30 cm above the bladder and allowed to flow under gravity. Suction irrigation to the outflow port should be avoided, as it is unnecessary and may increase the risk of inadvertent bladder perforation. The prostatic anatomy is carefully assessed and the prostatic urethral length from the bladder neck to the proximal aspect of the verumontanum is inspected. The laser fiber is then passed through the working port of the cystoscope and visualized in the prostatic urethra in preparation for beginning laser application.

Laser energy is directed at the locations along the prostatic urethra that are obstructed, such as medial, lateral, and anterior lobe tissue. A systematic and aggressive approach to laser prostatectomy will ensure complete laser treatment of all obstructive tissue elements. Laser resection may begin with either the medial or lateral lobes, but should always begin proximally and be continued distally, working away from the bladder neck and toward the verumontanum; after the proximal prostate near the bladder neck is opened by superficial tissue vaporization, there will be improved irrigation flow for the more distal laser treatment.

Laser energy may be applied in a continuous fashion over an area, barring excessive tissue resection (e.g. perforation). PVP, the technique described for 532 nm laser prostatectomy, is often described as "painting" systematically over the surface of the prostate until a TURP-like cavity is formed. However, a more correct analogy is "mowing the lawn," since a systematic sweeping technique is utilized to remove tissue in layers. In addition, the optimal distance from the tissue is small, within one fiber cap in a noncontact technique. Excellent vaporization results in a stream of bubbles, which represent the steaming away or vaporization of tissue. The laser source is used first to vaporize the median lobe to the level of the trigone. Once a channel has been created that allows adequate irrigation, the lateral lobes are next vaporized. This is followed by apical vaporization. At the end of the PVP procedure, a cavity should be present where the adenoma once was. If bleeding is encountered during PVP, the laser setting is lowered to allow coagulation instead of vaporization and the target area is coagulated.

Optimally, the fiber tip should be held just off the mucosal surface such that a clear plane of water stands between the tip and tissue; by moving the beak of the cystoscope close to the fiber tip, the scope can be used to hold tissue away from the tip in many instances. In addition, resecting proximal before distal prostate tissue aids in freeing tissue from the fiber. Finally, when all else fails and occlusive prostate tissue must remain in contact with the metal mirror during treatment, a very slight vibratory motion of the fiber tip (i.e. no more than 1–2 mm longitudinal oscillation), combined with good water flow can keep tissue from adhering to the metal fiber tip. For all fibers with a mirror reflecting mechanism, routine cleaning of the fiber is recommended. The build-up of spattered particulate on the fiber surface during treatment can cause superheating with fiber degradation. Prophylactic cleaning between each laser application and ensuring adequate room temperature water flow throughout the duration of each individual laser application are the most important means of preserving fiber integrity.

### Vaporesection/enucleation techniques

Once the basic technique is mastered, the 532 nm laser can be used to enucleate, vaporize, and resect tissue. This technique is referred to as transurethral laser enucleation of the prostate (TLEP). The procedure allows pathology to be collected and analyzed, improves surgical debulking of obstructive prostate tissue, and increases tissue removal efficiency, shortening operative times. This advanced technique is essentially a hybrid between TURP, laser vaporization, and enucleation utilizing the 532 nm laser [54]. The technique can be quickly learned by those with prior transurethral resection skills. However, there is a learning curve to transurethral navigation of complicated and long anatomy that is clearly related to experience of transurethral resection anatomy [54]. Pathology is provided and resection/enucleation is very complete. An incision is made through the median lobe until the bladder neck fibers can be seen. Sweeping motions with the side-fire laser fiber ensure that a wide channel is made, which allows for strong flow of cooling irrigant. Incisions are made lateral to the median lobe while visualizing ureteral orifices to ensure their safety. The intervening tissue between the incisions is divided into smaller chips. Multiple vaporization–enucleation–incision cycles are made down to the fibers of the prostatic capsule. The intervening tissue is vaporized, incised, and pushed into the bladder. Apical tissue proximal to the verumontanum is carefully ablated with care to preserve the verumontanum.

Son et al. investigated the use of the HPS 120 W laser, which utilizes a modified vaporization–resection technique, known as the Seoul technique [54, 55]. The procedure involves “vaporization of the prostate along the previously outlined margins and retrieving the resulting wedge-shaped prostatic tissue” [55]. This was a retrospective study including 104 patients with BPH who had undergone PVP and a prostate volume >40 ml. Sixty-four patients received the Seoul technique and 40 patients received vaporization only. $Q_{\max}$, PVR, IPSS, and QOL scores were evaluated for both groups at 1, 3, 6, and 12 months postoperatively. These parameters after PVP compared to baseline significantly improved ($P < 0.05$) [55]. Those patients receiving the Seoul technique showed significant reduction in prostate volume per operating time, as well as lasing time and laser energy ($P < 0.05$) [55]. In both groups the complication rates were low. Son et al. proved the Seoul technique for PVP has good short-term efficacy and is a safe treatment for patients with BPH. Furthermore, this procedure shortens operating time, lasing time, and energy. It allows urologists to preserve prostatic tissue for pathological evaluation.

Gomez Sancha et al. described the use of a high-power LBO en bloc enucleation to treat BPH in patients with larger prostates [56]. The laser equipments used were a GreenLight HPS 120 W and a GreenLight XPS 180 W, with a 2090 fiber and a MoXy fiber, respectively. Patients are first placed in a lithotomy position. Next, a “26-F continuous flow resectoscope is inserted in the uretha avoiding urethal or prostatic trauma or bleeding” [56]. In stage 1, the anatomic photoselective vaporization creates a central cavity in the prostate using a standard vaporization technique. Next, stage 2, a hybrid vapoenucleation technique is employed to create grooves in order to reach the surgical capsule also known as photoselective vapoenucleation. Finally, stage 3 includes the photoselective en bloc enucleation to resect the tissue and to deliver the “adenoma ‘en bloc’ into the bladder” [56]. This technique proved to be efficient, producing “excellent vaportization and coagulation properties in prostatic tissue,” especially in larger prostates [56].

## Postoperative care

At the conclusion of laser prostatectomy, a urinary catheter is left in place to provide drainage. A suprapubic catheter may be left in place to facilitate early or repeated voiding trials if desired. Many centers routinely discharge patients following complete recovery from anesthesia, making laser prostatectomy essentially an outpatient procedure. Catheter drainage to a urinary leg bag if necessary can be maintained and easily mastered by most patients. Patients should note that if they have a history of preoperative urinary retention or detrusor hypocontractility with a large preoperative residual urine volume, they may require longer catheterization times. Postoperative management with suprapubic catheter drainage in these individuals may be ideal to allow easy or repeated voiding trials if needed.

Following catheter removal, immediate improvement in voiding may not occur. This may be due to inefficient vaporization resulting in a greater degree of coagulation necrosis. In fact, patients may have little or no change in voiding during the first 1–2 weeks postoperatively and they may experience slightly worse symptoms while the treated prostatic transition zone sloughs. During this time, patients may note a cloudy, white appearance in the urine, caused by proteinaceous material from the dissolving prostate; others may note the passage of minute particulate matter in the urine. This phase of active tissue dissolution can be associated with symptoms of mild dysuria, which are usually relieved by NSAIDs as needed. Phenazopyridine appears to be much less effective for this syndrome, but may also be used as needed. By 4–6 weeks following laser prostatectomy, most patients begin to note a significant improvement in their voiding pattern. Improvement will continue in most men for an additional 6–12 weeks and longer, until maximum voiding outcome is achieved. By three months, voiding outcomes are similar to those expected after electrocautery TURP. With the more efficient vaporization and limited coagulation necrosis with high-power 532 nm laser applications, improvement may occur as soon as a few days to a week following application, with minimal dysuria.

Because of the superior surgical hemostasis associated with laser prostatectomy, significant restrictions on physical activity are not as limiting, even in the immediate postoperative period. After catheter removal, sexual intercourse is allowed immediately if desired, but a wait of about one month is recommended postoperatively. Patients should be warned of the possibility that the ejaculate may be temporarily dark or bloody. The most significant risk from activity is hematuria, which is usually clinically insignificant but can on occasion result in clot retention requiring transient catheterization and irrigation.

Serum levels of PSA rise approximately 10-fold following laser prostatectomy, generally peaking on the first postoperative day [57]. This seemingly corresponds with the height of capillary leakage and tissue edema after the laser burn injury. By three months, we have observed serum PSA levels to be at or below baseline in more than half of our patients. Approximately 90% have returned to or are below baseline values by six months [58]. Those with significant and persistent elevations of PSA levels beyond this time probably should be evaluated for subclinical prostatic infection or occult carcinoma.

## Complications

All published studies have reported decreased morbidity associated with laser prostatectomy as compared with traditional surgical approaches. Bleeding is the main complication of traditional electrocautery TURP, often necessitating transfusion and causing associated problems such as clot retention, premature termination of the procedure, and inadequate relief of obstruction [59]. Bleeding can also result in continuous catheter irrigation and complications, such as stricture secondary to traction on the Foley catheter. Rarely, uncontrolled bleeding can even require open packing of the prostatic fossa. Poor visibility because of bleeding is also thought to be a cause of sphincteric damage and incontinence resulting from TURP. The incidence of hemorrhage requiring blood transfusion is 3.9% and this increases twofold if the amount of resected tissue exceeds 45 ml or if the resection time is longer than 90 minutes. In contrast to TURP, which cuts across the prostatic parenchyma and opens prostatic venous sinuses, laser prostatectomy seals blood vessels as it coagulates the transition zone and prevents both absorption of irrigating fluid and hemorrhage; the hemostasis associated with laser prostatectomy is thus superior, with even multiple studies of anticoagulated patients undergoing resection without bleeding complications [27, 49, 50].

Irrigant fluid absorption during electrocautery TURP results in a 2% incidence of transurethral resection syndrome because of dilutional hyponatremia, glycine-induced ammonia intoxication, or the direct toxic effect of glycine [59]. As with bleeding, fluid absorption increases with larger glands and longer resection times. Laser prostatectomy minimizes this complication, again through its sealing zone of coagulative effect on tissue which prevents fluid absorption.

The incidence of urethral stricture after electrocautery TURP is 3.1%; if bladder neck contractures are included, this figure approaches 5%. Stricture formation is thought to be secondary to trauma induced by the large size of the resectoscope as well as the use of low-intensity, coagulating current, which penetrates deeper into tissue than cutting currents. Since laser procedures do not use electrical current, the cystoscopes utilized are smaller in size, and the overall operative time is usually shorter, the incidence of stricture is lower. The incidence of reoperation for residual obstructive tissue is difficult to determine since most published series of laser prostatectomy have documented initial experiences only with this technology. Our experience is that the incidence of strictures and bladder neck contracture is higher in patients with bladder dysfunction or bladder diverticulum, or following long procedures utilizing larger diameter scopes.

Postoperative infections may also occur after TURP. The incidence of urinary tract infection following TURP is 15.5% (median) while epididymitis occurs in 1.2% [59]. Urinary tract infections have been reported in 1–20% of patients following laser prostatectomy and epididymitis in 5–7% of patients [5, 60–64]. The treatment of such infections may be more problematic in laser prostatectomies secondary to the residual necrotic prostate tissue that remains *in situ* for several weeks after laser coagulation. When this occurs, the most common manifestation is subacute prostatitis, characterized by significant and persistent irritative voiding symptoms, with mild prostatic and/or epididymal tenderness on examination, persistent pyuria, and positive urine cultures. Two cases of frank urosepsis have been reported following laser prostatectomy, both requiring TURP to remove infected necrotic prostate tissue [65]. Aggressive antibiotic therapy is therefore warranted in these patients.

Finally, retrograde ejaculation represents another potential side-effect of electrocautery TURP, occurring in up to 90% of patients. The incidence of impotence following electrocautery TURP ranges from 3.4% to 32% [66, 67], while its overall incidence following all forms of laser prostatectomy is rare.

Since its inception in 2010, the 180 W laser system has demonstrated its ability to be effective when treating patients with BPH. One study found some of the most common complications following this procedure to be: urinary tract infections (9%), dysuria (22.8%), incontinence (11.8%), and stricture (5.1%) [43]. Hueber et al. found complication rates to be similar across prostate groups with the incidence of bladder neck or urethral stricture ranging from 3.9% to 4.6% ($P = 0.66$) [48]. Rates of patients experiencing urinary tract infections postoperatively were 4.9–5.1% ($P = 0.90$) [48]. Another possible complication is resultant retrograde ejaculation. Altay et al. reported a 41.8% incidence of retrograde ejaculation, which was lower than the GOLIATH trial which reported a 64.7% incidence [43, 46]. The largest concern with using the GreenLight system has been the conversion to traditional TURP. This is due to intractable bleeding occurring in men with larger prostates. A study by Bachmann et al. reported a conversion rate of 16% in their cohort [39]. In the study by Hueber et al. the only major complication was the conversion rate to TURP for patients with prostates >80 ml as compared to those <80 ml (8.4 vs. 0.6%, $P < 0.01$) [48]. In another study, the conversion rate to TURP was 7.3%, with these patients requiring TURP loop for hemostasis [46].

## Contraindications

There are scenarios when laser coagulation of the prostate is not indicated, and where electrocautery resection may still be advantageous. These include certain cases of bladder cancer, in which acute electrocautery resection of the bladder neck or enlarged prostate may be necessary to access tumors behind the bladder neck, especially anteriorly. Rarely, this maneuver may also be needed for ureteroscopic access. In cases in which histologic assessment of the prostate for invasion by transitional cell carcinoma is required for staging of malignancy, electrocautery resection is indicated. Finally, in the uncommon case of chronic, recurring prostatitis where electroresection of the prostate may be used to remove infected tissue and/or prostatic calculi, laser prostatectomy cannot substitute for an aggressively performed TURP. In the rare case of a prostatic abscess that must be unroofed transurethrally, electrocautery resection may also be indicated.

## Conclusions

Laser prostatectomy has proved to be a safe and efficacious surgical intervention to relieve symptomatic bladder outlet obstruction. Overall morbidity contrasts favorably with standard surgical approaches. Moreover, laser technology is generally accessible to the practicing urologist. These attributes have positioned laser prostatectomy as an accepted and sometimes preferred surgical treatment of bladder outlet obstruction secondary to BPH.

See accompanying Video 146.1.

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## 147

# Thulium Lasers

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## Animal studies

The first animal studies in the field of urology with thulium:YAG (Tm:YAG) lasers were published by Theisen et al. in 2003 [1]. They demonstrated the tissue-cutting ability of a Tm:YAG laser on a pig liver with coagulation zones of 0.8 mm or less [1]. El-Sherif and King tested the ablation abilities of thulium fiber lasers on various soft tissues *in vitro*, such as muscle, cartilage, and liver [2].

In 2005, Fried reported the vaporization capabilities of a thulium fiber laser using canine prostates as an *ex vivo* model [3]. He used a mean of 88.5 ± 2.3 W of a 110 W high-power laser at a wavelength of 1.91 µm. Thus, his results may not be absolutely comparable with the commonly used Tm:YAG lasers working at 2013 nm, since absorption coefficient and penetration depth depend on wavelength and even small changes may have a relevant impact (Figures 147.1 and 147.2). With the setting used by Fried, the laser works in both a continuous wave (cw) and a chopped mode. The focus of interest in this study was the measurement of the tissue vaporization rate in a given time, which was 0.83 ± 0.11 g/min at 88.5 W laser power [3].

Thulium laser settings at 26 W were not powerful enough, however, to make efficient and accurate incisions [4, 5]. The zone of thermal damage had a wide variance of 500–2000 µm in two studies [4, 5]. Fried and Murray stated that a higher power laser could be used to deliver more energy during a shorter pulse duration, with the intention of reducing collateral tissue damage. Fried confirmed his original data in further *ex vivo* studies in canine prostates, and additionally in animal ureters and bladder neck tissue [3–5]. He was not concerned about unacceptable collateral tissue damage, which was documented to be several hundred microns of thermally damaged tissue [4].

Whereas the first *ex vivo* studies were with soft tissue, Fried also published data on urinary stone fragmentation [6]. A cw high-power thulium fiber laser operating at a wavelength of 1.94 µm was modulated to operate in a pulsed mode with an output pulse energy of 1 J, pulse duration of 20 ms, and repetition rate of 10 Hz. The fragmentation time to reduce various stones into particles of less than 2 mm was measured. In principle, a high-power cw thulium fiber laser, when operated in pulsed mode, could fragment both soft and hard urinary stones, not accounting for the time taken.

## Clinical experience with thulium laser treatment of the prostate

Clinically, thulium lasers were studied first in otolaryngology, pneumology, gynecology, gastroenterology, and neurosurgery [7–9]. An early paper in the field of urology was published in 2005 by Xia et al. [10]. They performed a low-power vaporesection of benign prostate hyperplasia (BPH) using a 50 W Tm:YAG laser [10]. Subsequently, laser treatment of the prostate has evolved to be the main field of thulium laser applications in urology (Figure 147.3).

### Vaporesection

Xia et al. reported their initial experience with the Tm:YAG laser on 30 patients using the so-called “tangerine technique” for BPH treatment [10]. They sliced the prostate in tangerine-like pieces *in situ* and extracted these mechanically with a syringe. The ability of the Tm:YAG laser to cut prostate tissue chips small enough

*Smith’s Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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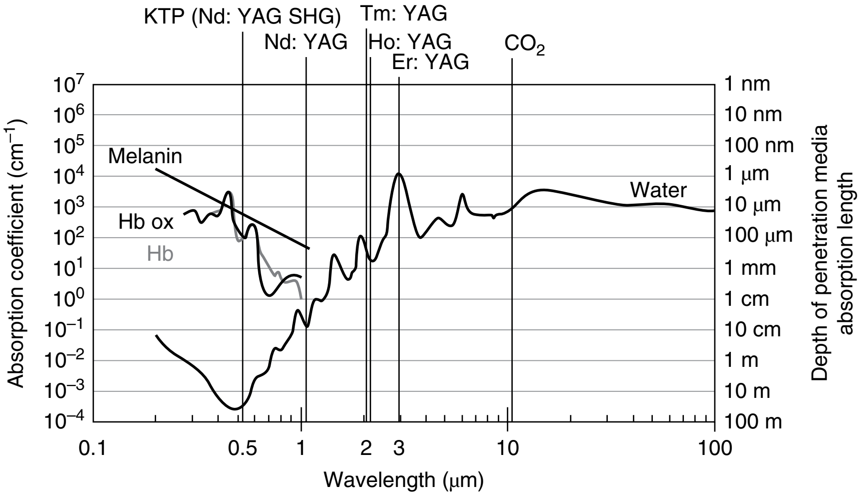

**Figure 147.1** Absorption spectrum for melanin, hemoglobin (Hb; oxygenated hemoglobin, Hb ox), and water in comparison to selected laser wavelengths and carbon dioxide.

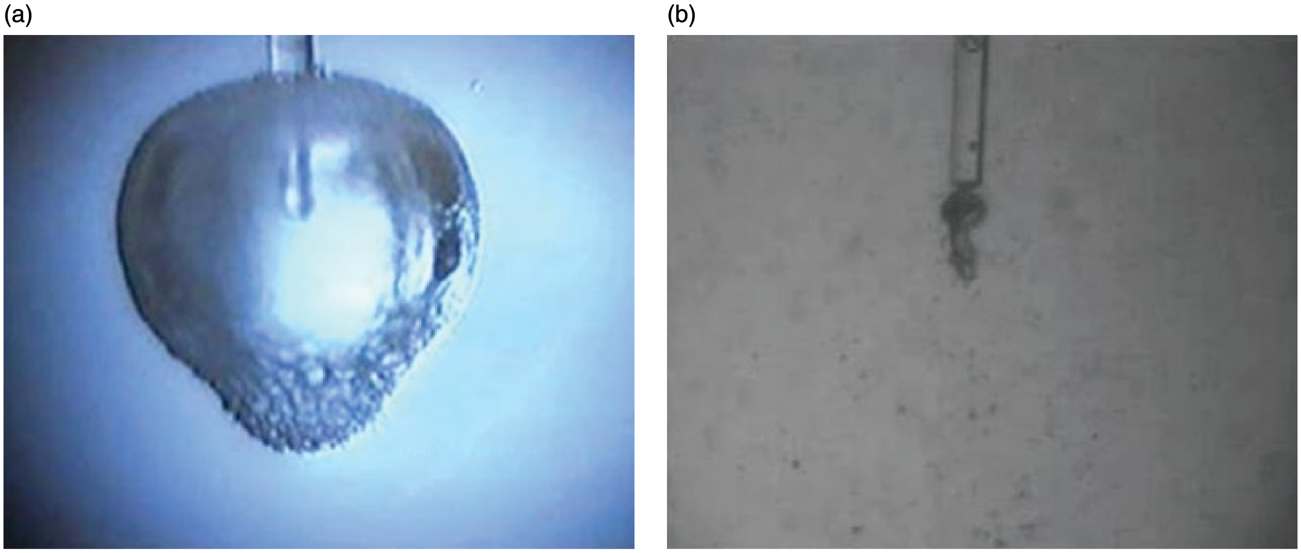

**Figure 147.2** (a) Large steam bubbles in a pulsed laser (holmium laser; 2 J, 32 W). (b) Small steam bubbles in a continuous wave laser (2 µm, 50 W).

for the resectoscope sheath was an important difference from the previously introduced lasers, especially the holmium:YAG (Ho:YAG) laser, which cannot cut or resect. This is the most important difference between thulium and holmium lasers, since the application and surgical techniques of thulium lasers in BPH treatment are very similar to those of holmium lasers.

The patients in this first paper by Xia et al. had a mean prostate volume of 58 ml, an average International Prostate Symptom Score (IPSS) of 19, and a maximum urinary flow rate ($Q_{\max}$) of 8.0 ml/s [10]. The Tm:YAG laser was used at 50 W. During a mean operating time of 56 minutes, an average of 1 g tissue was removed per minute. This tissue retrieval rate was in the range of contemporary holmium laser enucleation of the prostate (HoLEP) series of that time, which reported enucleation rates of up to 0.71 g/min [11]. In the first series by Xia et al., neither perioperative blood transfusions nor postoperative bladder irrigation were necessary [10]. The Foley catheter remained *in situ* for 1–3 days. Three months after surgery, $Q_{\max}$ (24.7 ml/s) and IPSS (7.1) had improved significantly. No cases of new onset of impotence were found. These data were confirmed at 1-year follow-up [12].

In 2007 Bach et al. reported their initial results with 54 patients being treated with 70 W Tm:YAG high-power vaporesection of the prostate (mean volume 30.3 ml) and the subsequent 1-year follow-up [13]. At that time, holmium laser enucleation of the prostate had already been described [14]. However, one disadvantage of the

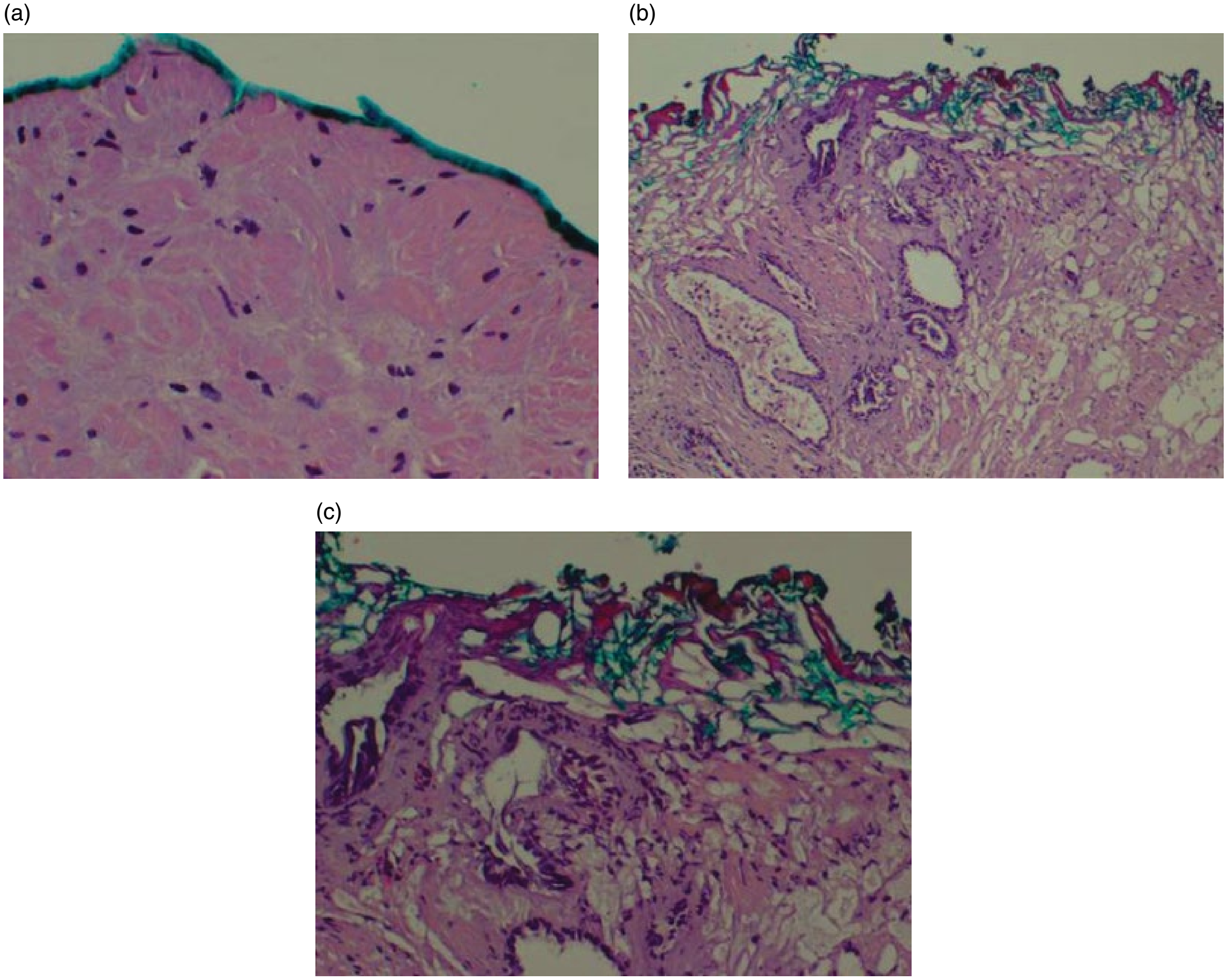

**Figure 147.3** Human prostate following treatment with a 70 W, 365 µm fiber thulium laser in contact mode. (a) Magnification × 20; (b) × 40; (c) × 100.

enucleation procedure was the difficulty in removing the tissue from the bladder: either a mechanical tissue morcellator was used for removal of the enucleated lobes off the bladder or the so-called "mushroom technique" [15]. In the latter, the prostate is left attached by a pedicle at the bladder neck and the tissue is then resected with a monopolar or bipolar loop into transurethral resection of the prostate (TURP)-like chips. Vaporesection is a protocol where small chips are produced with a Tm:YAG laser and washed out with a syringe, similar to the standard resection technique. In the series of Bach et al., mean preoperative $Q_{\max}$ was 8.1 ml/s after exclusion of 14 patients with acute urinary retention (AUR). In this first study, removal at a resection speed of 0.6 g/min was achieved, which increased with growing experience to 1.5 g/min. Mean catheter time was 1.7 days (range 1–3 days). Blood transfusions were not required in any patient. However, six patients had urinary tract infections (UTIs) with irritative voiding symptoms 1–2 weeks postoperatively, which required antibiotic therapy. At 1-year follow-up, no bladder neck stricture or urethral stenosis had occurred. IPSS, $Q_{\max}$, postvoid residual urine (PVR), and quality of life (QOL) had improved significantly at 1-year follow-up and continued to do so at 18 months follow-up [13, 16].

After these reports from clinical practice, a systematic *ex vivo* evaluation of the thulium laser was performed by Wendt-Nordahl et al. [17]. The ablation capacity and hemostatic properties were tested at different power settings in a previous well-established model of the isolated blood-perfused porcine kidney. Histologic examination of the ablated tissue was used to compare changes after thulium laser treatment with results after TURP and use of a 80 W potassium titanyl phosphate (KTP) laser. At a power setting of 70 W, the thulium laser achieved a higher tissue ablation rate (average 6.56 g in 10 minutes).

This is, of course, far more than is achieved in clinical practice, since no time is lost for surgical orientation. The KTP laser ablated 3.99 g of tissue in the same time, whereas with TURP 8.28 g was removed in 30 seconds. The bleeding rates were 0.16, 0.21, and 20.14 g/min, respectively. The corresponding depths of the coagulation zones were 264, 666.9, and 287 μm, respectively. In conclusion, this study showed that the thulium laser offered a higher tissue ablation capacity and similar hemostatic properties to the KTP laser, and in comparison to TURP the bleeding rate was significantly reduced. The smaller quantity of removed tissue compared to TURP was due to the fact that the thulium laser was used for vaporization only.

The first prospective randomized prospective trial was performed by Xia et al. [18]. One hundred patients were randomized into two groups: 52 underwent Tm:YAG laser resection using the tangerine technique mentioned above and 48 underwent standard TURP. Preoperative assessment included IPSS, QOL, $Q_{\max}$, PVR, International Index of Erectile Function-5 (IIEF-5), and urodynamic studies. Those parameters were re-evaluated at 1, 6, and 12 months. Catheterization time was significantly shorter in the laser group (45.7 vs. 84 hours; $P < 0.0001$). Blood loss was less in the laser group and hemoglobin was lower (0.92 vs. 1.46 g/ml; $P < 0.001$) than in the TURP group. IPSS, QoL, Qmax, PVR and IIEF-5 as well as urodynamic studies did not reveal any significant difference between the groups. Both groups benefitted from the respective interventions.

Results from a larger series of patients ($n = 200$), also with larger prostate sizes (up to 120 g), were published by Mattioli et al. [19]. They used a 70 W laser with bare-ended and side-firing laser fibers. Bare-ended fibers used with the cw thulium laser are applicable for all BPH protocols, such as vaporization, vaporesection, and vapoenucleation; however, side-firing fibers are used for vaporization only. Mattioli et al. advocated the use of both fibers. They used a laser that enabled switching with a foot pedal between the two modes, and preferred to resect first and vaporize thereafter. In patients with prostates smaller than 35 g, vaporization was performed; in those with prostates larger than 35 g vaporesection and/or vaporization was performed. Mean catheterization time was 16 hours (range 12–72 hours). The efficacy of the procedures was evaluated with $Q_{\max}$, PVR, and the IPSS questionnaire. The authors concluded that clinical outcome was comparable with TURP and the KTP and Ho:YAG lasers.

Szlauer et al. have published a DVD on the vaporesection procedure with a thulium laser [20]. This DVD shows the main steps of the technique as introduced by Bach et al. [13]. The laser fiber is moved semi-circumferentially from the verumontanum towards the bladder neck, thereby undermining tissue and cutting chips. Szlauer et al. reported the results from 56 nonconsecutive patients. The mean procedure time was 60 minutes, postoperative irrigation was necessary in 19 of 56 patients (29%), and the mean time of catheterization was 23 hours. The decrease of hemoglobin was at 0.2 mg/ml until the day of discharge. Mean $Q_{\max}$ improved from 8.1 to 19.3 ml/s ($P < 0.001$) and the PVR decreased from 152 to 57 ml ($P < 0.05$). This study included the first report of the need for blood transfusions (two patients, 3.6%) after thulium laser procedures. Two patients needed recatheterization postoperatively. After a mean follow-up of nine months, IPSS improved from 19.8 at baseline to 8.6 ($P < 0.001$). During the learning curve, persisting obstructive symptoms in four patients necessitated a second procedure. Szlauer et al. chose TURP, while a few other authors have reported satisfactory second procedures for persisting complaints utilizing the Tm:YAG laser in a resection technique [21]. During the learning curve for a new technique, such as any laser procedure, it is appropriate to fall back on the standard procedure. Two patients in this series developed postoperative complications (one urethral stricture and one bladder neck contracture).

Over time, vaporesection has become less important as there is a strong trend towards enucleation techniques – no matter what energy source is used. But vaporesection still has its uses in thulium laser treatment of the prostate as it is an important step during the learning curve from vaporization to complete enucleation.

## Vapoenucleation

Following their work on vaporesection with thulium lasers, Bach et al. looked at holmium laser enucleation and implemented thulium lasers for this technique (so-called vapoenucleation of the prostate) in 2009 [21]. This represented a development because vaporesection and, indeed, any kind of pure vaporization, was limited to smaller glands, as the amount of tissue that can be removed by vaporization techniques is time limited, necessitating prolonged operating times with increasing prostate volumes. It became obvious that for larger glands tissue removal using mechanical morcellators must be an integral part of the procedure. Bach et al. again used a 70 W laser to remove the tissue, as in the previously described three-lobe technique in HoLEP [22], in 88 patients with a mean prostate size of 61.3 g. In brief, the procedure starts with the marking of the distal resection border close to the verumontanum. Turner–Warwick-like incisions down to the surgical capsule are made at the 5 and 7 o'clock positions up to the previously marked distal resection border. Then the entire median lobe of the prostate is enucleated. After that, the first lateral lobe and consequently the second lateral lobe are enucleated and positioned into the bladder for morcellation. After enucleation, tissue is morcellated within the bladder [22].

In 2015, Kim et al. published a variation of enucleation, the "all-in-one" technique [23]. The mean operative time was 82.1 ± 33.3 minutes and the mean enucleation and morcellation times 52.7 ± 21.7 minutes and 8.2 ± 7.0 minutes, respectively. The mean resected tissue weight and decrease in hemoglobin were 36.9 ± 24.6 g and 0.4 ± 0.8 g/dl, respectively. These results are consistent with two- or three-lobe techniques [23].

Bach et al. demonstrated the feasibility of laser enucleation of the prostate using the thulium laser, as previously shown for Ho:YAG lasers [21]. The authors discussed the advantages of this laser in comparison with open simple prostatectomy and Ho:YAG laser enucleation [21]. The operative time was 72 minutes, of which laser time (beam on) was 32.4 minutes. The remainder of the operative time, as in any other transurethral procedure, was taken up by instrumentation, catheterization, and morcellation. According to the authors, a suprapubic trocar could be used to perform a low-pressure procedure. An average of 127 kJ of laser energy was applied. An average of 31.7 g of prostatic tissue was available for histologic examination. The percentage of tissue lost through vaporization was estimated to be 30%, and it should be noted that the amount of retrieved tissue is often underestimated because of this. The average Foley catheter time was the same as in other laser procedures, being 2.1 days. Three patients (4.2%) had persistently high residual urine after removal of the Foley catheter and were discharged with suprapubic catheter *in situ*. At 1-year follow-up, improvements in urodynamic parameters appeared to be durable, with an increase in $Q_{\max}$ from 3.5 to 23.3 ml/s ($P < 0.001$) and decrease in PVR from 121 to 33 ml. IPSS decreased from 18.4 to 6.8. Early complications were UTI in 6.8%, hematuria in 5.6%, and the need for immediate retreatment in 2.2%. One patient developed an urethral stricture. Postoperative dysuria was reported in 27%, a rate similar to that with any other ablative procedure in the prostate [24]. At 48-month follow-up, $Q_{\max}$, PVR, IPSS, and QOL were still significantly better compared with baseline ($P < 0.001$). Bladder neck contractures and urethral strictures developed during follow-up in 1.6% and 0.8% of the patients, respectively. No patient had to be retreated during follow-up for recurrent prostatic tissue [25].

A slight variation of thulium vapoenucleation of the prostate (ThuVEP) is called thulium laser enucleation of the prostate (ThuLEP). ThuLEP is blunt transurethral anatomical enucleation of the prostate using the beak of the resectoscope with Tm:YAG laser support [26]. A large series with 1080 patients treated with ThuVEP confirmed the previously published data; median prostate size was 51 ml and median operation time was 56 minutes. Median enucleation time in this group was 32.5 minutes. Median resected tissue weight was 30 g, confirming that 60% of tissue should be resected. Incidental carcinomas were detected in 5.5% of the patients. $Q_{\max}$ (8.9 vs. 18.4 ml/s) and PVR improved significantly at discharge ($P < 0.001$). Clavien 1 and 2 complications occurred in 24.6% and Clavien 3 in 6.6%. There was only one Clavien 4 complication (0.09%). The overall complication rates decreased significantly over time with increasing individual and institutional experience of the ThuVEP procedure [27].

Open prostatectomy has been considered the standard technique for larger glands. It is effective and durable, but the rate of severe complictions is high. In one of the last large series of open prostatectomy, Serretta et al. in 2002 reported a complication rate of 15% [28]. Although the average overall complication rates for open prostatectomy and Tm:YAG laser prostatectomy appear to be comparable, the rates of severe unexpected complications, bleeding-related complications, and transfusion drop significantly with Tm:YAG laser prostatectomy. This is particularly important because surgical treatment for BPH tends to be performed in an older age group. Transfusion rates of 8.2–26.5% have been reported with open prostatectomy [29]. In a recent series of 2648 patients, Bach et al. differentiates different groups of prostate sizes and compares their blood loss during the respective procedure (Table 147.1) [30]. The infection rate was 8.6% in open prostatectomy, whereas in a series of 687 patients treated with thulium laser, Netsch et al. reported an infection rate of 4.66% [31].

To overcome these bleeding-related complications with open prostatectomy, HoLEP was introduced as a size-independent technique for BPH treatment [14]. Elzayat and Elhilali reported a blood transfusion rate of 1.3% after HoLEP in patients with BPH and a mean prostate volume of 126 ± 45.1 ml [32]. To overcome some disadvantages of the Ho:YAG laser, thulium lasers are now used for the same indication, mimicking the HoLEP technique. The main advantage of the thulium laser is the cw-mode that allows clear cuts and therefore better vision of the surgical site [21, 24]. The incision in the tissue is clear and the penetration depth is shallow. Thus, the surgeon can cut at any desired point and is not dependent on finding the exact layer of the surgical capsule between the adenoma and peripheral zone [21, 24]. If this path is lost, it may be easier to return to the preferred layer using the thulium laser or stop the enucleation procedure if the layer of enucleation is lost and change to vaporization of the tissue. For those in the early stages of learning the enucleation protocol, this may be a major problem with any other kind of laser. Clear cuts with a thulium laser therefore lead to a shorter learning

**Table 147.1** Transfusion rate in relation to resected tissue in transurethral resection and thulium vapoenucleation of the prostate, stratified according to preoperative transrectal ultrasonography volume.

| Preoperative TRUS volume | Procedure | Resected tissue (g) | Transfusion rate (%) |
|---|---|---|---|
| <40 ml ($n$ = 790) | TURP | 14.6 ± 27.5 | 1.3 |
| | ThuVEP | 15.9 ± 11.8 | 1.7 |
| 40–79 ml ($n$ = 1102) | TURP | 31.0 ± 34.6 | 2.8 |
| | ThuVEP | 35.1 ± 18.1 | 2.0 |
| ≥80 ml ($n$ = 480) | TURP | 38.5 ± 23.2 | 7.1 |
| | ThuVEP | 70.8 ± 33.6 | 7.0 |

TURP, transurethral resection of the prostate; ThuVEP, thulium vapoenucleation of the prostate; TRUS, transrectal ultrasonography.
Data presented as mean ± standard deviation or % where appropriate.
*Source:* Bach T et al. Prospective assessment of perioperative course in 2648 patients after surgical treatment of benign prostatic obstruction. *World J Urol* 2016;35(2). Reproduced with permission of Springer-Verlag.

curve [33]. El-Hakim and Elhilali reported that a minimum of 50 cases have to be undertaken to achieve a reliable learning curve for HoLEP [34]. For thulium laser treatment with either simulator or mentor-based training a learning curve of 50 and 32 patients, respectively, seem to be sufficient to achieve safety during the procedure [35, 36].

The results of long-term follow-up for HoLEP, which is the earlier introduced technique, are available [37], but there is no reason to presume that outcomes for thulium laser enucleation would differ. Netsch et al. submitted an abstract for publication with a prospective randomized trial comparing HoLEP with ThuLEP [38]. In this prospective randomized trial, 96 patients were enucleated with either one of the two lasers, and no difference was found in any of the evaluated parameters.

In conclusion, both procedures give equivalent and satisfactory immediate micturition improvement with low perioperative morbidity. Thus, thulium laser enucleation appears to be repeating the experience with Ho:YAG lasers, but with an improvement in the ability to resect and consequently a shorter learning curve. With both ThuLEP/ThuVEP and HoLEP, simple open prostatectomy becomes obsolete.

At this stage, four surgical protocols using thulium lasers for the treatment of BPH have been introduced: vaporization, vaporesection, vapoenucleation, and mechanical blunt enucleation with Tm:YAG laser support. The following discussion considers subgroups of patients, cost, and recent developments in the standard protocols.

## Patient subgroups

Bach et al. evaluated the feasibility and efficacy of thulium laser enucleation of the prostate in 65 patients with an indwelling transurethral catheter due to recurrent urinary retention secondary to BPH [39]. They were compared to 143 patients scheduled for the same procedure, but without catheterization for urinary retention. Both groups were comparable in terms of clinical parameters. At discharge, mean $Q_{\max}$ and PVR had improved in both groups and were similar. The incidence of bleeding was similar, but UTI were more frequent in the catheterized group. Since up to 40% of patients scheduled for surgery for BPH can develop AUR, this study has an important impact on decision-making regarding the adequate procedure. Carmignani et al. confirmed these data in their series of 93 patients [40]. Compared to other laser techniques treating similar groups of patients, the thulium laser appears to offer advantages [41].

With an aging population, the percentage of patients on oral anticoagulants is high and increasing. In a large group of 2648 patients undergoing surgical treatment of BPH, Bach et al. had 36.7% receiving some form of anticoagulation therapy. Interestingly, the transfusion rate remained stable at a low level during a time when the percentage of patients under oral or systemic anticoagulation doubled. In 61.4% of the patients, anticoagulation was not stopped before surgical intervention, because bridging may alter the risk of thromboembolic complications [30]. Ong et al. showed that regular users of anticoagulants who had enoxaparin bridging are at a higher risk of both perioperative bleeding and thromboembolic complications [42]. Maccione et al. observed 76 patients with oral anticoagulants. Thirty-five discontinued the treatment with oral anticoagulants 10 days before thulium vaporesection of the prostate (ThuVARP) and 41 were treated under ongoing therapy. No differences between the procedures with regard to surgical time, hospital stay, or functional outcomes were noted [43]. In a next step, Netsch et al. performed a three-center retrospective matched-paired comparison of patients treated with either ThuVARP or ThuVEP under ongoing oral anticoagulants [44]. They concluded that both ThuVEP and ThuVARP were equally efficacious in patients on oral anticoagulants. The only difference noted was a higher $Q_{\max}$ at six months for patients treated with ThuVEP. All other functional parameters measured were not significantly different.

The impact of any surgical or interventional treatment of benign prostatic obstruction (BPO) on erectile function is an important issue. In his review, Li et al. worked up 18 randomized clinical trials with 2433 patients. Pooled data of the four various laser systems revealed that all surgical procedures for BPO except photoselective vaporization of the prostate did not have any negative impact on erectile function when preoperative and postoperative IIEF-5 scores were compared directly [45]. Tiburtius et al. prospectively evaluated 72 patients who underwent ThuVEP. At 12-month follow-up, they found a marginal nonsignificant erectile function improvement [46]. Carmignani et al. followed up 180 patients after ThuLEP and reported in up to 56% of the patients preservation of antegrade ejaculation [47]. These numbers are a little better than those published by Yee et al. with a preservation of 44% in their cohort of 113 patients treated with ThuVARP [48].

## Economic issues in practice

Scientific data on the cost-effectiveness of surgical techniques for BPO are scarce. A wide array of different international health systems have to be compared. From a medical point of view, the following parameters should be addressed: operating time, concomitant medication, hospital stay versus outpatient treatment, operation success, reoperation rate, and work incapacity. On the other hand, providers of certain surgical techniques have to deal with costs of purchase and maintenance: Is it better to buy or to lease? Is it possible to share? How much disposable material comes (or goes) with each procedure? Is the main instrument a multiple purpose device or designed for a solitary operation? With these numbers it is possible to calculate how many cases have to be done to achieve a financial break-even point.

## Recent developments and modifications to the standard procedure

Early studies with thulium lasers were performed with 70 W laser output, but, pushed by developments in other laser systems, thulium lasers with 120, 150, and 200 W have been introduced and have made it necessary to reassess the ablative and hemostatic properties [49]. In particular, it has to be clarified whether higher power would create a deeper zone of tissue coagulation and tissue penetration, which might lead to an increased risk of collateral damage. Bach et al. recently showed that the amount of tissue ablation increased with increased power output, but with increasing fiber diameter (800 µm fiber instead of 550 µm), the depth of the cut decreased [49]. As shown by Wendt-Nordahl et al. in their previous study [17], tissue ablation with the thulium laser appeared to be more effective than reported for other systems. This study indicated also that the bleeding rate did not increase with the higher power output. In contradiction to that, it has been shown that bleeding rates increase at higher power settings in other laser systems [50, 51]. There were no differences in the clinical outcomes as shown in 28 patients treated with a 200 W Tm:YAG laser [52].

A more interesting consideration with the higher power laser is the effect on deeper tissue layers, leading to a lower possibility of histologic assessment or even collateral damage. Using standard H&E staining, the extent of the coagulation zone with the 70 W thulium laser is reported to be 0.36 mm with the 550 µm bare-ended fiber and 0.49 mm with the 800 µm fiber [49], which is smaller than that reported for other laser systems [51]. Deep tissue penetration is responsible for obstructive necrotic tissue, leading to a high reoperation rate [53]. Dissipation of heat does not end at the border of the coagulation zone.

There have been two recent reviews of laser treatment for prostates, including thulium lasers. Herrmann et al. included articles published between 1995 and 2009 encompassing 3669 patients [54], and concluded that most contemporary laser treatment modalities provide similar $Q_{\max}$ improvement compared to open surgical treatment. To differentiate one treatment from another, they advocated comparative computer urodynamic investigations.

Bach invited all authors of scientific thulium laser publications to define the terminology for different surgical techniques, and he proposed the use of this terminology to ensure a homogeneous nomenclature [55]. In brief, the authors recommended the following terms: ThuVaP for vaporization of the prostate, ThuVaRP for resection, ThuVEP for enucleation in combination with vaporization, and ThuLEP for blunt enucleation with laser support, respectively (Table 147.2).

## Thulium lasers in the treatment of urinary tract conditions

There is less experience using thulium lasers for the treatment of strictures or transitional cell carcinoma (TCC) of the upper and lower urinary tract.

**Table 147.2** Proposed nomenclature for thulium laser protocols.

| Technique | Basic principle | Consensus nomenclature |
|---|---|---|
| Vaporization | Destruction | Tm:YAG vaporization of the prostate (ThuVAP) |
| Vaporesection | Resection into small tissue chips (to be washed out) | Tm:YAG vaporesection of the prostate (ThuVARP) |
| Vapoenucleation | Enucleation in combination with vaporization of the median and lateral lobe | Tm:YAG vapoenucleation of the prostate (ThuVEP) |
| Enucleation | Blunt enucleation with laser support | Tm:YAG laser enucleation of the prostate (ThuLEP) |

*Source:* Bach T et al. Thulium:YAG 2 μm cw laser prostatectomy: where do we stand? *World J Urol* 2010; 28(2). Reproduced with permission of Springer-Verlag.

## Bladder neck contractures

Bach et al. reported the treatment of bladder neck contractures in 14 patients using a 70 W 2 μm cw Tm:YAG laser [56]. The unsatisfactory results with other interventions, such as bladder neck incision either by cold knife or electrocautery, stents, or balloons, led them to try thulium lasers. The use of lasers for the treatment of strictures was not new, but due to their operational mode and disadvantageous wavelength, they were of limited use; the coagulation zone was suspected of causing recurrent strictures. The technical features and biologic effect of thulium lasers make them more appealing for the treatment of strictures. It should be remembered that the thulium laser can cut through any kind of tissue, no matter whether perfused or scarred. Bladder neck incision also offers a good way to learn the handling of thulium lasers, as the procedure is short, bleeding does not occur, and orientation *in situ* is clear.

In the study by Bach et al., bladder neck incision was carried out successfully in all patients [57]. Mean operative time and catheter time were short: 7 minutes and 6.5 hours on average, respectively. The $Q_{max}$ improved from 9 to 25 ml/s after two months and 23 ml/s after 12 months, while the American Urological Association Symptom Index (AUA-SI) score improved from 22 to 8. Two patients developed restenosis during that time.

In a much larger series of 238 patients [56], Guo et al. confirmed the positive results of Bach et al. There were no complications such as significant blood loss, urine leakage, or rectum injury. $Q_{max}$ increased from 3.2 ml/s preoperatively to 16.7, 18.7, and 19.2 ml/s directly after removal of the catheter, three and five months after the intervention, respectively. IPSS improved from 28.3 to 7.1 to 5.3. Forty-three patients developed restenosis and seven were incontinent 1–3 weeks after catheter removal. All cases of incontinence were temporary. Mattioli et al. published their experience with a single laser incision for treatment of congenital bladder neck sclerosis [58]. This procedure was performed successfully in 214 patients with either unilateral or bilateral incision. At 1-year follow-up, antegrade ejaculation was unchanged in 179 patients (91.3%). All other parameters on sexual function were not permanently changed. Even women with bladder neck obstruction underwent thulium laser incision. In a direct comparison between an electric and a thulium resection group, thulium resection was advantageous with regard to intraoperative blood loss and postoperative catheterization time. There was no urethral stricture or stress incontinence in the thulium group as compared to three patients with either one of these conditions in the electric resection group [59].

## Ureteral strictures

Thulium lasers have been used in a completely new technique for the treatment of subtotal ureteral strictures [60]. Using a combination of endourology and fluoroscopy, the laser fiber is pulled through the stenosis "blindly." In these extreme cases of strictures, the restenosis rate was as high as 38.8%, although the rest of the group were spared from major surgical intervention. Thus, although the results of thulium laser intervention for this application are practicable, they are not superior to any other procedure.

## Transitional cell carcinoma

Endoscopic management of upper urinary TCC has been assumed to have an important role in diagnosis and treatment. The well-known disadvantages of laser treatment also became obvious in the treatment of this entity; either the depth of laser penetration was too great or the pulsed mode disrupted the tissue to be treated. Consequently, Scoffone et al. suggested thulium lasers as an option in this type of procedure [61]. Defidio et al. compared the use of holmium and thulium lasers for the treatment of upper tract TCC in 59 patients [62]. Thulium lasers had a noninferior recurrence-free survival as compared to Ho:YAG laser ablation, but they showed better median parameter performance scores in precision, fiber-tip stability, bleeding, and mucosal perforation.

Gao et al. has reported the use of thulium lasers for the treatment of recurrent bladder tumors [63], a condition for which transurethral resection of the bladder (TURB) is considered to be the standard procedure. According to the authors, histology may not necessarily be required in these cases. They performed thulium laser resection of bladder tumors (ThuRBT) via a flexible cystoscope in 32 patients. All patients were treated successfully with no hemorrhage, obturator nerve reflex, or bladder perforation. Biopsies taken after the procedure revealed no residual tumors. During the first year of follow-up, local and heterotopic recurrences were found in three and six patients, respectively. The accumulated recurrence rates at 3, 6, and 12 months were 9%, 22%, and 28%, respectively.

The first paper on Tm:YAG laser *en bloc* mucosectomy for accurate staging of primary bladder cancer was published in 2011 [64]. Wolters et al. demonstrated the feasibility of resecting bladder tumors *en bloc* with detrusor muscle in the specimen. A re-resection after six weeks was negative for residual TCC in all six patients. Muto et al. confirmed these results in their series of 32 patients [65]. After a mean follow-up of 16 months the recurrence rate was 14.5%, all locations being outside the site of the first resection. Even in larger tumors of a mean diameter of 2.5 cm *en bloc* enucleation proved to be possible [66]. The advantage of laser treatment of bladder cancer is that it may be performed as outpatient treatment, with less blood loss, no occurrence of obturator nerve reflex, and, therefore, a reduced bladder perforation rate.

## Other transurethral procedures

There has been recent interest in the use of thulium lasers in other transurethral procedures, due to their shallow depth of penetration and good coagulation abilities. Mattioli et al. reported on their initial experience with partial nephrectomy, either open or laparoscopically, in nine patients [67]. In six patients, the big vessels were clamped, while in three they were not. Mean tumor size was 3.5 cm and mean operative time was 135 minutes for the open procedure and 210 minutes for the laparoscopic procedure. Blood loss was 260 ml in the open procedure and 156 ml in the laparoscopic procedure. One case was done under renal hypothermia. The authors were able to outline the precise dissection as there was an absence of bubbles and minimal formation of gas during the laparoscopic procedure. The laser coagulated vessels up 1.6 mm, which allowed good sealing of the surface. Operative time was relatively short because suturing of renal parenchyma was not required. Gruschwitz et al. have also reported successful results for Tm:YAG laser-supported partial nephrectomy [68]. Their data were confirmed by a study on 10 patients with nephron-sparing surgery by Sciarra et al. [69].

See accompanying Video 147.1.

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# The Prostatic Urethral Lift Procedure Using UroLift Implants: Novel, Minimally Invasive Therapy for Benign Prostatic Hyperplasia

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## Introduction

A male infant who was born in the United States in 2013 would be expected to live until age 80, with many men living substantially longer than that length of time. Given the variety of improvements in both preventative and interventional healthcare, it is likely that this man will remain active and avoid many of the usual concerns, such as cardiac disease, that have caused disability in previous generations of men. However, it remains likely that this man will experience prostatic growth over time that results in noticeable voiding symptoms. In fact, it is fair to consider benign prostatic enlargement from prostatic hyperplasia as an obligate condition of the aging male [1]. This argument is supported through analysis of published autopsy series in which the prevalence of histologic benign prostatic hyperplasia (BPH) has been shown to increase with age from 23% in the fifth decade of life to 87% by age 80 [2]. In addition, the prevalence of clinically identified prostatism, currently identified as lower urinary tract symptoms (LUTS), correlates closely with the development of histologic BPH [3].

The estimated volume of the prostate has also been shown to increase as men age from a normal 20 g size at age 20 to a median volume on autopsy of 33 g with 4% of prostate glands measured as over 100 g in men over the age of 70 [4]. Although the experience of voiding dysfunction is not directly correlated with the estimated size of the prostate these findings further support the expectation of progressive prostatic enlargement with aging.

Since it has been established that BPH is more common in older men and is associated with an increased risk of intervention for the associated symptoms from infravesical obstruction it may be valuable to estimate the number of men who could be in need of any interventions. The average life expectancy for men in 2001 was 76.8 years, which at that time represented an increase of 27.5 years since the year 1900 [5]. The overall death rate has continued to fall with an increase in life expectancy to 78.2–82.7 years in 2010, with a likely further 8–10 year increase by 2050 [6, 7]. In addition, men are living longer without other medical disabilities, suggesting that a growing number of healthy older individuals will experience progressive voiding dysfunction from BPH and desire intervention beyond medications [8].

Although BPH represents the pathophysiologic disorder for which many therapeutic interventions have been developed it is actually the health of a man's bladder that determines his experience with the prostatic enlargement. There is little information regarding bladder health, in general, and the length of time a man's bladder will remain healthy once obstructed by an enlarged prostate. The development of a standardized patient-reported questionnaire regarding voiding symptoms has provided a surrogate marker for overall bladder health in aging men [9]. This instrument was not developed to diagnose BPH but rather to objectively measure bladder-related voiding symptoms and to monitor the progression or improvement in these symptoms with intervention [10]. Information from the International Prostate Symptom Score (IPSS) questionnaire has demonstrated an age-related increase in LUTS for both men and women, with the most severe symptoms present in older men [11]. This suggests that age independently impacts bladder heath but prostate enlargement likely plays an additional role in men. Morphologic studies in animals and humans also suggest that infravesical obstruction from BPH alters bladder smooth muscle and connective tissue with likely adverse consequences [12]. Ultrasound analysis of bladder weight also appears to identify detrusor-related consequences of prostatic enlargement. Kojima found that the ultrasound-measured bladder weight improved

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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toward normal values in 29 of 33 men by 12 weeks following a prostate-directed bladder outlet procedure [13]. Interestingly, men with bladder weights higher than 80 g did not improve, suggesting that there is a threshold of bladder deterioration beyond which improvement is unlikely despite intervention.

Therefore, as more men age without disability but with obligate prostatic enlargement, it can be predicted that the demand will grow for therapeutic options that can treat the bladder outlet obstruction and maintain a healthy bladder. Importantly, these therapies should successfully manage the obstruction without toxicity and with acceptable cost. Pharmacologic agents have been developed, such as alpha-adrenergic antagonist agents or 5-alpha reductase inhibitors, that can reduce the urinary voiding symptoms but do not alter the underlying physiologic obstruction [14]. It appears that the mechanical obstruction necessitates a mechanical solution. The prostatic urethral lift (PUL) procedure using the UroLift® implant system (Neotract, Inc., Pleasanton, CA, USA) may represent that solution.

## Anatomic considerations for the prostatic urethral lift procedure

Histologic BPH develops within the transition zone of the prostate, which represents a region around the prostatic urethra that gradually enlarges to compress the urethral lumen. Although the exact cause of the pathologic enlargement is incompletely understood it likely involves inherited genetic factors, hormonal dysregulation, and ongoing inflammation that induces the release of proliferative mediators [15]. Urodynamic testing has identified urethral obstruction secondary to both compression by the enlarged prostate as well as a constrictive component that may be related to specific tissue factors such as fibrosis [16]. Traditional extirpative interventions all involve a reduction in the prostate volume (directly with resection or indirectly with thermal ablation) that creates a more open prostatic urethral lumen with clear demonstration of improved voiding parameters. It is the associated toxicity of these procedures that has created a clinical need for a novel therapeutic approach.

The PUL technique using the UroLift implant system is conceptually designed to also create a more open prostatic urethral lumen that can overcome both the compressive and constrictive aspects of BPH. The stromal capsule that surrounds the prostate gland is strong, while the prostatic parenchyma is sponge-like and able to be compressed. The placement of a transprostatic implant between the capsule and the urethral urothelium can compress the intervening parenchyma and create an open lumen.

The specific location for placement of the implants is designed to avoid injury to the bladder neck, ejaculatory ducts, posterolateral neurovascular structures, and the rectum. The prostatic parenchyma is compressed in an anterior and lateral direction that creates an open anterior channel through the prostatic lumen.

## Equipment

The PUL procedure has been designed as an endoscopic technique that can be performed under a variety of anesthesia conditions. The equipment includes a 20 Fr rigid cystoscope with a 2.5 mm 0° endoscope (currently manufactured by Karl Storz, Tuttlingen, Germany) with a longer custom bridge that allows direct visual placement of the cystoscope into a man's bladder.

The permanent UroLift implant consists of a nitinol capsular tab attached to an adjustable length of polyethylene terephthalate (PET) monofilament that traverses the prostatic parenchyma. The inner urethral endpiece is constructed of stainless steel and is applied to the appropriately tensioned PET suture. The delivery system is currently a single-use device that contains all components of one implant and is delivered through a spring-loaded 19 gauge needle under direct endoscopic guidance. The 0° endoscope is inserted through each individual delivery device. A photograph of the equipment is provided in Figure 148.1.

## Surgical indications for the prostatic urethral lift

The majority of men who are candidates for treatment of LUTS secondary to BPH with the PUL procedure will have suffered from bothersome voiding symptoms for a prolonged period of time and may have developed evidence of bladder wall thickening or trabeculation that can be seen on diagnostic cystoscopy or pelvic ultrasound [17]. Since the treatment of BPH-related LUTS with medications has been codified into various guidelines it is likely that most men will also have taken and failed the standard options of an alpha-adrenergic antagonist or a 5-alpha reductase inhibitor [18]. Therefore, it is expected that the predominant surgical indication for performing a PUL will be bothersome LUTS that have not responded to medical management. There may also be individuals who have suffered intolerable toxicity from medical therapy or who have contemporaneous medical contraindications for such treatment.

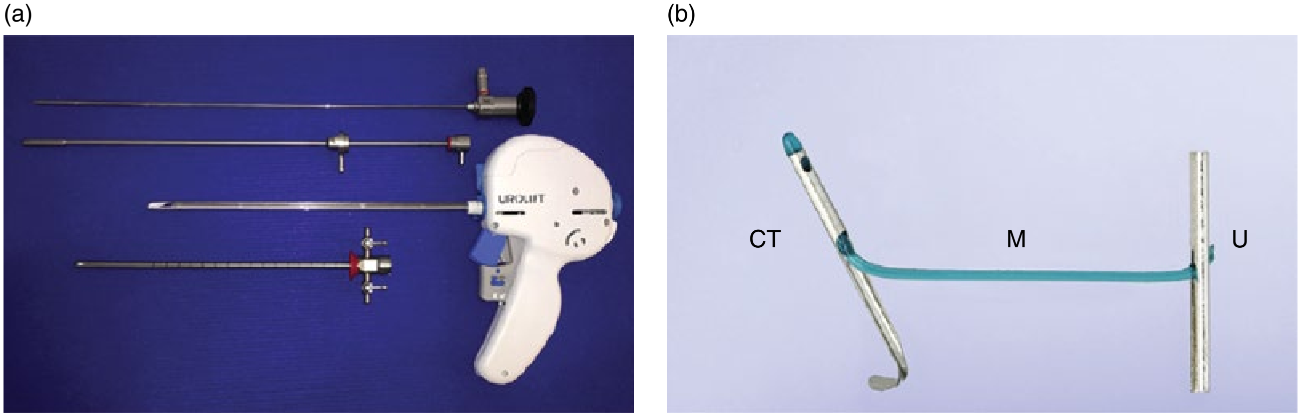

**Figure 148.1** UroLift system and associated equipment. (a) UroLift delivery device with 2.9 mm telescope, 20 Fr sheath, and visual obturator. (b) UroLift implant comprising capsular tab (CT), polyester monofilament (M), and urethral endpiece (U). *Source:* NeoTract, Inc., California, USA. Reproduced with permission of NeoTract.

Interestingly, the PUL procedure may also be an appropriate choice for men on chronic anticoagulation when this therapy is unable to be safely halted for surgery. Finally, there are likely to be some healthy men with a predictably long life expectancy for whom the palliative treatment with medications provides an inadequate long-term approach to maintaining a healthy bladder.

The preoperative evaluation for a man with bothersome LUTS should be guided by established approaches as outlined in the published guidelines [19]. Although a diagnostic cystoscopy is not required for all men who have elected treatment for LUTS this test can be helpful in determining the optimal candidate for the PUL [20]. A transrectal or suprapubic pelvic ultrasound can also provide useful information about prostatic anatomy, prostate volume and the presence of a middle lobe that could alter the surgical approach [21, 22]. Current selection criteria for men as candidates for the PUL likely mirror, but not exclusively, the inclusion criteria for the L.I.F.T. randomized placebo-controlled clinical trial that resulted in the US Food and Drug Administration (FDA) approval for the UroLift implant device [23]. These criteria included men over the age of 50 with an American Urological Association Symptom Index (AUA-SI) (equivalent to the International Prostate Symptom Score or IPSS) greater than 13 and a maximum urinary flow rate of ≤12 ml/s. In addition, the optimal candidate should have a measured or estimated prostate volume between 30 and 80 $\text{cm}^3$ without a visually obstructing middle lobe.

It is also worth considering other potential indications for performing a PUL in an individual with BPH-related voiding dysfunction. The procedure can be performed under local anesthesia or intravenous sedation making this approach appropriate for medically compromised or frail elderly men who could not otherwise tolerate a bladder outlet surgery. In addition, anecdotal clinical experience has demonstrated that UroLift implants can be deployed safely in men on anticoagulation therapy with only mild hematuria.

Perhaps another common indication is a healthy man who selects the PUL approach in an effort to avoid the risk of sexual dysfunction that has been associated with other bladder outlet procedures. In particular, the creation of an open prostatic urethral channel with the UroLift implants system has been associated with stable or improved erectile function as well as improved ejaculatory function in several clinical investigations [24].

## Surgical technique

The endoscopic technique for PUL is designed to allow the customized placement of each individual implant according to the anatomy of the lateral lobes of the prostate. A cartoon depiction of the surgical approach is provided in Figure 148.2. The spring-loaded needle is of adequate length to perforate through the prostatic parenchyma in an anterior and lateral position to deploy the capsular tab on the external prostatic capsule. The length of the PET monofilament is determined relative to the thickness of the prostatic tissue by compressing the prostatic tissue with the tip of the delivery device. Finally, the inner urethral endpiece is secured to the tensioned monofilament in such a manner that it results in the invagination of the stainless-steel endpiece into the urethral wall. The inert endpiece is rapidly covered by the urothelium within the prostatic urethra, preventing exposure of the device to urine. The specific details of the procedure have been well described by McNicholas et al. in 2013 and will be briefly reviewed again in this chapter [25].

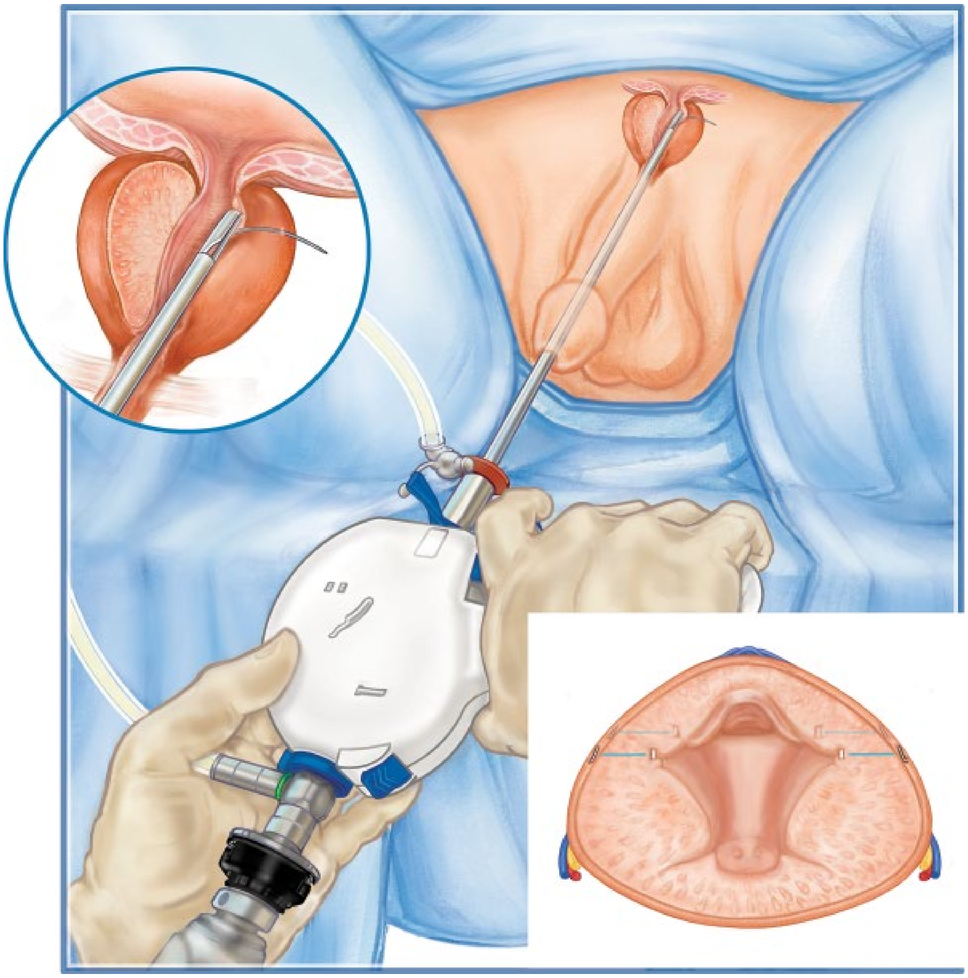

**Figure 148.2** The rigid cystoscope is used to compress the anterior and lateral prostatic parenchyma such that the flexible needle can be extended to deploy the capsular tab and ultimately secure the urethral endpiece. As the figure depicts, the placement of the implants compresses the parenchyma and holds open the prostatic lumen.

The endoscopic technique is performed on an appropriately anesthetized man (either with local lidocaine urethral anesthetic or with intravenous sedation) positioned in the routine dorsal lithotomy position. The most effective anesthetic approach is best determined by the skillset of the treating urologist and the preferences or medical requirements of the patient.

The rigid cystoscope is advanced into the bladder under direct vision using the custom bridge with care taken to avoid urothelial injury that could result in unnecessary bleeding. The care taken in this portion of the surgery can avoid the delays in treatment that would be associated with diminished visualization due to bleeding. The treating urologist will need to evaluate the prostatic anatomy and develop a treatment plan for positioning the individual implants on both sides of the prostate into the anterior and lateral prostatic urethral walls. The endoscopic lens is then placed into the UroLift device, which is subsequently inserted into the rigid cystoscopic sheath and into the bladder. Since the active end of the device protrudes approximately 2 cm beyond the end of the cystoscope, care must be taken to avoid injuring the bladder wall.

The device is then turned 90° to the right or left side and withdrawn into the prostatic urethral lumen. The initial pair of implants is often placed in the proximal urethral lumen approximately 1.5 cm distal to the bladder neck. The device is not activated until the specific location for the implant has been determined. The prostatic tissue is compressed approximately 20° from the midline with the tip of the device. The initial compression may have been positioned at the 9 o'clock location on the right side (or 3 o'clock on the left side) but upward pressure is required to create the anterior lift that will ultimately result in an open anterior channel. Once adequately compressed and lifted, the device is activated and the needle advanced to deploy the capsular tab.

The blue PET suture will be visible within a small window in the tip of the device. The tip of the cystoscope is then advanced slowly toward the bladder, creating a tension on the suture. A white reflection on the blue suture will come into view through the small window once adequate tension has been applied and the luminal endpiece can then be deployed. The device applies the endpiece and cuts the suture simultaneously. This causes the endpiece to visually invaginate into the urethral wall. The implant procedure is then repeated as often as needed to create an open channel from the bladder to the veru montanum. In the L.I.F.T. trial the median number of implants required was 4.9 with a range of 2–11 [23]. Routine clinical practice has resulted in a range of 2–8 implants with the total determined by the individual prostate anatomy.

The procedure is determined as complete when a surveillance cystoscopic examination reveals an open anterior urethral channel without any urethral endpieces visible within the bladder lumen. Any of the endpieces that were inadvertently placed into the bladder lumen at the bladder neck can be easily removed with a flexible grasper. The PET suture will retract into the prostatic parenchyma. The man can then be discharged home either with or without a urethral catheter as consistent with the practice pattern of the treating urologist. The large majority of men will not require a catheter after this surgery.

## Prostatic urethral lift clinical outcomes

Woo and colleagues first reported in 2011 on the technical feasibility and safety of the PUL procedure in men [26]. This preliminary clinical investigation involved 19 men who received the implants under general anesthesia with two versions of the delivery device. All procedures were completed satisfactorily with no serious device- or procedure-related adverse events. Subsequently the delivery device has been standardized as a 20 Fr system and procedures have been performed under all forms of anesthesia including local instillation of lidocaine.

A prospective randomized and sham surgery controlled investigation, called the L.I.F.T. Study, was published in 2013 and provided the foundation for ultimate FDA approval of the UroLift device in the United States [23]. A total of 206 men were randomized to either the sham procedure or the PUL with the UroLift implants using a primary endpoint of comparison of the AUA-SI score at three months. Ultimately, this revealed a reduction in the AUA-SI of 11.1 ± 7.67 points in the PUL group compared to an initial reduction of 5.9 ± 7.66 points in the sham group ($P = 0.003$). A recent publication has compared the clinical outcomes at 2 years in the men who crossed over to the PUL procedure at six months following a sham treatment. In this analysis each man served as his own control and demonstrated a persistent 36% improvement in the AUA-SI from baseline. In addition, other endpoints – quality-of-life score (QOL), BPH Impact Index (BPHII), and maximum urinary flow rate – improved 40%, 54%, and 77% from baseline, respectively [27].

Subsequent to the initial publications there have been a number of prospective clinical trials that have detailed the favorable clinical outcomes of this new procedure [28–30]. Table 148.1 provides an overview of these outcomes.

Although the PUL has demonstrated high-quality outcomes in the context of voiding symptoms it was really the potential to reduce toxicity that was the compelling factor in the development of this new approach. The more established interventions for benign prostatic enlargement include the transurethral resection of the prostate (TURP), various laser-based extirpative approaches and thermal ablative techniques designed to reduce the volume of prostatic tissue that obstructs the bladder outlet. Each of these approaches demonstrates effective reduction of bothersome voiding symptoms but is associated with side-effects that likely cause men to delay or avoid altogether any beneficial therapy. The potential adverse consequences include incomplete resection with the need for repeat interventions, urinary tract infection, urethral stricture, incontinence, and sexual dysfunction. A thorough analysis of the risk for toxicity with each treatment strategy is beyond the intent of this review but several publications may be informative to the interested individual [31–35].

The mechanical principle of the PUL procedure is to endoscopically place a transurethral implant that compresses the prostatic parenchyma to create a more open urethral channel. This can be accomplished with a very favorable toxicity profile when compared to the established extirpative approaches mentioned above. Sonksen and colleagues published a multicenter prospective randomized comparison of the PUL to the TURP in 2015 using a novel composite endpoint measurement called the BPH6. This tool combined measurements of six domains in order to assess overall outcome from each procedure. These domains included LUTS relief, recovery experience, erectile function, ejaculatory function, continence preservation, and safety. A total of 80 men (45 PUL and 35 TURP) were evaluated at 12 months with the PUL found to be noninferior to the TURP [36]. The transurethral resection was superior in achieving a reduction in LUTS but the overall outcome was superior for the PUL. Importantly, there was no statistical difference in the incidence of Clavien–Dindo grade 1, 2, or 3

**Table 148.1** Clinical outcomes for prostatic urethral lift.

| | 2 Weeks | 1 Month | 3 Months | 6 Months | 1 Year | 2 Years |
|---|---|---|---|---|---|---|
| **IPSS** | | | | | | |
| No. of studies | 4 | 4 | 3 | 3 | 3 | 2 |
| Total patients | 288 | 288 | 237 | 237 | 237 | 193 |
| Change from baseline | −5 | −10.4 | −11.2 | −11.2 | −10.2 | −9.3 |
| *P*-value | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| % Improvement | −18% | −45% | −49% | −47% | −45% | −41% |
| **QOL** | | | | | | |
| No. of studies | 4 | 4 | 3 | 3 | 3 | 2 |
| Total patients | 288 | 288 | 237 | 237 | 237 | 193 |
| Change from baseline | −1.3 | −2.1 | −2.3 | −2.4 | −2.3 | −2.2 |
| *P*-value | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| % Improvement | −22% | −43% | −47% | −49% | −49% | −46% |
| **BPHII** | | | | | | |
| No. of studies | 4 | 4 | 3 | 3 | 3 | 2 |
| Total patients | 288 | 288 | 237 | 237 | 237 | 193 |
| Change from baseline | −0.2 | −3 | −3.9 | −4.3 | −4 | −3.8 |
| *P*-value | 0.47 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| % Improvement | 21% | −38% | −55% | −58% | −55% | −56% |
| **$Q_{max}$** | | | | | | |
| No. of studies | 0 | 1 | 3 | 1 | 3 | 2 |
| Total patients | | 51 | 237 | 33 | 237 | 193 |
| Change from baseline | | 3.3 | 3.7 | 3.8 | 3.6 | 4.16 |
| *P*-value | | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| % Improvement | | 47% | 50% | | 49% | 58% |

IPSS, International Prostate Symptom Score; QOL, quality-of-life score; BPHII, BPH Impact Index.

adverse events between the two approaches. However, urinary incontinence, retrograde ejaculation and urethral stricture were significantly more common in the TURP group. Erectile dysfunction was also more common in the TURP group but the difference did not reach statistical significance.

The information regarding sexual function following a prostate-directed surgery continues to suggest that men consider these risks when making a decision to receive a bladder outlet procedure. Although the risk of erectile dysfunction is small following the extirpative procedures, other sexual dysfunction, such as loss of ejaculatory function, are significantly more common [37]. McVary and investigators for the L.I.F.T. trial reviewed the outcomes for sexual dysfunction using the Sexual Health Inventory for Men (SHIM) and the Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHG-EjD) [24]. There was no evidence for a negative effect of the PUL on erectile function. In fact, the 12-month SHIM analysis revealed a statistically significant improvement in erectile function for the men who reported severe erectile dysfunction at baseline. In addition, men reported a 40% reduction in an ejaculatory bother score by the 12 months endpoint of the study. These reports establish the PUL as the only surgical procedure for BPH that can improve ejaculatory function while minimizing any negative effect on erectile function.

Overall, the current clinical experience with the PUL procedure has revealed the technique to be well tolerated with only mild toxicity. Box 148.1 lists the adverse events that were identified during the L.I.F.T. randomized trial. The likely unique adverse event that has been identified with the UroLift implants is encrustation of the urethral endpiece. This was identified during the randomized trial in 2.1% (14 out of 642 total implants). Only those implants with the urethral endpiece inadvertently positioned within the bladder lumen at the bladder neck are at risk for this toxicity. None of the correctly placed devices were found to encrust and the involved endpiece could be easily removed endoscopically with a flexible grasper.

**Box 148.1 Adverse events from L.I.F.T. trial.**

**Serious events**

- Clot retention on coumadin
- Bladder stone (not from implant)

**Related adverse events**

- Dysuria (34%)
- Hematuria (25.7%)
- Pelvic pain (17.9%)
- Urgency (7.1%)
- Urge incontinence (3.6%)
- Urinary tract infection (2.9%)
- Urinary retention (0.7%)
- Erectile dysfunction (0)
- Retrograde ejaculation (0)

## Conclusion

BPH is an obligate condition of the aging man and a source of both QOL and medical health consequences. The development of prostatic enlargement with infravesical obstruction has been shown to alter the structure of the bladder wall and, over time, this alteration likely results in a permanent disorder. A variety of extirpative procedures that remove tissue from the prostate to enlarge the urethral lumen have been found to effectively reduce the bothersome voiding symptoms. These procedures are associated with a risk of adverse events that may cause a man to delay intervention beyond the time at which a complete return to normal bladder health is possible. The PUL procedure with the UroLift implants represents a new mechanical approach for the management of bladder outlet obstruction from prostatic enlargement. A straightforward cystoscopic technique, which can often be performed under minimal anesthesia, allows placement of the implants that compress the prostatic parenchyma and establishes an open channel through the prostatic urethra. This procedure can be performed safely with minimal risk for sexual dysfunction and at an acceptable cost [38, 39].

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# 149

# Goals and Expectations of Ablation Techniques and Emerging Therapies for Benign Prostatic Hyperplasia: An Editorial

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## Introduction

Benign prostatic hyperplasia (BPH) and its associated lower urinary tract symptoms (LUTS) continue to be a significant burden to healthcare systems around the world. There is an estimated prevalence of histologic BPH of 10% in men in their 30s, with this number rising to 80% in men over the age of 70 years [1]. LUTS due to BPH are associated with significant morbidity and reduced health-related quality of life [2], with the prevalence of moderate-to-severe LUTS increasing with age [3]. An estimated 90% of men aged between 45 and 80 years have some form of LUTS [4].

For the last 80 years, surgical management of the prostatic component of these symptoms has been dominated by the transurethral resection of the prostate (TURP). For many years the only endoscopic option, there is an extensive body of research on the technique, its propensity to improve LUTS, and anticipated adverse events. The TURP is still considered the gold standard in management of the 30–80 ml prostate [5, 6]. The drawbacks of a TURP include the duration of hospital stay, associated adverse events, the long-term sequelae of erectile dysfunction and retrograde ejaculation, blood transfusion rates, and its limitations in high-risk patients.

In recent decades there has been a significant effort to increase the number of techniques available to the urologist to manage LUTS due to BPH [7]. This has been brought about not only by a desire to improve functional outcomes and efficacy, but also in an effort to develop treatments that can be offered to higher risk men, while reducing both morbidity and cost [8]. Such patients include those with larger prostates, increasing age, and those who are anticoagulated or otherwise present a high anesthetic risk.

Laser ablation can be considered as the first alternative to traditional TURP, and was pioneered throughout the 1990s. The neodymium:YAG laser was initially used by Costello et al. [9], with subsequent development of the holmium laser [10] and the 532 nm wavelength, commonly known as GreenLight [11]. Diode and thulium lasers represent newer techniques with a limited numbers of studies, particularly with regard to long-term follow-up [12, 13]. Holmium and GreenLight lasers now appear in both American Urological Association (AUA) and European Urological Association (EAU) guidelines [5, 14] as an effective alternatives to TURP. One of the difficulties in developing new prostatic ablative techniques is that, with surgical options already cited in international guidelines as a gold standard, the urologist must determine how newer techniques compare.

As with any new technique, there are several areas that must be examined in order to determine whether it can be considered as an alternative to an already established treatment. In the treatment of BPH, these include both short- and long-term efficacy, patients' ability to tolerate treatment, potential complications, impact on quality of life (QOL), and economic costs [15].

Ablative techniques currently in use include laser, thermoablation, radiofrequency ablation, aquablation, and injection of ethanol. Although some of these techniques are now approaching 30 years in clinical use, others are much more recent, meaning that only short-term outcomes are available. A lack of high-quality randomized controlled trials and limited head-to-head data, means that the majority of trials are set up to demonstrate noninferiority to another treatment, usually TURP. Whether these newer treatments represent equivalence to established techniques must therefore be based on similar outcome data, with long-term outcomes inferred.

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The LUTS associated with BPH have been found to affect how men organize their day, and may prevent them from performing their preferred daily activities [16]. The primary goal of any therapy should therefore be relief of symptoms and prevention of long-term adverse outcomes that will adversely affect QOL. Accepted methods of measuring outcomes in the treatment of LUTS due to BPH include the use of uroflowmetry, postvoid residual (PVR), urodynamics, AUA Symptom Index (AUA-SI) or International Prostate Symptom Score (IPSS), incontinence, sexual function outcomes as assessed by the International Index of Erectile Function (IIEF), and the need for further procedures.

The 2010 AUA guidelines [14] define three important outcome measures when considering therapies for BPH: (i) a comparison of the efficacy of available treatments; (ii) treatment-associated adverse events; and (iii) identification of subpopulations in which efficacy and adverse events differ from the general population. In developing these guidelines the panel used symptom and QOL scores (primarily AUA-SI/IPSS) and peak urinary flow ($Q_{\max}$) to assess efficacy. These outcome measures should therefore be considered as a minimum in the assessment of newer therapies. Comparison of adverse events (AEs) is more difficult, primarily due to the heterogeneity among trials in how AEs are reported. Many newer therapies seek to take advantage of the subpopulations that may benefit from alternative treatment methods, particularly the elderly or those at high risk from anesthesia.

Uroflowmetry, originally developed from research into pressure-flow studies, as a means of indirectly evaluating the presence of obstruction [17], is an important component of the assessment of many BPH interventions. The majority of studies therefore use the uroflow as an outcome measure of the success of a given intervention. The most commonly used value in clinic practice is the $Q_{\max}$, but unfortunately this correlates poorly with subjective symptoms and the degree of bother experienced by the patient. Despite this limitation, it provides an excellent means of comparing functional outcomes between treatment groups.

The AUA-SI was developed in the early 1990s as a standardized instrument to assess the degree of bladder outflow obstruction in men [18]. This was further modified to develop the IPSS with the addition to the original of a "bother" score, as a QOL measure [19]. Symptom scores are stratified with a score <7 being mild symptoms, score 8–19 moderate, and 20–25 severe. Both of these scoring systems have been extensively validated and are sensitive enough to be used in the evaluation of symptoms and to assist in selection of treatment [20–22].

One of the most important things to note regarding the IPSS system is the frequent discrepancy between symptom severity and QOL scores [23]. A significantly improved symptom score may represent treatment success, but if there is ongoing reduced QOL then the patient may continue to be dissatisfied and seek medical attention. The Veterans Affairs Cooperative Study showed that the significant factor predicting elective crossover from watchful waiting to TURP was high baseline bother due to urinary symptoms, with outcomes better in men most bothered by urinary symptoms at baseline [24]. It is therefore important to consider both these scores in the success or failure of new therapies.

Complications such as failure to void, recatheterization, symptoms of dysuria and frequency, and need for reoperation represent a significant burden for both the patient (QOL and satisfaction outcomes) and healthcare systems (the cost of repeat hospital attendances and interventions). TURP has a well-documented range of complications, as follows: failed trial removal of catheter (TROC) (6%), transfusion (1–4%), clot retention (3%), infection (2%), contracture/stricture (6%), transurethral resection syndrome (2%), incontinence (1%), and erectile dysfunction (13%) [25–28]. Newer techniques should provide comparable or improved complication profiles in order to be considered competitive.

One of the appeals of several of the newer treatment modalities is that they can be effectively used in higher risk patients who might otherwise be considered unsuitable for a traditional TURP. The ability to perform ablation procedures on anticoagulated patients without significant complications, or the fact that a technique can be performed in the outpatient setting might make it competitive compared to established techniques.

In order to capture long-term outcomes it appears that a median of at least 3 years of data in a large number of men are required [29], and for many newer therapies the data are simply not mature enough to allow this. Long-term efficacy is important in order to assess the economical viability of newer therapies, with low retreatment rates important. Although early results may be promising, it is clear that longer follow-up is required for many ablative techniques.

The true economic cost of BPH treatment is multifactorial, involving not only the cost of drugs, imaging, clinic and hospital attendances, equipment and staffing, as well as the actual procedures, but also the repercussions of lost earnings and time off work. It has been estimated that in the United States the treatment of BPH costs approximately US$4 billion annually [30]. A recent study reveals that 12.2 million BPH patients are treated each year, with 55% being treated with medication and 1% treated surgically [31]. It is expected that, with an aging population, the economic cost of treating BPH will only increase.

There is an ever-increasing range of surgical therapies available for the management of BPH, many of which have only short-term follow-up data available in order to assess outcomes. Here we outline some of the more recently developed techniques that have been used in the treatment of LUTS due to BPH.

## Transurethral microwave therapy

Transurethral microwave therapy (TUMT) involves the placement of an intra-urethral antenna to facilitate heating of the prostate to temperatures above 45 °C, causing tissue destruction by coagulation necrosis. Although this technique has been found to improve both IPSS, which decreased by 65% over 12 months, and $Q_{max}$, which improved by 70%, neither of these results were as good as TURP, with a 77% decrease and 119% increase, respectively [32]. A single randomized controlled trial (RCT) compared TUMT to medical therapy with terazosin, rather than surgical techniques, with significantly better outcomes in the TUMT group over 18 months follow-up.

TUMT has been shown to be successful in the management of patients in urinary retention, with 80–93% of patients regaining spontaneous voiding after treatment [33, 34]. The majority of this follow-up data are, however, in the order of less than 12 months and one study suggests that there is a cumulative risk of treatment failure in this subgroup of patients in the order of 59% at 5 years [35].

The majority of AEs related to this technique involve perineal pain, dysuria and urgency, with few of the more significant morbidities associated with TURP. In particular, sexual dysfunction and urethral stricture rates have been found to be lower. The technique cannot, however, be used in patients with a middle lobe or short prostatic urethra. In favor of TUMT is the fact that there is no requirement for general anesthesia, making it appealing in those patients with significant comorbidities or anesthetic risk. It is, however, important to bear in mind the trade-off in terms of lower flow improvements and higher retreatment rates when compared to TURP.

## Transurethral needle ablation

Transurethral needle ablation (TUNA) involves cystoscopic insertion of needles into prostatic parenchyma under direct vision. Low-level radiofrequency energy is then transmitted down these needles, causing coagulation necrosis in the transition zone. A meta-analysis of 35 studies [36] has demonstrated a significant improvement in both IPSS and $Q_{max}$, in the order of a 50% decrease in symptom score and 70% improvement in flow, but as with TUMT these outcomes are significantly inferior to TURP. At 5 years of follow-up in a single study, approximately 50% of patients had maintained their improved outcomes, but there was a 21% additional treatment rate [37].

The most common adverse event of TUNA is that of postoperative urinary retention, which occurs in 13–42% of patients. 90–95% of patients are catheter free within a week, but storage LUTS are common for 4–6 weeks following treatment [38, 39]. This method cannot be used in patients with a prostate size greater than 75 ml, nor is it suitable in those with a middle lobe. It can, however, be performed as a day case, and has a lower rate of bleeding and sexual dysfunction when compared to TURP. The 5-year retreatment rates are high, and do raise concerns about the durability of this technique when compared to others that are available.

## Prostate stents

A variety of stents have been trialed, differing in design and materials and whether they are permanent or not. The majority of studies have high dropout rates, almost certainly related to poor tolerability due to migration, misplacement, encrustation, and subsequent exacerbation of LUTS [40]. UroLume, a permanent stent, enabled 84% of catheter-dependent patients to regain their ability to void, but also reported a failure rate of 16% at 12 months, increasing to 27% at 5 years [41]. It is no longer commercially available.

Various temporary blind-placement stents have also been trialed, but have been found to have significant side-effects and a high migration rate, leading to the conclusion that they are unsuitable for clinical use [42, 43]. The Memokath system, a self-expanding, removable metallic stent has also been used in this setting. Results are more favorable here, with a reduction in IPSS of 11–19 points and increase in $Q_{max}$ of 3–11 ml/s [44]. Current EAU guidelines suggest that prostate stents should only be considered in men unfit for surgery or as a temporary measure [5].

## Intraprostatic ethanol injections

Ethanol is injected directly into the prostatic parenchyma using either a transurethral, transperineal, or transrectal approach. Studies have used anything between 2 and 25 ml of ethanol at a variable number of injection sites. Most patients require catheterization following the procedure. Several nonrandomized open trials report a significant reduction in IPSS of 40–70% and $Q_{\max}$ improvement of 35–155% [45, 46].

Again there are concerns about the durability of treatment, with a single trial reporting a 41% retreatment rate at 3 years [47]. In addition to pain, storage LUTS, hematuria, retention, and infection, two cases of bladder necrosis were reported [48]. Both patients required cystectomy and urinary diversion. The lack of evidence and severity of AEs has meant that intraprostatic ethanol injections are regarded as unsuitable for use outside clinical trials.

## Intraprostatic botox injections

Botulinum toxin A is injected into the prostatic parenchyma using the transperineal, transurethral, or transrectal route. The drug induces apoptosis in epithelial cells, leading to tissue atrophy and neuronal inhibition, which may contribute to smooth muscle relaxation. A variety of different doses have been used. A single review of 20 studies [49] demonstrates significant IPSS reduction in 13 studies, $Q_{\max}$ improvement in 14 studies, and durability ranging from 3 to 30 months. The largest placebo-controlled study [50] did not, however, show any significant difference in any parameter at 12 weeks posttreatment. At this stage the lack of evidence that botulinum toxin is effective in this situation, coupled with a paucity of controlled trials, means that intraprostatic botulinum toxin is still considered experimental.

## Aquablation

This technique uses a high-velocity saline stream to resect parenchymal tissue, with subsequent hemostasis achieved using brief thermal coagulation. The AquaBeam® system (Procept BioRobotics, Redwood Shores, CA, USA), combining real-time transrectal ultrasound imaging and robotics, has been through phase I and II studies, and a large multicenter RCT is ongoing [51]. Initial trials show significantly improved functional parameters with an IPSS decrease of 63–90% and $Q_{\max}$ increase of 54–101% [52–54].

Reported complications have been minor and included dysuria, retention, mild hematuria, and infection. Sexual function and continence have been preserved with no reports of significant AEs. The technique is still in its early stages with long-term data lacking.

## Water vapor energy ablation

The Rezūm® system (Rezūm Water Vapor Therapy, Maple Grove, MN, USA) injects water vapor at 103 °C via a transurethral approach into the transition zone and median lobe as needed, causing thermal ablation. The number of injections is determined by the size of adenoma and length of prostatic urethra. Results from a multicenter RCT [55] show significant improvement in IPSS of 53% and $Q_{\max}$ of 54% at 12 months.

The procedure appears to be well tolerated and is performed in the outpatient setting. AEs include retention, dysuria, hematuria, and infection, with no serious complications reported. Again, long-term data are lacking, but results appear durable over at least 12 months.

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# 150

# Monopolar Transurethral Resection of Prostate

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## Introduction

Transurethral resection of the prostate (TURP) has been the gold standard in surgical management of patients with benign prostatic hyperplasia (BPH). The procedure has stood the test of time while many new, alternative “minimally invasive” procedures have failed to last in an era of procedure avidity. The place of conventional TURP using monopolar energy has recently come under scrutiny with the emergence of bipolar electrosurgical systems, which have become increasingly popular. The underlying principles of both monopolar and bipolar electrosurgical systems are similar, but the manner in which the current returns to the generator is different. However, owing to its widespread availability and use, monopolar TURP will continue to be an important tool in the therapeutic armamentarium of urologists dealing with BPH patients.

## History

Electrosurgery had its beginning in 1882 when d’Arsonval found that high-frequency alternating current, when passed through the body, caused heating without muscle and nerve stimulation [1]. Young (1909) improved the endoscopic application of electrosurgery by using a fenestrated tube in place of an inner cutting tubular knife for the cold punch operation for prostatectomy [2]. This innovation allowed water to be infused between the electrode and the sheath, thereby improving vision and cooling the instrument. Edwin Beer (1910) is credited with being the first to make use of electrosurgery endoscopically by placing an electrode through a Nitze cystoscope to remove tumors of the bladder neck [3]. Stevens and Bugbee performed the first electrosurgical endoscopic incision of the prostate in 1913 [4, 5].

The development of the spark gap generator was a landmark invention which came into existence with the pioneering efforts of Liebel and Bovie in 1924 [6]. This generator was able to produce both cutting and coagulating waveforms, which greatly facilitated hemostasis while resecting the prostate. Shortly after this invention, Stern developed the early resectoscope using a cutting loop consisting of a small ring of tungsten wire of approximately 0.5 cm in diameter [7]. The loop was placed at right angles to the end of an insulated shaft and was connected such that the loop could be made to slide easily. The radiofrequency current was then delivered continuously under water to excise prostate tissue. However, securing hemostasis was still an important issue. Davis, by using the Bovie generator, not only overcame this problem, but also became the first to use it for excision of large amounts of prostate tissue. Joseph McCarthy in 1932 subsequently developed the McCarthy resectoscope, which bears significant resemblance to the modern resectoscopes. The invention of rod–lens optical systems by Harold H. Hopkins in 1959 and the addition of fiber-optic light transmission by Karl Storz in 1960 marked further breakthroughs in modern endoscopy [8]. Since then, several refinements in instruments and technique have been made by outstanding urologists, but the basic principles have remained the same.

## Electrosurgical basis of transurethral resection of the prostate

The entire concept of TURP (monopolar or bipolar) is based on the principles of electrosurgery. Ablation of the prostate is achieved by employing alternating current with wavelengths in the radiofrequency range. The standard alternating current, with frequencies in the 60 Hz range, is unsafe for use in this setting as it subjects

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Companion website: www.wiley.com/go/smith/textbookofendourology

the patient to the risk of excessive neuromuscular stimulation, leading to tonic–clonic contractions with rhabdomyolysis and cardiac arrhythmias. The role of an electrosurgical generator is to increase the frequency of this current to over 200 kHz, because at all frequencies above 100 kHz current can pass through the body with minimal neuromuscular stimulation and no risk of electrocution.

While using a monopolar system for TURP, the active electrode (cutting loop) is placed in contact with the prostate tissue. Inside the resectoscope, the electrical connection from the generator to the cutting loop is carefully insulated. When activated, the generator produces a high-frequency voltage which drives a high-frequency current through the patient. The current passes from the small active electrode (cutting loop) at the tissue interface, through the patient to a proportionately larger indifferent electrode, and subsequently back to the generator (Figure 150.1). Thus, in a monopolar TURP, the patient is part of the system. Alterations in the frequency of oscillation and waveform alter the quality of coagulation and cutting.

The current flowing through the patient heats the tissue in contact with the loop, the heat generated being proportional to the current density (current flowing per unit area). The current density is high only in the tissue neighboring the current loop, leading to vaporization of the fluid in the cells near the loop, which can be moved through the tissue almost without any mechanical force.

## Types of current waveforms

The basic function of an electrosurgical unit is to fulgurate or coagulate tissue by use of low-frequency current and the incision of tissue with high-frequency current. Depending on the characteristics of the generator, a variety of current waveforms can be produced (Figure 150.2). The individual settings are governed by the machine and requirements of the surgical procedure. The historical terms “coagulation” and “cutting” waveforms can be misleading as low-power settings in the cut mode produce excellent contact coagulation, while high-power settings in the coagulation mode will produce a cutting action.

### Cutting waveform

Cutting current uses a pure, nonmodulated sinusoidal waveform. Electrosurgical cutting requires the generation of small arcs from the electrode to the tissue, which occur twice during each cycle at the maximum and minimum voltage of the sine wave. This implies that the frequency of these arcs will be double the frequency of the sine waves produced by the generator, thereby facilitating a smooth cutting action without extensive thermal damage. This waveform achieves a higher average power when compared with any other alternating waveform of equal peak voltage (>500 V), allowing the voltage to be limited when compared with coagulation current. It is important to remember that the described cutting effect depends only on the magnitude of the current density,

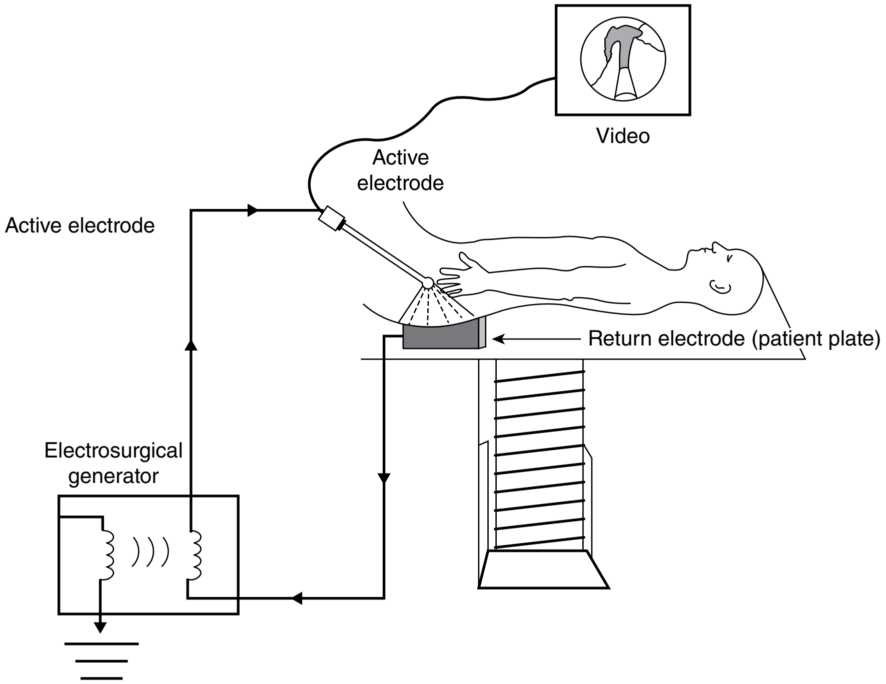

**Figure 150.1** Monopolar circuit.

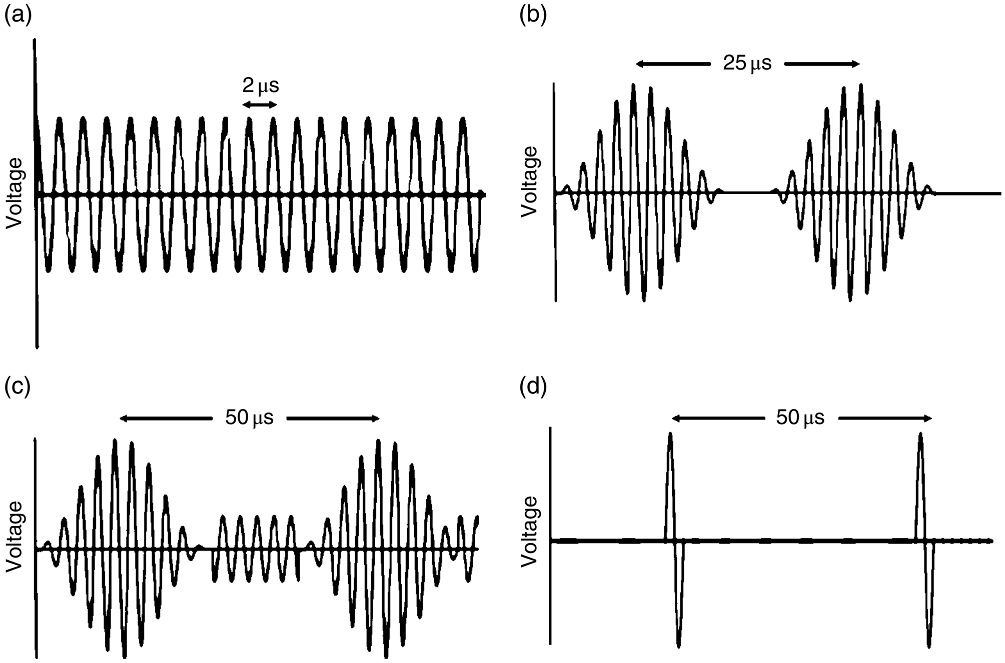

**Figure 150.2** Waveforms. (a) Cutting current; (b) coagulating current; (c) blended current; (d) spray coagulation.

not on the frequency of the current. In general, cutting is produced by high tissue temperatures (>100 °C), whereas coagulation is produced by tissue heating between 70 °C and 100 °C.

While performing TURP, a higher setting for the cutting current increases greatly the efficiency of the cut, while adding little to the danger of the procedure. On the other hand, too much cutting current produces a noticeable blue flame between the electrode and the tissue, which should be avoided. In general, small fibrous glands or bladder neck contractures are best treated by using a small-caliber loop with a high-intensity cutting current.

## Coagulation waveform

Coagulation current is a highly dampened current characterized by extensive wave modulation in which the generator supplies current for less than 50% of the activation time. This produces intermittent bursts of damped sine waves of high peak voltages, up to 10 000 V (Figure 150.2b). When employed, with the active electrode in contact with the tissue, these peak voltages result in high tissue temperatures, and hence significant thermal destruction, making this type of current particularly suited for the coagulation of bleeding vessels. Therefore, when this type of current is used in TURP, the intensity should be as low as will reasonably coagulate the tissue, and the time of application should be as short as possible.

## Blended waveform

Blended currents are actually a combination of the above two waveforms, created by modulating a second, lower frequency, higher amplitude sine wave with the sine wave from the cutting generator, producing a higher peak-to-peak voltage. This waveform typically supplies current for only 50–80% of the activation period. The new waveform is then delivered in intermittent bursts at a rate determined by the settings of the electrosurgical generator. Blended currents allow the surgeon to cleanly divide tissue while maintaining a variable degree of hemostasis, depending on the amount of coagulating current used. Because more vascular glands have higher moisture content, this type of tissue is best resected using a blended current to maximize cutting and coagulation properties.

## Spray coagulation waveform

This waveform is highly intermittent, with the generator supplying current for only 5% of the activation time. It is also high voltage (up to 10 kV) to produce long sparks between electrode and tissue. Operating in this mode, the active electrode does not touch the tissue, but instead, the high voltage causes air ionization and sparking. This mode uses relatively low current output (approximately 0.1 A) and thus leads to a thin layer of tissue necrosis with little depth of thermal damage.

## Irrigation fluids

A hypo-osmolar irrigation fluid (1.5% glycine) is used that is nonconducting and not too rapidly absorbed. Despite having an osmolality of 200 mOsm/kg, it has played a role in reducing the risk of hemolysis and death by more than 50% from the days when distilled water was used for irrigation [9]. A variety of other electrically nonconducting irrigation fluids such as 5% dextrose, 3% mannitol, and 3% sorbitol have also been used. Normal saline is not suitable for monopolar TURP as it may prevent the creation of a cutting arc because of its conductivity.

## Indications for transurethral resection of the prostate

In 1989, the American Urological Association (AUA) initiated the Guideline Panel for Diagnosis and Management of BPH, which was later taken over by the Agency for Health Care Policy and Research (AHCPR) [10]. The panel subsequently recommended the AUA-7 Symptom Index for formal assessment of a patient's symptoms. The current indications for performing TURP are listed in Box 150.1.

**Box 150.1 Current indications for transurethral resection of the prostate.**

- Moderate (8–19) to severe (20–35) lower urinary tract symptoms (LUTS) not responding to medical treatment
- Refractory urinary retention with at least one failed attempt at catheter removal
- Chronic retention with back pressure changes, leading to:
  - Hydronephrosis
  - Renal insufficiency
- Complications of benign prostatic hyperplasia (BPH), including:
  - Recurrent urinary tract infection
  - Recurrent gross hematuria
  - Bladder diverticula
  - Bladder stones

## Preoperative evaluation

### Patient assessment

As most patients undergoing TURP are elderly, assessment of the renal, cardiac, pulmonary, and general physiologic status is of paramount importance because major derangements in these vital organs are important predictors of postoperative outcome. In addition to routine blood investigations, including hemoglobin, complete and differential blood counts, blood sugar, prothrombin time, and partial thromboplastin time. Renal function tests (including serum creatinine and blood urea nitrogen) should be obtained, and surgery should be postponed and catheter drainage done in patients with impaired renal function due to obstructive uropathy. Such an approach allows maximum possible improvement in renal function before the patient is taken up for surgery. An ultrasound abdomen with special emphasis on the kidney, ureter, and bladder (KUB) region should be obtained to assess the prostate size and postvoid residual volume (PVR). In patients who have not been catheterized, uroflowmetry is considered the single best noninvasive test to detect lower urinary tract obstruction. Pressure flow studies should only be done when the diagnosis is unclear or neurological disorder is suspected. A prior cystoscopic assessment is generally not necessary and it can be done at the time of the procedure.

## Perioperative antibiotics

Patients with evidence of infection should be treated prior to the planned procedure. Although the impact of prophylactic antibiotics in reducing postoperative infection was refuted by some authors, most of the available literature supports their beneficial role [11–16]. The antibiotic should cover both Gram-positive and Gram-negative organisms. Patients with an indwelling catheter are at a higher risk, even if no preoperative evidence of infection is detected. It is our practice to routinely administer a single intravenous dose of a broad-spectrum prophylactic antimicrobial 1 hour before the procedure. The patient is subsequently continued on oral antibiotics until they are catheter free.

## Anesthesia

The choice of anesthetic should be individualized, and the procedure can be performed under spinal epidural or general anesthesia with similar results [17–19]. Small-volume glands (<40 g) can also be resected under local anesthesia, especially when associated major comorbidities are present [20, 21].

## Surgical technique

The patient is placed in the modified lithotomy position. Care is taken to avoid overextension at the hip joint, and adequate padding is used for bony prominences.

Cystourethroscopy is done as the first step to assess the distal urethra, position of verumontanum, size and

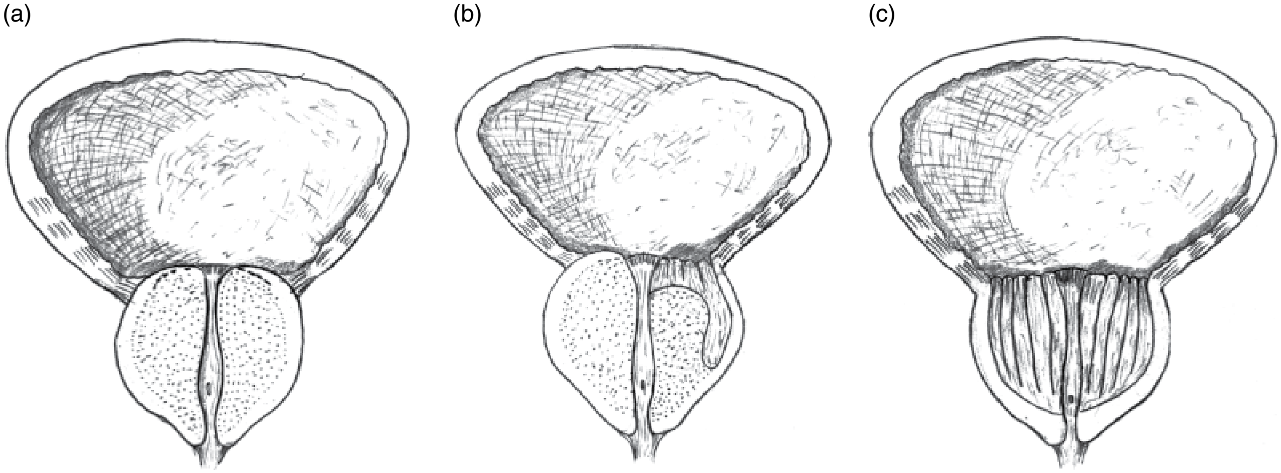

**Figure 150.3** Stages of transurethral resection of the prostate: coronal representation.

configuration of the prostate, bladder neck, urinary bladder, and both ureteric orifices. In case of urethral narrowing, urethral dilators are used to dilate it to 28 Fr. Sometimes internal urethrotomy may be required to accomplish this. Meatal dilatation or dorsal meatotomy is done if the meatus is narrow.

The resection technique may vary according to the size or configuration of the prostate, but should be based on an orderly plan. There are several different surgical techniques described for TURP adenoma; however, the principle remains the same, (i.e. step-by-step resection and coagulation of each quadrant of prostatic lobes) (Figures 150.3 and 150.4). The operator is expected to get familiar with any one approach, and then to master it with experience. A commonly used approach, popularized by Nesbit, utilizes the principle of resecting anteriorly first so that the adenomatous tissue drops down, allowing the surgeon to resect from the top downwards rather than from the floor upwards.

A 24 or 26 Fr size resectoscope, the continuous irrigation variety (Iglesias), is the most commonly employed equipment. The resectoscope is placed at the level of the verumontanum and the adenoma is resected in quadrants. Resection begins at 12 o'clock at the bladder neck, and is then carried down anticlockwise to the 9 o'clock position in a stepwise fashion to a depth where circular fibers of the bladder neck become visible. The resection is carried down to the surgical capsule, which is recognized as a rather fibrous structure compared with the granular appearance of the prostatic adenoma. The other anterior quadrant, from 12 to 3 o'clock, is next resected clockwise.

Resection of the anterior quadrants results in the lateral lobes falling toward the floor. Resection of right lateral lobe is started at approximately the 9 o'clock position and continued in an anticlockwise fashion. The resection is carried to the right side of the verumontanum. For the left lobe, a similar procedure is started at approximately 3 o'clock and carried clockwise to the left side of the verumontanum. After completion of the lateral lobes, the tissue at 6 o'clock, including the median lobe if present, can then be resected up to the verumontanum. Care must be taken not to resect too deeply in the region of the posterior aspect of the vesical neck to prevent undermining of the trigone.

Large adenomas can be resected using "encirclement," a modification of the above-mentioned technique. During resection of the lateral lobes, a groove is created between the bulk of adenoma tissue and the surgical capsule by working the resectoscope loop along the capsule, allowing the lobe to fall to the floor. The loop works somewhat like the finger of the operating surgeon in the open transvesical prostatectomy, separating the lobe from the surgical capsule of prostate. The procedure is done first on one side and then on the other side. Finally, the remaining bulk of tissue on the floor, which by now is mostly devascularized, can be resected quickly to complete the procedure.

Another variation of the technique, popularized by Blandy, starts with resection of the floor at the 6 o'clock position, including the median lobe if present. This is followed by resection of each lateral lobe from the 12 o'clock down to the 6 o'clock position in the standard fashion. The advantage of this approach is to establish the tissue planes and landmarks at the beginning of the operation. This approach can be especially useful in prostates with a large median lobe.

Toward the end, the apical portion of the lobe remains; this is resected last. Care must be taken to avoid extending the resection beyond the level of verumontanum to protect the external sphincter mechanism, which lies just distal to it. The most common area of damage to the external sphincter is at the 12 o'clock position. Thus, care must

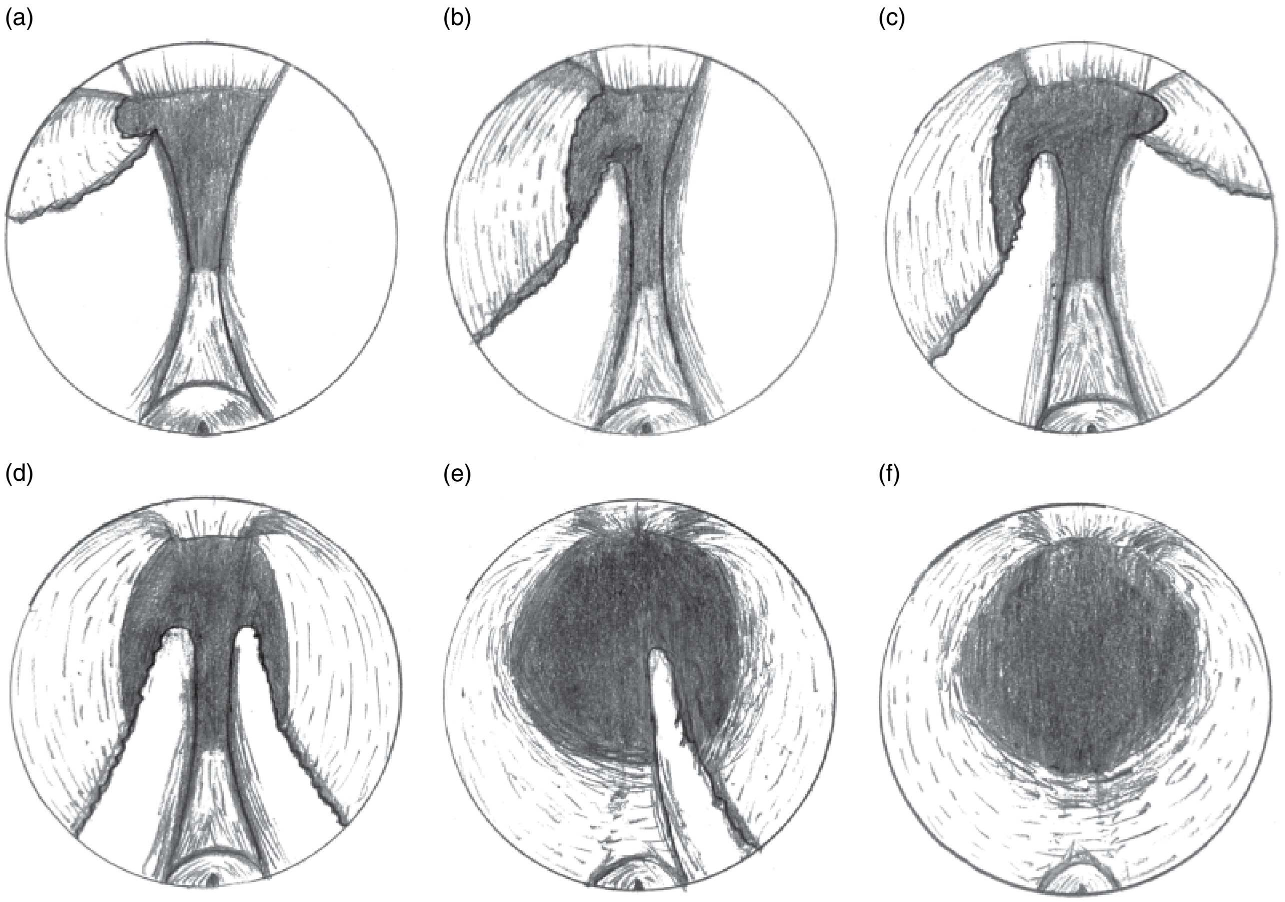

**Figure 150.4** Stages of transurethral resection of the prostate: endoscopic view.

be taken as the 12 o'clock position is approached. The resection, especially the apical portion, may be performed with a finger in the rectum, for which a rectal shield can be put in place at the beginning of the operation. When the resection is completed, the resectoscope is pulled just distal to the verumontanum, to see that there is no falling or obstructing tissue. Any remaining adenoma tissue can be judiciously trimmed down to the surgical capsule, taking care not to damage the sphincter mechanism.

Hemostasis is of prime importance, and must be maintained meticulously throughout the operation. The arterial bleeders are best coagulated at the level of the surgical capsule using spray coagulation. Complete hemostasis must be achieved at each stage, before resection proceeds to the other quadrant.

## "Hemiresection" of the prostate

TURP for large glands may be associated with significant morbidity, mainly due to absorption of irrigant and blood loss. When extensive resection of the prostate tissue is carried out, opening of venous sinuses can be associated with troublesome bleeding and/or excessive absorption of fluid, resulting in "TUR syndrome."

Similarly, in medically compromised elderly individuals (cardiomyopathy, ischemic heart disease, chronic obstructive respiratory disease, renal insufficiency, etc.) standard TURP may carry greater risk. In such patients the procedure may sometimes need to be terminated prematurely due to blood loss and/or excessive fluid absorption, because of the prolonged operating time.

However, incomplete resection leads to a large raw surface. Good hemostasis is not achieved because of the retraction of the blood vessels within the adenoma, leading to a greater incidence of hemorrhage and infection. In addition, incomplete resection of the prostate leads to poor flow rates postoperatively, and recurrent retention due to the "falling in" of the residual adenoma. It is also associated with a higher complication rate of reactionary and secondary hemorrhage, persistent postoperative urinary infection, and early recurrence [22].

In such a situation, an alternative solution is termination of the procedure after "complete" resection of one

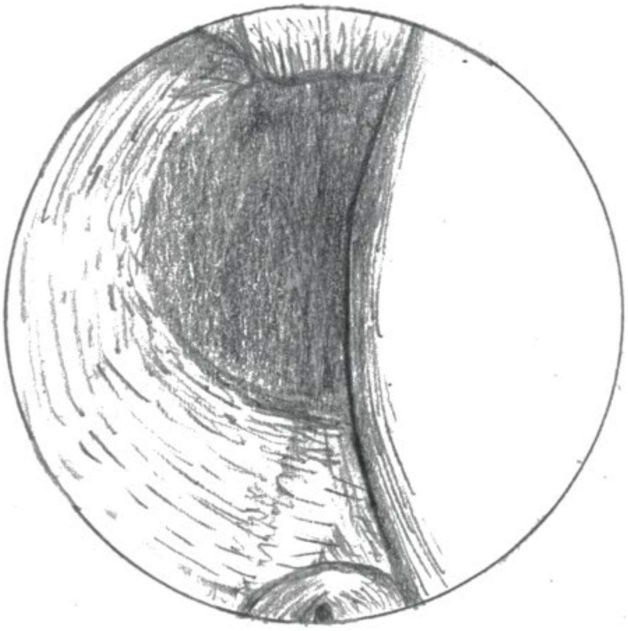

**Figure 150.5** "Hemiresection": endoscopic view.

lateral lobe (and the median lobe, if present) of the prostate. This procedure, termed "hemiresection" of the prostate (Figure 150.5), allows completion of the procedure quickly to avoid complications of excessive blood loss and/or fluid absorption, while at the same time avoids the problems associated with "incomplete" resection.

The patients undergoing hemiresection have the advantage of shorter operating time and less blood loss compared to those undergoing standard TURP. At the same time, complete resection of one lateral lobe (and the median lobe if present) prevents the complications of hemorrhage and persistent infection associated with incomplete resection, and ensures a good channel for adequate flow. The other lateral lobe that is left untouched remains attached to the surgical capsule of prostate and therefore does not "fall in" to obstruct the channel and increase the incidence of postoperative retention of urine. In addition, there is no raw area of incomplete resection as the mucosa over the unresected lobe remains intact.

In a prospective randomized trial at our center in a series of 163 patients, the results of standard TURP and prostatic hemiresection were found to be comparable in terms of reduction of PVR, improvement in symptom score, and peak flow rate [23]. No patient developed retention of urine in the postoperative period. The incidences of blood loss and TUR syndrome were lower in the hemiresection group.

Prostatic "hemiresection" allows early termination of TURP in case of need, to avoid complications of excessive blood loss and fluid absorption. At the same time, it avoids the problems associated with "incomplete" resection. "Hemiresection" or "hemi-TUR" may be considered an acceptable option if the surgeon gets into trouble in the middle of an operation, or even as an elective operation in men with large glands and severe medical comorbidity, without compromising the basic principles of TUR surgery.

## Postoperative care

Most urologists prefer to apply traction on the irrigation catheter for a period of 2–6 hours. Continuous irrigation is provided with prewarmed fluids, with care taken to ensure proper outflow. The early postoperative period requires careful monitoring for prompt recognition of any complications. It is desirable to have an assessment of hemoglobin and electrolytes in this period. Patients are made to ambulate after traction is removed. Antimicrobials are continued until the patient is catheter free (i.e. 3–5 days).

## Outcomes

The AHCPR panel conducted a meta-analysis of various clinical studies and found the results of TURP to be significantly better in comparison to other less invasive procedures [24]. TURP improved symptoms in 70–96% of patients (mean 85%).

The mortality rates following TURP have shown a significant decline since the introduction of the procedure. The current mortality rates range from 0% to 0.25% [25]. This reduction indicates that progress has been made in making the procedure safer than it originally was. Technologic advances, such as microprocessor-controlled units, better armamentarium such as video TURP, and better training have contributed to this improvement.

## Complications

### Early complications

**Hemorrhage**

Hemorrhage is the most frequent complication. Larger glands and resection times of longer than 90 minutes are associated with a higher incidence of bleeding. The bleed can be arterial or venous and complicates both intraoperative and postoperative management. Arterial bleeding should be suspected if the irrigation catheter shows continuous passage of bright red blood. As a general principle, during resection all bleeding from an area of the prostatic fossa should be controlled using coagulation before moving to another area. Venous bleeding is darker and generally occurs after a period of initial clear irrigant in the postoperative period. Reapplication of traction on the catheter with or without overinflation of the balloon can be useful in these cases. Excessive bleeding, especially if suspected to be arterial, may require repeat cystoscopy with electrosurgical coagulation to control the bleeding.

#### Resection errors

Over-resection with perforation of the prostatic capsule leads to extravasation of irrigant. It is characterized by restlessness, vomiting, and abdominal pain localized to the lower abdomen and back (a noticeable feature in a patient who has undergone spinal anesthesia). Immediate termination of the procedure with control of bleeding is of paramount importance in these patients. Most patients respond well to a period of catheter drainage and antibiotics.

#### TUR syndrome

This complex syndrome of fluid overload, dilutional hyponatremia, and hemolysis due to systemic absorption of large amounts of irrigant, especially in patients with a gland size larger than 45 g and a resection time of more than 90 minutes. Mebust et al. observed that TUR syndrome occurred in 2% of patients [10]. The syndrome may occur as quickly as 15 minutes after the resection starts or up to 24 hours postoperatively [26–29]. It is characterized by confusion, nausea, vomiting, hypertension, bradycardia, and visual disturbances. Monitoring the serum sodium concentration is important as the syndrome does not occur until the serum sodium falls below 125 mEq/dl. Intravenous hypertonic saline, diuretics, and termination of the procedure may be required when this happens. Madsen and Naber observed that limiting the height of the irrigation bottle to 60 cm above the prostate reduced the intravascular fluid absorption [30]. Leaving a rim of tissue on the capsule until the end of the procedure, where it can be left if signs of TUR syndrome are evident, may reduce the risk of absorption due to opening of prostatic sinuses [31, 32].

#### Obturator nerve stimulation

Most instances of obturator nerve stimulation occur following transurethral resection of bladder tumors and TURP is very infrequently implicated. When it occurs, stimulation of the obturator nerve produces a sudden thigh movement that can cause the cutting loop to bite more deeply, and often at an undesired location. Various modalities have been tried to prevent adductor spasm during spinal anesthesia, ranging from local blockade of the obturator nerve, periprostatic and subvesical lignocaine infiltration, changing the site of the inactive electrode, reduction of the electrocoagulation voltage, and general anesthesia with muscle relaxants. However, local blockade of the obturator nerve seems to be the most effective in preventing this complication [33–35].

#### Intraoperative priapism

Intraoperative penile erection may be managed by injecting small boluses of an alpha-adrenergic agent (dilute ephedrine or phenylephrine) into the corpora cavernosa.

#### Sepsis

Pre-existing urinary tract infection should always be rectified and managed before undertaking TURP. Patients with longstanding indwelling catheters are at greater risk. Once infection is recognized, broad-spectrum empirical antibiotic therapy is started. Perioperative antibiotic prophylaxis has been shown to reduce the risk of events related to postoperative infection.

### Late complications

#### Bladder neck contracture

This complication occurs 4–6 weeks after surgery and should be suspected in a patient complaining of poor stream who initially had a good flow postoperatively. Zwergel et al. reported bladder neck contracture in up to 2.7% patients following TURP [36]. It can be treated by bladder neck incision with a Collings knife.

#### Urethral stricture

Urethral strictures following TURP have been reported in 1.7% patients and can occur at the fossa navicularis (most commonly), bulbar urethra or prostato-membranous junction [36]. Strictures can be treated with sequential urethral dilatation and optical internal urethrotomy. The incidence of post-TURP stricture has declined significantly with the availability of better electrosurgical equipment and smaller sized resectoscopes, limiting the resection time, and use of lubricant jelly.

#### Incontinence

Thermal injury to the sphincter is the underlying mechanism in most patients who develop this complication of TURP. Detrusor instability and residual adenoma blocking the external sphincter mechanism may also contribute to this complaint. Transient incontinence is relatively common following the procedure, and most patients show spontaneous improvement in a few weeks or months. Kegel exercises and anticholinergics are useful in these patients. For refractory cases, collagen injections and artificial sphincters are needed.

### Impotence

A small number of patients report impotence following the procedure, which may be psychogenic or due to age and prolonged abstinence following the operation. This complication needs to be studied well to eliminate the discrepancy in the reported literature (incidence 4–40%). In fully potent men, the risk of impotence after transurethral prostatectomy is fairly low, but it is higher in men who already have a degree of erectile failure. This risk has also been reported to be related to the incidence of capsular perforation at the time of surgery [37].

Tscholl et al. used the Snap Gauge tests to assess the incidence of erectile impotence in patients with intact potency preoperatively. Of the 98 patients studied, they observed that erectile dysfunction persisted in eight (8.3%) patients three months after the procedure [38]. Importantly, in their study 26 patients who had potency-related problems postoperatively improved in the subsequent three months.

## Comparison with bipolar transurethral resection of the prostate

Monopolar TURP does suffer from a few inherent limitations. First, the patient is a part of the electrosurgical circuit, which can cause deep heating and the possibility of nerve damage. Second, the use of a hypo-osmolar irrigant implies that electrolyte imbalance and TUR syndrome will always remain bothersome concerns.

In recent years, bipolar TURP has emerged as an alternative to the standard monopolar TURP. Advocates of bipolar TURP cite comparable clinical efficacy with a better safety profile, especially in terms of lower instances of TUR syndrome and better hemostatic capability, as the primary reason for its superiority. A systematic review by Tang et al. indicates that bipolar TURP was significantly better for decreasing the incidence of TUR syndrome and clot retention. However no significant differences were observed in the nature of adverse events such as transfusions, retention after catheter removal, and urethral complications between the groups [39].

Another study by Mamoulakis et al. indicated that no clinically relevant differences in short-term efficacy exist between the two techniques, but that bipolar TURP is preferable due to a more favorable safety profile (lower TUR syndrome and clot retention rates) and shorter irrigation and catheterization duration [40].

These studies are promising, but large randomized _ trials with long-term follow-up are needed to further clarify issues related to long-term complications and cost. Bipolar TURP has the potential to become the next generation "gold standard" for benign prostatic obstruction but only time will tell if it can replace monopolar TURP.

See accompanying Video 150.1.

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# 151

# Ablation of Prostate: Bipolar Resection

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## Introduction

Bipolar transurethral resection of the prostate (BiTURP) is an endoscopic technique used in the surgical management of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH).

Monopolar TURP, as described in Chapter 150, is a transurethral endoscopic procedure that relies on electrosurgical resection of prostate adenoma, followed by removal of "prostate chips" from the bladder with an aqueous evacuator. It has been performed since early in the last century, has evolved to be the procedure of choice for surgical treatment of LUTS secondary to BPH, and is often called the "gold standard" surgical treatment for BPH/LUTS. Although monopolar TURP is known to be efficacious in this context, it is associated with reasonably high rates of complications, including hematuria, reoperation, dilutional hyponatremia, and the need for blood transfusion [1]. Advances in optics and energy generation/delivery systems have decreased complications significantly in modern times [2]. However, the number of TURPs performed in the United States continues to decrease yearly, perhaps because of the perception of increased morbidity [3].

The rationale for BiTURP, therefore, is straightforward – to limit the risk of dilutional hyponatremia while leveraging transurethral resection skills that most urologist acquire during training and practice. Most authorities suggest limiting monopolar TURP operating times to 60 minutes because absorption of fluid is proportional to the operative time. Longer operative times lead to increasing risk of dilutional hyponatremia, also known as "TUR syndrome" due to absorption of glycine irrigation [4]. The fact that BiTURP uses normal saline as an irrigant effectively eliminates the risk of dilutional hyponatremia and allows operators to use this technique for as long as needed. This is particularly advantageous in patients with large-volume prostates or for use in medical education.

It should be noted that BiTURP is actually an evolution of transurethral vaporization of the prostate [5], which is a monopolar technique that uses higher current and electrodes with broader contact with tissue to "vaporize" tissue at the cut edge of the resection. BiTURP has been referred to as bipolar vaporesection of the prostate, plasmakinetic vaporization of the prostate, or bipolar resection of the prostate. This nomenclature adds to confusion, particularly with strictly ablative techniques such as photoselective laser vaporization of the prostate or bipolar button vaporization electrode. The "vaporization" referred to in BiTURP is actually the vaporization that occurs of tissue in contact with the cutting loop (active electrode). This is similar to what happens to tissue in contact with the cutting electrode during monopolar TURP. BiTURP relies on the creation of a "plasma corona" at the electrode and this results in roughly 20% of the tissue being vaporized, with the rest resected as prostate chips [6].

BiTURP was first introduced in humans in the early part of this century [7]. The initial reports touted this technique's ability to use bipolar current through an isotonic irrigant media with results similar to TURP. Most subsequent reports have focused on technologies from different manufacturers and primarily compared results to TURP via either randomized control trials or comparative trials.

## Patient selection

Surgical therapy is the mainstay for treatment of LUTS secondary to BPH, refractory to medical therapy. Current practice is to offer minimally invasive surgery to patients

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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who do not want or are unfit for a more involved operation. Endoscopic surgery is the gold standard for treatment of LUTS secondary to BPH, with open surgery reserved for those patients with large glands or those who need concomitant procedures [8].

The most recent American Urological Association (AUA) guidelines [8] on the management of BPH/LUTS recommend TURP as the surgical treatment of choice for men with moderate to severe LUTS who are bothered by their symptoms. These guidelines state that the "choice of a monopolar or bipolar approach should be based on the patient's presentation, anatomy, the surgeon's experience and discussion of the potential risks and likely benefits" [8]. The European Association of Urology has similar recommendations in its recently release guideline on the management of non-neurogenic male LUTS, but goes a little further by stating that "B-TURP offers an attractive alternative to M-TURP in patients with moderate to severe LUTS secondary to BPO [benign prostatic obstruction], with similar efficacy but lower peri-operative morbidity" [9]. An updated set of AUA guidelines is currently being formulated and should be available shortly.

## Surgical equipment

BiTURP is an endoscopic resection technique that uses a continuous flow resectoscope and a specially designed loop and inner sheath that varies by manufacturer and use. It is a design modification of the monopolar TURP, utilizing a specialized resectoscope and loop that incorporates the active electrode on the loop and return electrode on a separate insulated part of the loop or on the inner sheath of the resectoscope. This allows the procedure to be performed using normal saline as an irrigant, thereby limiting the risk of dilutional hyponatremia (or TUR syndrome), and with potentially less stray current because of the very short distance between the active and return electrodes. The electrode can be used to resect as well as coagulate. Modifications of the electrode also allow vaporization, which will be discussed in a subsequent section. In contrast to monopolar TURP, the irrigant media is usually 0.9% normal saline. Generators are also matched to the loop used and voltage is varied based on impedance to keep the current constant.

## Technology

Bipolar technology platforms currently available are the PK system by Gyrus/ACMI, an Olympus Corporation (Tokyo, Japan) company, the TURis system by Olympus Corporation (Tokyo, Japan), and a bipolar resection system by Karl Storz (Tuttlingen, Germany). Each of these systems uses a continuous flow resectoscope and relies on an active electrode on the cutting element of the loop, with the ability to generate a plasma corona vaporization field in normal saline media. The difference between these platforms is the location of the return electrode. Because BiTURP relies on the ability to generate a current between two poles and the closer the two poles, the lower the voltage needed to generate a current, the return pole (electrode) has to be in close proximity to the active electrode. As such, the return electrode of the PK system is on the loop itself, separated from the cutting element by a few millimeters of insulation. The return electrode for the TURis system is on the inner sheath of the resectosope, and the return electrode for the Storz system is on the loop opposite the cutting element. See Figures 151.1–151.3 for illustrations of the different available loops.

The BiTURP, which typically needs a lower voltage differential to generate a high current because of the short distance needed to close the circuit, relies on generators that can change voltage based on tissue impedence and therefore keep current constant. Specially designed generators are matched to each platform. All generators have preset default settings; typical settings for "cutting" are high power (200–280 W for TURis, 160–200 W for PK) and settings for "coagulation" are lower power (120 W for TURis and 80 W for PK). Different loops are also available for the PK system and the TURis system to allow resection of bladder tumors or to perform vaporization without resection. All currently available loop electrodes are single use. Figure 151.4 is an illustration of the Gyrus PK® generator.

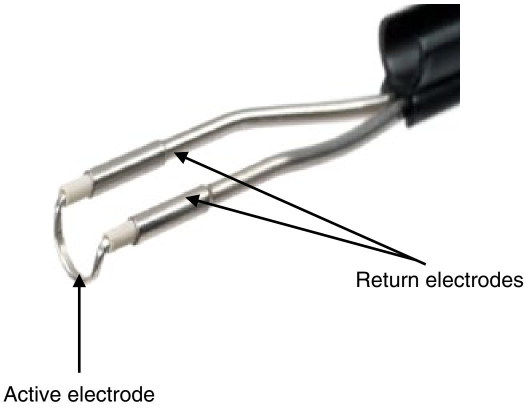

**Figure 151.1** The Gyrus PK Supersect loop.

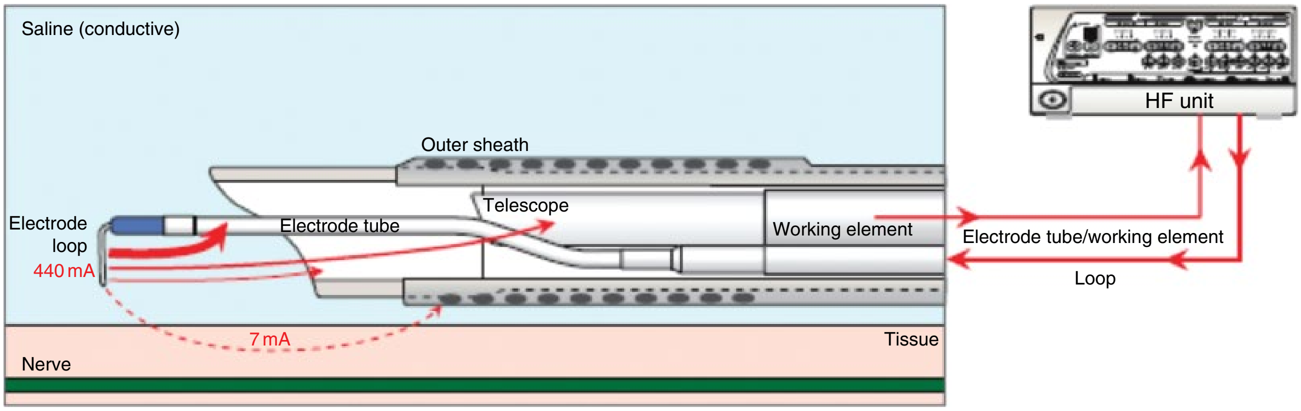
Saline (conductive)
HF unit
Outer sheath
Telescope
Electrode loop
440 mA
Electrode tube
Working element
Electrode tube/working element
Loop
7 mA
Tissue
Nerve

**Figure 151.2** Olympus TURis bipolar loop.

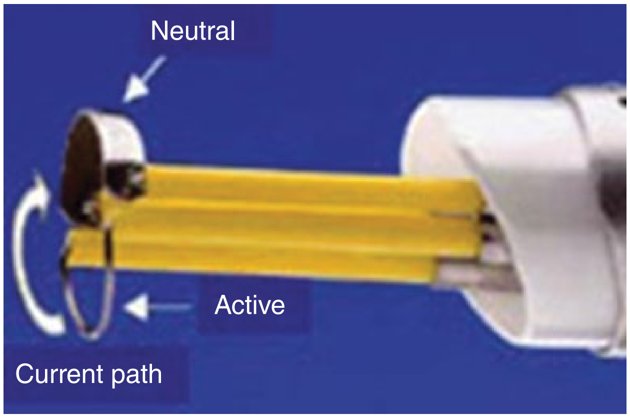
Neutral
Active
Current path

**Figure 151.3** Karl Storz bipolar loop.

**Figure 151.4** Gyrus PK generator.

## Surgical technique

The surgical technique for BiTURP is similar to that for monopolar TURP, with a few unique aspects. As in other transurethral procedures, preoperative antibiotics should be given. Regional anesthesia (e.g. spinal) or general anesthesia may be used. It is important to note that there should be no dilutional hyponatremia with BiTURP, eliminating the need to monitor mental status and allowing general anesthesia to be used at the anesthesiologist's discretion.

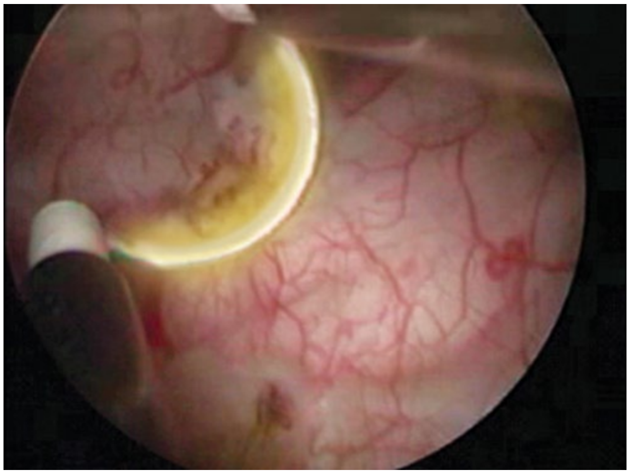

**Figure 151.5** The plasma corona firing in the bladder.

Initial intubation of the urethra should be performed with the help of a visual obturator. If needed, a urethrotomy may be performed to allow entry of larger resectoscopes. Once the bladder is reasonably filled, continuous irrigation should be started, typically with the outflow port open to gravity drainage. Resection is started by first resecting the intravesical component and the median lobe of the prostate. Unlike the monopolar TURP, the cutting electrode loop needs to develop a "plasma corona" prior to the start of resection (see Figure 151.5 for an illustration of a loop with plasma corona active). The loop should be in close proximity to prostate tissue when the operator initiates the cutting current via the foot pedal. At the beginning of the case, this is typically done with the electrode in the bladder and slightly off the prostate surface. Once the corona is formed, resection proceeds in an antegrade fashion for the length of the loop excursion. Prostate chips are formed similar to monopolar TURP and are forced into the bladder by the inflow of normal saline irrigant.

The resection should be performed systematically with prostate landmarks used to limit resection, in particular the verumontanum near the apex. Typically, the intravesical component is first resected, followed by the median lobe from the bladder neck to verumontanum. Care should be taken to avoid injury to the ureteral orifices during this step. Next, one of the two lateral lobes is resected in its entirety prior to proceeding to the other one. Finally, apical tissue and anterior tissue is resected. During resection, the plasma should always be visible. This is especially important as the procedure proceeds, because the cutting loop will add charred tissue to its surface and add impedence to the circuit. As stated above, the corona should be initiated within the bladder or in the lumen of the prostatic urethra without contacting prostate tissue. If the time between stepping on the cutting pedal and the formation of the plasma corona starts to become long, the operator should place the loop in the center of the bladder and allow the plasma to fire for a few seconds. This will clean the loop electrode and allow more efficient vaporization.

Once the surgical endpoint is reached, specifically the entire adenoma has been resected from bladder neck to verumontanum and capsular fibers are visible, hemostatis should be achieved. This is done with the coagulation current. During coagulation, no plasma is formed. Instead of point coagulation, as in monopolar TURP, BiTURP relies on coagulating a surface around the bleeding vessel. This is likely due to the shallow penetration of current during BiTURP. Of note, coagulation should be performed intermittently throughout the procedure if significant bleeding is encountered as this will improve visibility during the case.

Prostate chips deposited in the bladder throughout the resection are removed near the end of the case with help of an aqueous evacuator. Once all chips have been removed and this has been confirmed by a final survey of the base of the bladder and prostate fossa, a three-way urethral catheter is inserted and continuous bladder irrigation is begun. Typically, this irrigation is titrated off by the first postoperative day, and the catheter removed. Patients are discharged with a few days of antibiotics. The prostate chips are evaluated by surgical pathologists in a manner similar to prostate chips removed during a monopolar TURP and the same conventions are used to report findings, including T1a or T1b prostate cancer in cases of previously unsuspected prostate cancer. If T1a or T1b prostate cancer is found and the patient is a candidate for prostate cancer treatment, a prostate biopsy should be performed once the patient has healed from the BiTURP – typically six weeks to three months after the procedure.

Postdischarge management is similar to that with monopolar TURP and is dependent on the surgeon. Typically, patients can expect mild hematuria which resolves within days and can also expect temporary increase in frequence and urgency of urination. There may be a period of recurrent hematuria 2–6 weeks after the procedure, managed by increasing oral hydration. Follow-up visits are usually at 3, 6, and 12 months. At each follow-up visit, the International Prostate Symptom Score (IPSS) is collected along with uroflowmetry data and measurement of postvoid residual urine (PVR). A serum PSA should be obtained at the 12 month visit if indicated. Of note, if patients were candidates for prostate cancer screening at the time of BiTURP, a preoperative serum PSA and digital rectal exam should have been performed and if either one was abnormal, a prostate biopsy should also have been performed.

## Efficacy

The first reports of BiTURP in humans came in the early part of this century. Botto et al. [7] published a pilot study in 2001 of 42 patients who underwent electrovaporization of the prostate using saline bipolar electrocautery using the Gyrus system. These investigators reported three-month results following treatment of men with symptomatic BPH without suspected prostate cancer. They noted that no men had significant postoperative bleeding and the mean catheterization time was 1.4 days. Two out of the 42 patients developed urethral strictures requiring treatment. Mean length of stay was 2.2 days. At three months, IPSS decreased from 16 at baseline to 9 and peak flow rate on uroflowmetry increased from 7.9 ml/s to 19.7 ml/s. Based on these short-term results, the authors concluded that the Gyrus system for electrovaporization of the prostate is useful and safe.

Yang et al. [10] subsequently performed a randomized prospective study comparing the Gyrus BiTURP to conventional monopolar TURP. They enrolled 117 patients, 58 in the BiTURP group and 59 in the monopolar TURP group, and followed these patients for three months. The authors noted that both groups reported significant improvements in IPSS (BiTURP: 20.9 preoperatively to 10.8 at three months; TURP: 21.6 preoperatively to 11.1 at three months) and peak flow rates (BiTURP: 10.4 ml/s to 17.1 ml/s; TURP: 10.9 ml/s to 14.8 ml/s), but noted no statistically significant difference between groups. In their study, complications occurred at the same rate in both groups; notably, only one patient developed TUR syndrome in the monopolar TURP group and none in the BiTURP group. These authors concluded that monopolar TURP and BiTURP yielded similar results but that longer follow-up was necessary to establish long-term efficacy.

Starkman and Santucci [11] retrospectively reviewed their results and compared 18 consecutive patients who underwent monopolar TURP with a subsequent consecutive group of 25 patients who underwent BiTURP. After an observation period of approximately 1.5 years to evaluate long-term complications, weights of resected tissue were similar in both groups; catheterization times were shorter (3.2 days for monopolar TURP vs. 1.8 days for BiTURP) and length of stay shorter with BiTURP (2.1 days for monopolar TURP vs. 1.2 days for BiTURP). Acute complications included 2 out of 18 monopolar TURP patients with dilutional hyponatremia and, interestingly, one out of 25 BiTURP with dilutional hyponatremia. Other acute complications were minor, but higher in the monopolar TURP group compared to in the BiTURP group (33% vs. 16%). Long-term complications consisted of one bulbar urethral stricture in each group and a patient who developed a bladder neck contracture related to radiotherapy for a subsequent prostate cancer diagnosis in the BiTURP group and a patient with persistent stress urinary incontinence in the monopolar TURP group. Long-term complications were not statistically different between groups.

De Sio et al. [12] randomized 70 patients to Gyrus PK BiTURP or monopolar TURP groups. They reported results of their randomized cohorts after 12 months. Like the earlier groups, they found decreased mean catheter time (100 hours for monopolar TURP vs. 72 hours for BiTURP) and mean length of stay (107 hours for monopolar TURP vs. 78 for BiTURP) in the BiTURP group. They also noted no difference between groups in IPSS, peak flow rates, or PVR. IPSS decreased from 20 preoperatively to 4 at 12 months in both groups, peak flow rate improved from roughly 5 ml/s preoperatively to 20 ml/s at 12 months in both groups, and PVR decreased from roughly 80 ml preoperatively to roughly 20 ml at 12 months in both groups. These authors noted no significant difference in adverse events.

Seckiner et al. [13] similarly performed a randomized study comparing the Gyrus PK BiTURP to monopolar TURP. They compared 24 patients in each group and followed them for 12 months. No significant difference in operative and perioperative data were found except for decreased serum sodium in the monopolar TURP group, with two patients in the monopolar TURP group exhibiting mild dilutional hyponatremia. Like previous authors, these authors reported significant improvements in IPSS, peak flow rate, and PVR in both groups compared to baseline values but did not show any difference between groups.

Iori et al. [14] performed a clinical and urodynamic evaluation in a randomized manner to compare Gyrus PK BiTURP to monopolar TURP. These authors operated on 51 patients with urodynamically proven bladder outlet obstruction; 26 of these patients underwent monopolar TURP and 27 underwent BiTURP. Mean follow-up was 12 months. There was no difference in resection time, catheterization time, or length of stay between groups and no difference in change in serum hemoglobin or serum sodium between groups. Of note, all patients underwent urodynamic evaluation prior to procedure and at 12 months postoperatively. The Schaefer obstruction class was significantly improved after both procedures and, as with other parameters, there was no difference between urodynamic effects after monopolar TURP and BiTURP.

Fagerström et al. [15] performed a randomized trial comparing operative performance of the Olympus TURis BiTURP to conventional monopolar TURP. These investigators randomized 202 patients, 185 of whom were evaluable. They noted that both groups had similar tissue resection weight, but that blood loss and hemoglobin decrease were greater in the TURP group than the BiTURP group. These authors concluded that BiTURP causes less bleeding than monopolar TURP technique.

Ho et al. [16] performed a randomized study comparing Olympus TURis BiTURP to standard monopolar TURP and followed these patients for 12 months. They compared 52 patients in the monopolar TURP group to 48 patients in the BiTURP groups and noted no difference in resection time or resection weight. A significant decrease in serum sodium was noted in the monopolar TURP group compared to BiTURP, and two cases of clinically significant dilutional hyponatremia occurred in the monopolar TURP group and no cases in the BiTURP group. Urethral strictures were observed in 3 out of 48 patients in the BiTURP group and 1 out of 52 patients in the TURP group. These authors also showed significant improvements in IPSS and peak flow rate at 12 months from baseline in both groups but no differences between groups. It was concluded that monopolar TURP and BiTURP were equally efficacious with BiTURP having a better safety profile.

Michielsen et al. [17] performed a large randomized trial comparing conventional monopolar TURP to Olympus TURis BiTURP. One hundred and twenty patients underwent monopolar TURP and 118 underwent a BiTURP. These authors focus on intraoperative parameters and immediate perioperative morbidity. They noted no difference is resected prostate tissue weight and duration of hospitalization between groups. They did note that BiTURP took longer to perform, but that decrease in serum sodium was significantly greater for the monopolar TURP group. They also noted one case of TUR syndrome in the monopolar TURP group and none in the BiTURP cohort.

BiTURP has been reported to be a safe alternative to monopolar TURP for use in resident teaching and for the management of large-volume prostates. Bhansali et al. [18] performed a randomized trial of 70 patients with prostate sizes greater than 60 g comparing Gyrus PK BiTURP to monopolar TURP. They noted no length of stay or function outcomes at 9 and 12 months postoperatively between the two cohorts. They did notice significantly more blood loss, significantly longer catheterization time, and significantly large changes in serum sodium in the monopolar TURP group compared to the BiTURP group. The authors concluded that it is safe to perform BiTURP in large-volume prostates.

More recently, Demirdag et al. [19] reported on 81 patients with prostates greater than 60 ml, 45 of whom underwent monopolar and 36 underwent BiTURP, and noted that the only difference between the two groups was a decrease in serum sodium in the monopolar group. Further, the authors noted that two of the monopolar patients had TUR syndrome whereas none of the BiTURP patients did.

Gilleran et al. [20] commented on using BiTURP in an academic setting to help teach residents how to perform an adequate TURP. These authors reported results of a series of 21 men who underwent Gyrus PK TURP in an academic setting. They noted that despite small-size prostates (median resected tissue weight was 20 g), they had a median resection time of 65 minutes, which is much more than would be expected for the amount of tissue resected. Although they did note a significant decrease in serum hemoglobin between preoperative and postoperative values, they did not report a significant difference in serum sodium and no patients needed blood transfusions. The authors concluded that BiTURP is a safe modality for resident medical education.

Large series of BiTURP have been reported recently. Martis et al. [21] reported their series of 401 patient who underwent Gyrus PK BiTURP and noted no intraoperative complications. They reported excellent and durable functional results measured by IPSS and peak flow rates though 36 months of follow-up. The authors did note three patients developed urethral strictures that were effectively managed with internal urethrotomy. Puppo et al. [22] reported outcomes and complications after the first 1000 cases of Olympus TURis system resections, including 376 BiTURPs. Other procedures using the saline bipolar technology in this report were 480 bladder tumor resections and 144 transurethral incisions of the prostate. The authors noted no cases of TUR syndrome and operative and function results better than comparable series of monopolar TURP.

Mamoulokis et al. [23] reported a systematic review and meta-analysis of all randomized control trials of BiTURP. They found a total of 16 randomized controlled trials with 1406 patients which were included in the meta-analysis. The authors noted that efficacy of BiTURP was comparable to monopolar TURP, with respect to IPSS and quality-of-life metrics. They did note, however, that peak flow rate was significantly improved with BiTURP over monopolar TURP at 12 months. This was weighted by one trial which showed marked improvements for BiTURP over monopolar TURP. The meta-analysis also evaluated decreases in serum sodium and incidences of TUR syndrome. They noted a significant larger difference in serum sodium decrease in patients undergoing monopolar TURP compared to BiTURP. Of note, while none of the individual studies showed a difference in the incidence of TUR syndrome, the pooled analysis did detect a significantly higher rate of TUR syndrome in patients who underwent a monopolar TURP compared to a BiTURP. The number needed to treat to prevent one case of TUR syndrome was 50.

Lee et al. [24] and Omar et al. [25] subsequently performed systemic reviews and noted somewhat differing results. Lee et al. found improvements in IPSS, maximum flow rates, residual volume, better satisfaction, and decreased complications in the BiTURP patients, whereas Omar et al. noted decreased complications but no significant improvement in efficacy in the BiTURP. They also noted no significant difference in IPSS and while there was a significant difference in maximum urinary flow there was evidence of heterogeneity between groups.

Cornu et al. [26] recently published a comprehensive systemic review that evaluated functional outcomes and complications following multiple transurethral procedures for LUTS. When comparing BiTURP to monopolar TURP, the authors noted complication rates were lower in the BiTURP patients but that efficacy was similar between groups.

## Morbidity/complications

BiTURP appears to be safer than monopolar TURP, especially with regard to decreases in serum sodium and incidence of dilutional hyponatremia. All studies that report on serum sodium show decrease and the meta-analysis performed by Mamoulokis et al. [23] confirmed that serum sodium decreases and incidences of TUR syndrome are both significantly higher in monopolar TURP arms as compared to BiTURP. BiTURP has not been compared to other prostate ablation modalities such as laser prostatectomy that also use normal saline as an irrigant.

Urethral strictures were noted to be higher in the early BiTURP studies, particularly in a study by Tefekli et al. [27] that evaluated a hybrid vaporization/resection technique using Gyrus equipment. These authors compare their saline bipolar technique to monopolar TURP and noted similar efficacy but a significantly higher rate of urethral strictures in the bipolar cohort. Other authors have suggested that the large cystoscope needed to perform continuous flow BiTURP and possibly longer operating times may be associated with increased incidence of urethral strictures [17]. A unique aspect of Olympus TURis BiTURP has also been implicated – the fact that current returns through the inner sheath [16]. An equipment malfunction could potentially expose the urethra to active current, potentially leading to urethral strictures. Despite the fact that the cutting loops for TURis are single use, some authors have speculated that reusing the loops leads to higher stricture rate. The pooled analysis of all BiTURP randomized control trials [23] has not shown a higher rate of urethral stricture, and in fact shows stricture and bladder neck contracture rates comparable to those of BiTURP and monopolar TURP. Mamoulakis et al. [28] performed a multicenter RCT of 295 patients comparing BiTURP to monopolar TURP and found 10 urethral strictures in each arm, but noted two bladder neck contractures in the monopolar arm compared to eight in the BiTURP arm. The differences in bladder neck contractures, however, was not significant.

The perception of increased intra- and postoperative blood loss with BiTURP remains controversial. Although early reports after saline bipolar resection showed a smaller zone of coagulation than monopolar TURP [29], more recent report have shown a larger zone [30] and others have shown differences in size of zone between that measured immediately postoperatively and that measured after a few days [31]. It remains unclear which is beneficial as far as hematuria is concerned – decreased or increased zone of coagulation. Regardless, the pooled meta-analysis [23] showed no difference in intraoperative or postoperative blood loss following BiTURP compared to monopolar TURP. Stucki et al. [32] performed an RCT comparing bipolar to monopolar focusing on bleeding complications and noted no significant difference in blood loss, rates of blood transfusion, or TUR syndrome, but did note a significantly higher rate of bladder neck contracture in the biTURP arm (8.5% vs. 0%).

Rates of TUR syndrome are certainly lower for BiTURP than monopolar TURP due to absorption of isotonic instead of hypotonic irrigant media. However, fluid absorption does occur with BiTURP and Porsch et al. [33] showed that this absorption is higher in patients who undergo BiTURP than in those who undergo photoselective laser vaporization of the prostate, even though both procedures use normal saline as irrigant. This means that care should be taken when performing BiTURP in larger glands because of the potential for fluid overload.

## Cost

The cost of BiTURP is an important consideration, especially with pressures on most healthcare systems to control costs. The Urologic Diseases in America project estimated that over US$1 billion was spent in the United States for the management of BPH, not including costs of medicines [3]. It appears that BiTURP may be less expensive than monopolar TURP despite increased capital costs and increased disposable costs. This has been postulated to be because of potential decreased length of stay and possibly decreased postoperative complications due to BiTURP.

BiTURP has not been compared to other modalities for prostate debulking, but is likely to be at least competitive when it comes to other methods of prostate ablation. The fact that BiTURP is a technique that most urologists have learned in graduate medical education may decrease the training costs associated with learning newer techniques such as laser prostatectomy. However, these new modalities may offer similar improvements in length of stay and morbidity as compared to BiTURP, as BiTURP did compared to monopolar TURP. Whether the differential in these recurring costs is greater than initial capital outlay remains to be seen.

## Education issues

The BiTURP has been touted as a useful adjunct for urology graduate medical education [6, 20] because the decreased risk of dilutional hyponatremia leaves more time available for resident operative teaching. Although this is a valid observation, it should be noted that the number of transurethral resections of the prostate, monopolar or bipolar, have been declining for decades [3]. In fact, over a 7-year period during which BiTURP was available, graduating chief residents performed approximately 25% fewer cases [34]. This might be due to increase in other ablative treatments such as laser prostatectomy and may be a reversible trend if BiTURP is adopted by the urologic community.

A more fundamental question is the role of TURP in management of BPH/LUTS. With the advent of effective medical therapy and a host of other ablative and minimally invasive techniques available for the surgical management of BPH/LUTS, the TURP procedure may be performed less and less often and therefore may not remain the "gold standard." If this were to happen, some of the advantages of the BiTURP may become less obvious.

## Conclusions

BiTURP is an effective modality for the surgical management of BPH/LUTS. It has been in use for only about a decade and during that time it has demonstrated efficacy similar to that of monopolar TURP, with potentially improved safety profile. It has not been compared to other transurethral ablative therapies for the prostate that use saline as an irrigant. If TURP remains the "gold standard" for surgical management of BPH/LUTS in the future, then BiTURP will continue to have an increasing role.

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# Bipolar Vaporization of the Prostate

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## Introduction

Transurethral resection of the prostate (TURP) has long been accepted as the "gold standard" surgical treatment for benign prostatic hyperplasia (BPH). It is the measuring stick against which all other minimally invasive treatments for BPH are compared, being highly effective in improving urinary flow rates and decreasing symptom scores. The Agency for Health Care Policy and Research (AHCPR) panel guideline meta-analysis showed that patients had an 88% chance of symptomatic improvement after TURP [1]. However, due to the morbidity associated with monopolar TURP, including the risk of bleeding, clot retention, impotence, urethral stricture, and transurethral resection (TUR) syndrome, as well as the length of hospitalization and catheterization, urologists have been tinkering with other minimally invasive treatments for BPH for decades.

Vaporization of the prostate was first described in the early 1990s using either conventional electrical surgery, termed electrovaporization, or laser techniques [2]. Transurethral vaporization of the prostate (TUVP) was first described by Kaplan and Te in 1995 [3]. The proposed advantages of TUVP included less blood loss, shorter catheterization time, and shorter hospitalization, all the while maintaining efficacy. Initially, electrovaporization techniques were performed using monopolar currents, but a monopolar current has its own associated problems. First, the use of a conductive irrigant, such as glycine or mannitol, is required, which may result in systemic absorption of hypotonic fluids, thus risking hyponatremia and TUR syndrome. Second, the patient is part of an electrical circuit that can pose a risk for patients with pacemakers and cause diathermy burns at the site of the return plate. Third, monopolar current does not allow simultaneous cutting and coagulation. To address these issues, bipolar electrocircuitry was developed for minimally invasive prostate surgery. Bipolar vaporization or resection allows normal saline to be used, which is isotonic, avoids the need for a return plate as the patient is not part of the electrical circuit, and allows simultaneous cutting and coagulation.

Bipolar electrovaporization of the prostate was first described in 2001 using a Gyrus device [4]. Since then, numerous centers have reported level 1 evidence for favorable short-term outcomes using bipolar vaporization of the prostate. Herein we present a review of the mechanism of action of bipolar vaporization, various electrode and generator designs, clinical experience, and relevant comparative studies.

## Mechanism of action

Vaporization is produced via the application of energy to the prostate, which results in heating of the tissues. The tissues are primarily composed of intracellular water, which subsequently boils at a rapid rate, thus producing steam. This results in cellular disruption and tissue destruction, leaving a void where the cells were previously present. In electrosurgery, the rate of electrical energy delivered ($W$) is measured in watts, the current ($I$) flows through the tissue, and the tissue creates electrical impedance ($R$). Heat is created due to the electrical impedance of the prostate to current flow, therefore:

$$W = I^2/R$$

Most of the energy delivered to the prostate results in vaporization of the surface layer of cells; however, some of the energy has been shown to disperse below the vaporization layer to create a zone of coagulation, resulting in improved hemostasis. This phenomenon of simultaneous

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

vaporization/ablation and coagulation is the principal benefit of TUVP techniques. The actual depth of coagulation depends on system and electrode design. The technique employed by the surgeon will also impact the depth of coagulation as this is increased by increased pressure on and time in contact with the tissue. Importantly, coagulation has to take place with bipolar technology at lower peak voltages compared to those used for monopolar surgery (80–100 V for the PlasmaKinetic™ (PK) system) as higher voltages will convert the liquid into a gaseous phase, resulting in higher impedance. The impedance therefore is changed from a resistive to a capacitive mode, reducing energy flow, dissipating heat, and decreasing the final coagulation effect.

In bipolar and monopolar cutting, the generator must initiate a momentary high-energy spike to initiate a plasma vapor layer. This layer is ionized in the form of a nonequilibrium plasma, where plasma ions and electrons are responsible for current flow. In monopolar circuitry, the current arcs to the tissue and passes through the patient to a large-surface return electrode on the skin, heating the intervening tissue by ohmic resistance. However, in bipolar surgery, the active and return electrodes are in close proximity to each other, separated by an insulator. The electron emission from the smaller active electrode heats and vaporizes the adjacent intracellular water to form a thin gas layer (plasma pocket) that grows and forms a larger bubble containing energetic species that can dissociate both water and organic molecules, resulting in the net tissue effect [5]. It is likely that the thermal effect noted with bipolar surgery takes place at much lower temperatures (<70 °C) than those in monopolar surgery (300–400 °C). Once the plasma vapor pocket is formed, it can be maintained at low voltages (100–350 $V_{rms}$) as the electrode is close to making contact with the tissue. Tissue destruction ensues due to the breakdown of carbon–carbon and carbon–nitrogen bonds. This results in the production of elementary molecules and low molecular weight gases, including carbon dioxide, oxygen, nitrogen, and hydrogen. Intraoperatively, the effect is precise cutting and vaporization with minimal collateral damage as the charged sodium ions contained within the plasma vapor pocket have only a short estimated range of penetration (50–100 μm). This is largely due to electrosurgical principles as minimization of collateral tissue damage is dependent upon resistive heating caused by any current flowing through tissue and by limiting thermal transfer from the electrode sources. The final result in the human prostate is precision tissue cutting/vaporization with minimal charring and burnt prostate odor traditionally equated with monopolar TURP.

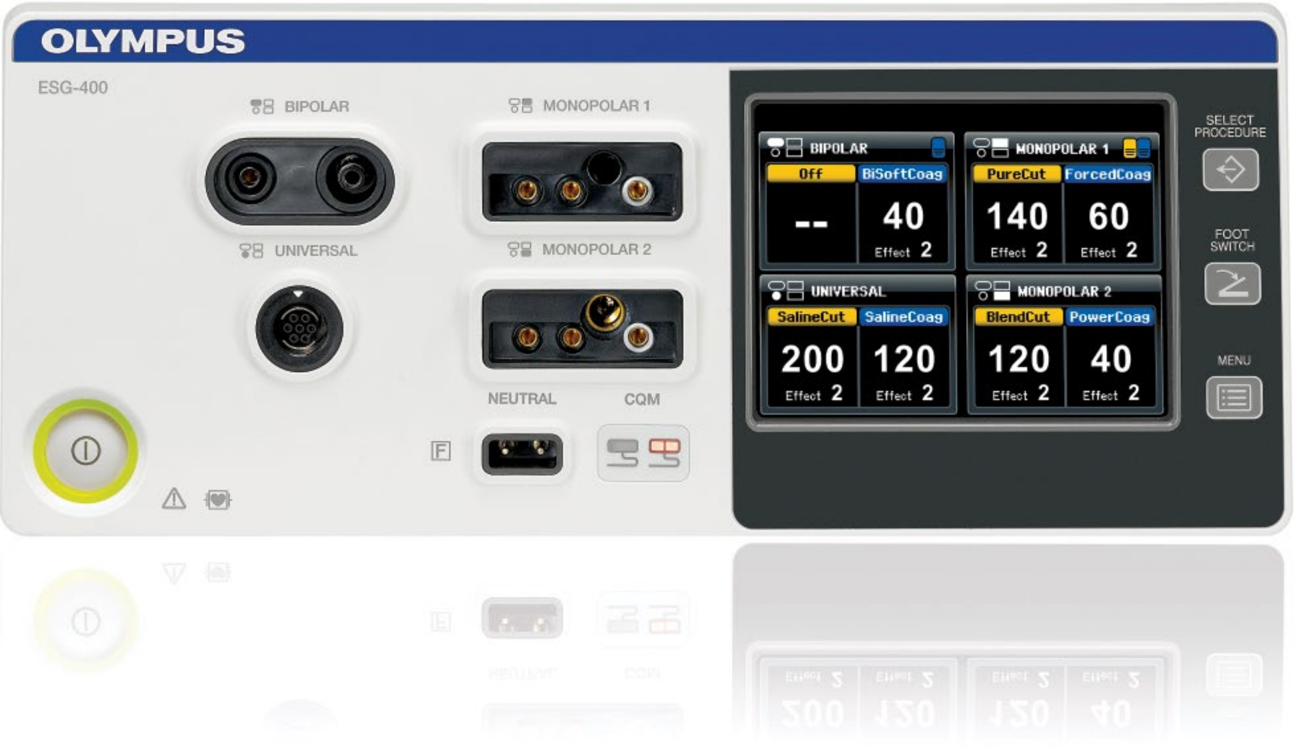
Specialized generators were developed along with the bipolar technology using radiofrequency (RF) energy output. The initial bipolar vaporization of the prostate used a Gyrus device and generator designed with a 200 W capability with an RF range of 320–450 kHz and a voltage range of 254–350 V [4]. However, the Vista Coblation system (ACMI Corporation, Southborough, MA, USA) used RF energy output from a specialized electrosurgical generator that is one-fifth that of monopolar generators (100 kHz square wave) [6]. The initial Olympus SurgMaster generated an RF output of 350 kHz and a recent report used the UES-40 SurgMaster (Olympus Medical/Winter & Ibe GmbH, Hamburg, Germany) with a power output of 290 W and 120 W for vaporization and coagulation, respectively (Figure 152.1) [7]. The frequency of the newest system from Karl Storz (Autocon® II 400 Electrosurgical System, Karl Storz, Tuttlingen, Germany) (Figure 152.2) generates an RF output of 350 kHz with a power output of 120 W for coagulation.

## Electrode and generator design

The bipolar technology was developed with the active and return electrodes in close proximity to one another, separated by an insulator. Energy from the generator travels through the active electrode, through the plasma pocket, through the conductive solution to the tissue bed, and returns via a thicker electrode to the active cord to the ground. Hence, there is no need for any energy to travel through the patient to a return electrode on the skin, eliminating the risk for inadvertent burns from inadequate contact. Also, the low operating frequency and voltage of bipolar surgery should eliminate any potential for interference with cardiac pacemakers.

There are several challenges to electrode design, including establishment of a reliable plasma corona preferentially at the distal active electrode, how to achieve a plasma condition with short delays from the time of foot-switch activation by the surgeon, how to provide adequate hemostasis from both cut and coagulation sources of foot-switch operation, and how to maintain this under all surgical conditions. With these challenges in mind, manufacturers and urologists are still in search of the “ideal” electrode for bipolar TUVP. The commercially available electrodes vary in size and configuration; however, in general, the active component is slightly thinner and separated from the thicker return electrode component by an insulator. The commercially available systems also vary in terms of resectoscope sizes, design of electrode housings, and coupling mechanism between active and return cords.

The Gyrus PK system was the first bipolar vaporization technology reported in the literature and therefore had to address several of these early technical issues. For bipolar vaporization to occur at the time of foot-pedal activation,


OLYMPUS
ESG-400
BIPOLAR
MONOPOLAR 1
UNIVERSAL
MONOPOLAR 2
NEUTRAL
CQM
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Off
BiSoftCoag
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Effect 2
MONOPOLAR 1
PureCut
ForcedCoag
140
60
Effect 2
Effect 2
UNIVERSAL
SalineCut
SalineCoag
200
120
Effect 2
Effect 2
MONOPOLAR 2
BlendCut
PowerCoag
120
40
Effect 2
Effect 2
SELECT PROCEDURE
FOOT SWITCH
MENU

**Figure 152.1** UES-40 Electrosurgical Generator. *Source:* Olympus America Inc. Reproduced with permission of Olympus.

STORZ
autocon II 400
205352 20
Saline-C-Cut
Saline-Coag
© 2017 KARL STORZ Endoskope

**Figure 152.2** Karl Storz Autocon® II 400 Electrosurgical System. *Source:* Karl Storz Endoscopy-America, Inc., California, USA. Reproduced with permission of Karl Storz Endoscopy-America, Inc.

the active electrode must be in close proximity to the tissue because if the gap is too wide or if there is insufficient power, current flow is dissipated by the large volume of electrolyte solution in a full bladder and there is no effect on the tissue. Furthermore, if the power/voltage spike is not great enough to maintain the plasma pocket, cutting and vaporization of the tissue will occur in a stuttering fashion, depending on the quality of tissue contact.

With these limitations and challenges in mind, the initial Gyrus PK system was modified, resulting in a second-generation model called the PK SuperPulse® Generator. There are several advantages of this system. First, this device is preconfigured for maximal allowable current under low impedance conditions. Second, the surgeon can choose between two sets of preset cutting voltages. Third, the generator is designed to recognize the active electrode offering default settings that are optimal for a wide range of conditions at the tip. Lastly, the PK SuperPulse generator is equipped with a row of internal capacitors acting as an energy reservoir to ensure sufficient voltage for instantaneous fire-up and for power ride-through under challenging conditions of impedance. These modifications have resolved the issue of stuttering cutting/vaporization that occurred previously. The capacitor reservoir can provide up to 4000 W of power for short periods of time (10 ms) if the tip impedance is low enough. This may be important because under conditions of high flow with cold saline, more power than normal is required to create and maintain the initial plasma pocket at the active electrode tip.

At baseline, prior to RF voltage application, the impedance differential between bipolar active and return electrodes is between 23 and 60 ohm with variability due to the irrigation temperature and the proximity of the active electrode to the tissue bed. The PK SuperPulse generator can generate a high enough power (4000 W) at low impedance (23 ohm) to sustain a voltage of close to 300 $V_{rms}$ that boils the saline immediately surrounding the active loop in a matter of milliseconds. This phenomenon is largely due to the electrode design. The electrical current crowds the reduced surface area of the active electrode, which results in a nonequilibrium vapor pocket containing charged sodium ions. The activated sodium ions form the plasma inside the vapor pocket and produce the orange glow that is visible to the naked eye. There is a time delay of 1–2 μs from the initial negative current spike until light is emitted. Once the plasma is formed, the impedance increases greatly from 500 to 3000 ohm, depending on whether the electrode is in contact with the vapor pocket or the irrigant, and/or the length of the vapor pocket (as there is higher impedance with longer plasma vapor pocket lengths). The power delivery now becomes focused around the active electrode and is not dissipated in the surrounding saline solution and prostate tissue, and therefore much less power is required to sustain the plasma vapor pocket. The energy reservoir can then be replenished as the output voltage falls by being repeatedly formed during each half cycle of the high-frequency exciting voltage waveform.

The PK SuperPulse generator has two sets of preset cutting voltages (termed SP1 and SP2). At the lower preset voltage of SP1, plasma volume is smaller and impedance is lower, and detected intraoperatively as a less intense orange glow around the active electrode. The SP2 setting can be used during suboptimal operative conditions when cutting/vaporization becomes difficult, to allow for an increased plasma volume and slightly higher preset voltage. Foot-pedal activation and fire-up should take no longer than 20 ms as a result of the energy reservoir of the internal capacitors. Once an activated electrode is in contact with tissue, *in vivo* studies have demonstrated that no more than 100 W are usually required to sustain the user-defined maximum voltages.

## Clinical experience

Bipolar TUVP has been in clinical use for a decade. The initial experience was reported in 2001 by Botto et al. using the Gyrus device and a rolling-type electrode (Axipolair®) [4]. This pilot study utilized the first-generation Gyrus PK generator and the electrode consisted of an active component (manufactured from 80/20 platinum/iridium alloy) and a return electrode (manufactured from stainless steel) placed on the same axis. A ceramic insulator separated the active and return electrodes. The initial technique describes vaporizing the obstructing tissue by placing the electrode in direct contact with the prostate in a systematic fashion similar to the technique for traditional TURP. The two major differences in performing bipolar TUVP are the modeling of the prostatic cavity in a circumferential action and the need to activate the current prior to bringing the electrode into direct contact with the tissue to allow the vapor pocket to build up. Therefore, for experienced endoscopists, the learning curve for bipolar TUVP is quite minimal. Forty-two patients with symptomatic BPH were included in this study and underwent bipolar TUVP using a standard 27 Fr resectoscope sheath and normal saline as irrigant. A majority of the patients (19) had a prostate volume between 30 and 60 ml and 93% of the operations took less than 60 minutes to complete. The mean postoperative hospitalization (including the day of surgery) was 2.2 days and all patients passed a voiding trial prior to discharge home. Early complications included bulbar urethral stricture in two patients requiring endoscopic urethrotomy, and dysuria in four patients, two of whom complained of dysuria for three months. Functional outcomes were assessed with International Prostate Symptom Score (IPSS) and maximum flow rate ($Q_{max}$) at baseline and at three months. Mean IPSS decreased from 19 to 9 and mean $Q_{max}$ increased from 7.9 ml/s at baseline to 19.7 ml/s at three months. These early clinical results showed feasibility, safety, and acceptable short-term outcomes that warranted further study.

Eaton and Francis performed bipolar TUVP in 40 patients with BPH symptomatology in a day surgical unit setting in the United Kingdom [8]. Similarly, bipolar TUVP was carried out using the Gyrus PK tissue management system (Gyrus Medical Ltd, Buckinghamshire, UK), which involved a 27 Fr continuous flow resectoscope sheath and normal saline irrigation. The mean operative time was 33 minutes (range 12–52 minutes) and mean prostate volume was 34.9 ml (range 15–76 ml). No patients had any electrolyte abnormalities or significant drop in hemoglobin level postoperatively. All but six patients were discharged home on the day of surgery, with an average hospital stay of 5.9 hours. All patients voided successfully at 48 hours, but two returned with obstructed catheters, thought to be due to coagulum and not blood clot or tissue fragments. At four months there was an improvement in IPSS and quality of life (QOL) by 64% and 83%, respectively, and an improvement in mean flow rate of 200%, but no baseline data were reported in any of these categories.

Dincel et al. reported on their initial experience with bipolar TUVP using the Gyrus PK tissue management system and a Plasma-V™ electrode (Figure 152.3) [9]. Twenty-one men with moderate to severe lower urinary tract symptoms (LUTS) attributable to BPH underwent bipolar TUVP, of whom 20 returned for follow-up and were available for final analysis. The median prostate volume was 42 ml and the operative time increased as the size of the prostate increased (median 55 minutes). The median duration of catheterization and time to discharge was three days. The only perioperative complication reported was constipation in one patient who required readmission due to clot retention and was transfused two units of blood. Median IPSS and urine flow rates were significantly better at 90 days postoperatively, and postvoid residual urine volume (PVR) had significantly decreased from a median of 54 ml to 19.5 ml. Serum prostate-specific antigen (PSA) values were measured preoperatively, on postoperative day 1, 30 days postoperatively, and 90 days postoperatively. Serum PSA values were significantly increased on postoperative day 1, and then trended back towards preoperative levels by 90 days postoperatively, prompting the authors to suggest that serum PSA levels should not be obtained in patients who have undergone bipolar TUVP until at least 30 days postoperatively. Furthermore, in these early studies, patients were heavily screened preoperatively for prostate cancer with serum PSA measurements and digital rectal examination (DRE), as it is important to note that no tissue is retrieved from TUVP for pathologic analysis. Therefore, patients with abnormal PSA/DRE were excluded from participation in these studies. Although the results of these nonrandomized clinical trials were promising and sparked the interest of the urologic community, large randomized prospective trials with long-term follow-up were needed to provide better evidence-based medicine rationale for the use of this new technology.

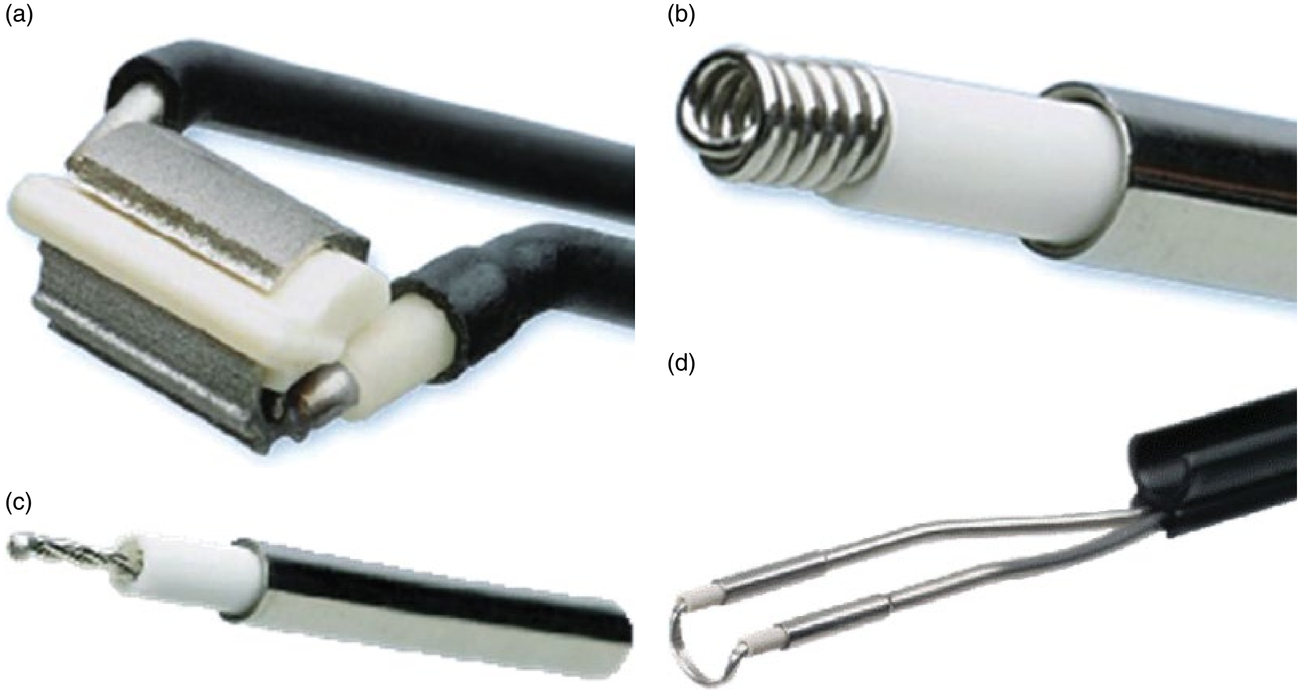

**Figure 152.3** (a) PK® Plasma-V PK "SuperPulse" Generator Vaporization Electrode (Gyrus, ACMI, Southborough, MA, USA). (b) PK PlasmaCise PK "SuperPulse" Generator Electrode (Gyrus, ACMI). (c) PK® PlasmaCut PK "SuperPulse" Generator Electrode (Gyrus, ACMI). (d) PK SuperSect (Wider Surface Loop) Generator Electrode (Gyrus, ACMI). *Source:* Olympus America Inc. Reproduced with permission of Olympus.

## Comparative studies

In 2003, Dunsmuir et al. reported the first randomized prospective clinical trial comparing bipolar TUVP to traditional monopolar TURP [10]. This study randomized 51 men with LUTS secondary to BPH to bipolar TUVP ($n = 30$) versus monopolar TURP ($n = 21$), of whom 40 (20 in each group) completed follow-up at 1 year. The bipolar TUVP arm underwent vaporization using a similar technique to that previously described using the Gyrus PK device with the Axipolaire electrode, and monopolar TURP was performed using standard techniques. In terms of perioperative outcomes, there was no difference in operative time, irrigation time, and time to catheter removal, or length of hospital stay between the two groups. These patients were followed up 1 year later and improvements in IPSS, flow rates, PVR, and QOL were similar between the two groups. Interestingly, four patients in the TURP group compared to zero patients undergoing TUVP required manual clot evacuation in the postoperative period, but the recatheterization rate for the TUVP procedure was 30% (compared to 5% for traditional TURP). All patients voided successfully 2–3 weeks later (range 14–19 days).

Hon et al. performed a randomized prospective clinical trial on 160 consecutive patients in their practice undergoing transurethral prostatectomy for bladder outlet obstruction [11]. They randomized the men to traditional TURP ($n = 81$) versus bipolar TUVP ($n = 79$) using the Gyrus PK system and the Plasma-V bar electrode. The two groups were similar preoperatively with regard to baseline characteristics. Mean operative time was 4 minutes shorter in the TURP arm, but this was not statistically significant (28.5 vs. 32.6 minutes, $P = 0.08$). There was no significant difference between the two groups with respect to intraoperative blood loss; however, the TURP group had a greater hemoglobin decrease postoperatively (1.4 vs. 0.8 g/dl, $P = 0.002$). Likewise, the TURP patients required more irrigant (28.3 vs. 20.1 liters, $P = 0.001$) and more manual bladder irrigations postoperatively (31 in 11 patients compared to 11 in seven patients who underwent TUVP, $P = 0.27$). The only difference in short-term adverse events included a total of 14 units of blood transfusion in the TURP arm compared to zero units of blood transfusion in the TUVP arm. The hospital stay was significantly longer for patients who underwent TURP compared to TUVP (3.4 vs. 3.0 days, $P = 0.04$). Interestingly, despite rigorous preoperative screening, eight patients in the TURP arm were found to have prostate carcinoma detected on prostate chip histology. Long-term outcomes were available in 93% of the patients at a mean follow-up of 258 days. IPSS, QOL, PVR, and $Q_{\max}$ improved significantly regardless of technique; however, there was no statistically significant difference detected in any of these categories other than for average urine flow when comparing TURP to bipolar TUVP. This fairly large trial with a decent length of follow-up concluded that bipolar TUVP has equivalent outcomes to monopolar TURP but with fewer earlier complications.

The disadvantage of bipolar TUVP is the lack of tissue for histologic processing. It is important to note that some clinically significant cancers may be missed, therefore highlighting the importance of screening these patients preoperatively and following them postoperatively with serial serum PSA and DRE.

Due to the potential for missing cancer and lack of tissue obtained from pure vaporization techniques, researchers began exploring a possible hybrid technique. This technique combined bipolar vaporization of the prostate with bipolar resection (TUVRP) and was described by Tefekli et al. in 2005 [12]. It should be pointed out that other researchers have shown that tissue sampling with a resection loop after vaporization of the prostate may not increase the likelihood of cancer detection [13]. In this randomized prospective clinical trial, 50 patients undergoing surgery for BPH were randomized to standard monopolar TURP and 51 patients were randomized to the hybrid bipolar TUVRP technique. The bipolar TUVRP procedure was performed with the Gyrus PK system using saline for irrigation. The lateral and median lobes were removed with a vaporization electrode and the final resection of tissue tags and apical tissue around the verumontanum were removed with a resecting loop. This technique was employed to not only remove tissue for pathologic analysis but also to aid delicate tissue resection around the apex and verumontanum. Complete data were available on 96 patients with a mean follow-up of 18.3 months (range 12–23 months). Mean operative time, catheterization time, and hospital stay were significantly lower in the TUVRP group compared to the TURP group. Mean improvement in $Q_{\max}$ was significantly better in the TUVRP group at 12 months, but mean improvement in IPSS from baseline was equivalent between the two groups. However, these authors did note an increase in irritative symptoms and recatheterizations in the TUVRP group, which, they hypothesized, was due to increased tissue edema due to the higher current with lower frequency exerted on the tissue. Of the three patients in the TUVRP group who required recatheterization, all were able to void after seven days. The increased recatheterization rate paralleled the findings of Dunsmuir et al. [10]. Urethral stricture was also a more common complication in the TUVRP group (three TUVRP vs. one TURP, $P = 0.002$) and was successfully managed endoscopically in all patients. The reoperation rate for persistent obstructive symptoms was not statistically significant, likely due to the low number of events in each group, with two patients in the TUVRP arm and only one in the monopolar TURP arm.

With several randomized prospective clinical trials emerging in the literature comparing bipolar TUVP to monopolar TURP, Neill et al. elected to compare holmium laser enucleation of the prostate (HoLEP) to bipolar TUVP in a randomized prospective clinical trial [14]. Forty patients were randomized 1:1 to either HoLEP or bipolar TUVP using the Gyrus PK device with the Axipolaire electrode. In their study, HoLEP performed better than TUVP with regard to mean operative times (43.6 minutes vs. 60.5 minutes, $P < 0.05$) and fewer patients in the HoLEP arm required bladder irrigation (5% vs. 35%, $P < 0.001$). The other outcomes analyzed, including hospital stay, catheterization time, complication rate, changes in IPSS, and maximum flow rate at 12-month follow-up, were all similar between the two groups. These authors concluded that bipolar TUVP has equivalent functional outcomes to HoLEP but increased intraoperative bleeding, which results in longer operative times and increased postoperative irrigation requirement. Surgeon preference, bias, and familiarity also play a large role and may have influenced these investigators to those conclusions.

## Button-type bipolar plasma vaporization

After introducing Gyrus plasma cutting system in clinical practice, bipolar technology, especially transurethral vaporization of prostate, became a common surgery for prostate resection [7, 15]. For bladder outlet obstruction, bipolar technology is as efficient as transurethral resection and has better long-term prognosis and fewer early complications [16]. This technology has made new progress recently with the utilization of the Olympus UES-40 high-frequency electric generator and “button-type” electrode vaporization resection in transurethral plasma vaporization of prostate in clinical practice. Reich et al. first reported the button-type electrode in the literature [7]. Plasma kinetic button vaporization of the prostate is an endoscopic approach which can be used as an alternative to monopolar TURP. The plasma kinetic technology uses RF energy to create an ionized plasma corona [17] using an axipolar electrode and electroconductive solution such as normal saline [1]. The axipolar vaporesection electrode is in the shape of a mushroom or the so-called “button.” It uses an RF range of 320–450 kHz, a voltage range of 350–450 V, and has a 200 W capability [16, 18]. The current passing over the ball-shaped button creates a plasma corona that vaporizes tissue while achieving hemostasis [19]. Since the axipolar electrode functions as both the working element and the return electrode, the risk of accidental skin burns is eliminated. This also provides decreased interference with cardiac pacemakers and decreased risk of stray currents causing an obturator reflex. Since normal saline is used as irrigation the risk of TUR syndrome is reduced. In bipolar plasma vaporization of the prostate with button electrode, bipolar energy is applied to the tissue using a button-type electrode that vaporizes the prostatic tissue without cutting prostatic fragments.

Button electrodes can work under a higher power because of their capacity for vaporization and strong coagulation. In large prostates, simple bipolar vaporization can be effective for nucleating large quantities of BPH tissue, therefore the button-type electrode, which has a larger contacting surface, was introduced as a novel endoscopic approach [18].

### Equipment and surgery technique

Button-type bipolar plasma vaporization (BTPV) systems require a UES-40 SurgMaster bipolar high-frequency generator, a 26 Fr continuous flow resectoscope, normal saline as irrigant at room temperature, and the aforementioned electrode (Figure 152.4). When the electrode surface is in direct contact with the prostate tissue, the spherical electrode shows a plasma corona. For effective system activation the power output is set at 280–320 W for vaporization (it can be adjusted depending on the tissue) and 120–140 W for coagulation modes. The vaporization technique is performed using the electrode in a near-contact technique (“hovering technique”). In other respects the procedure is performed like a traditional TURP, making the learning curve minimal.

### Clinical experience

In first clinical study, 30 patients with BPH underwent BTPV using the mushroom-like electrode [7]. The mean prostate volume was 59 ml (range 30–170 ml) and mean operative time was 61 minutes (range 20–140 minutes). No perioperative complications were noted, no patient required a blood transfusion, and no postoperative electrolyte abnormalities were noted. Postoperatively, four

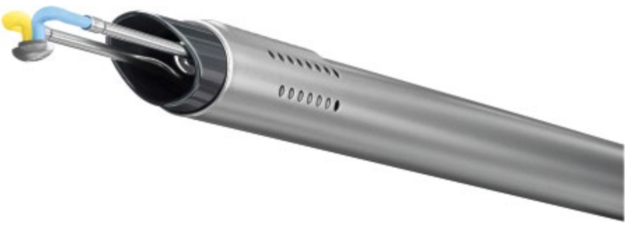

**Figure 152.4** Bipolar mushroom-like electrode. *Source:* Olympus America Inc. Reproduced with permission of Olympus.

patients (13%) required recatheterizations and the mean catheterization time was 41 hours (range 18–192 hours). Around half of the patients (53%) required continuous bladder irrigation postoperatively. The reoperation rate at six months follow-up was 3% (one patient required traditional TURP due to persistent obstructive symptoms). Transient mild-to-moderate dysuria was present in four patients (13%) and resolved within two weeks postoperatively with anti-inflammatory agents. Functional outcomes assessed at six months compared to baseline were excellent. Mean $Q_{\max}$ increased from 6.6 ml/s at baseline to 18.1 ml/s at six months ($P < 0.01$); mean IPSS decreased from 20.8 at baseline to 8.1 at six months ($P < 0.01$); and mean PVR decreased from 165 ml at baseline to 38 ml at six months ($P < 0.01$).

In another study 50 patients underwent prostate surgery by plasma kinetic button vaporization. The median preoperative PSA value was 2.98 ng/ml (0.3–7 ng/ml), median IPSS 22.8 (12–30), median $Q_{\max}$ 6.29 ml/s (3–14 ml/s), and median prostate weight 50 g (20–70 g). No perioperative complications were noted, no patient required a blood transfusion, and no postoperative electrolyte abnormalities were noted. Continuous bladder irrigation was <24 hours in 5 (10%) patients, between 24 and 36 hours in 40 (80%) patients, and >36 hours in 5 patients. Catheterization time was <36 hours in 38 (76%) patients, between 36 and 48 hours in 10 (20%) patients, and >48 hours in 2 (4%) patients. The length of stay was <48 hours in 44 (88%) patients, and between 48 and 72 hours in 6 (12%) patients. In 7 hospitalized patients, acute urinary retention with hematuria and clots was observed, but only in 1 case (2%) was a "second look" endoscopic hemostatic procedure performed. After catheter removal, 3 (6%) patients showed acute urinary retention before discharge and another 3 required rehospitalization for the same problem with the placement of a new catheter. Functional outcomes were assessed at 3, 6, and 12 months; patients showed a significant improvement in $Q_{\max}$ (19.3 ± 5.6 ml/s, 20.3 ± 4.6 ml/s, and 21.2 ± 3.6 ml/s, respectively) ($P < 0.001$). After 12 months, 39 (84.7%) patients had an IPSS <12 ($P < 0.05$). Before surgery, 56% of patients had a QOL >3 and 90% of patients with PVR >50 ml; after 12 months, this result was stable with a QOL >3 in 0% ($P < 0.05$) and a PVR >50 ml in 4.3% ($P < 0.05$). No patient after the procedure experienced incontinence [20].

## Comparative studies

Wroclawski et al. conducted a systematic review and meta-analysis of randomized prospective studies to determine the effectiveness and morbidity of BTPV in comparison with standard transurethral resection (five monopolar and one bipolar) [16, 18, 21–25]. According to this review the mean preoperative IPSS was similar between both groups and both treatments similarly significantly improved symptoms and postoperative IPSS. The need for retreatment due to symptom continuation was mentioned with 6 and 31 events in patients undergoing BTPV and TURP, respectively. Blood transfusion was necessary in two BTPV cases (0.006%) and in 16 TURP cases (0.032%). The mean duration of catheterization was significantly lower in the BTPV group (2.7 days) versus the TURP group (3.9 days). Urethral stricture was mentioned in 13 cases in the BTPV group and in 37 cases in the TURP group. Urinary incontinence was mentioned in 1 case with BTPV and in 6 cases with TURP. The retreatment rates were 3.5%, 9.4%, and 8.8% for BTPV, bipolar TURP, and monopolar TURP, respectively.

Geavlete et al. reported a single-center prospective randomized controlled study on 320 patients in 2015. They randomized the patients with BPH into four groups: bipolar TURP (B-TURP) ($n = 80$), bipolar electrovaporization of the prostate (TUVP) ($n = 80$), BTPV ($n = 80$), and open prostatectomy (OP) ($n = 80$). In terms of preoperative outcomes, there was no difference in age (67.5–69.5 years), prostate volume (122–129 ml), $Q_{\max}$ (6–7 ml/s), IPSS (24–25), PVR (134–158 ml), PSA (7.6–8.2 ng/ml), and QOL scores (4–4.4). According to perioperative outcomes, mean operation time was significantly shorter in the BTPV and OP groups (100 minutes, 118 minutes, 87 minutes, and 80 minutes, respectively). Mean resected adenoma weight was significantly higher in the BTPV and OP groups (78 g, 0 g, 99 g, and 110 g respectively). TUVP was characterized by the lowest mean hemoglobin level drop, followed by B-TURP and BTPV (1.7 g/dl, 0.9 g/dl, 1.6 g/dl, and 3.1 g/dl, respectively). The transvesical prostatectomy group displayed the longest mean catheterization period and hospital stay, next followed by B-TURP, BTPV, and TUVP (2.2–3.2 days, 1.3–2.1 days, 1.6–2.5 days, and 5.4–6.7 days, respectively). During the 1-year evaluation period, statistically similar outcomes were found in all study groups at the checkups at 1, 3, 6, and 12 months with regard to mean IPSS, QOL, and PVR features. On the other hand, the TUVP approach was marked by significantly less pronounced $Q_{\max}$ progress (24.9 ml/s, 22.8 ml/s, 25.6 ml/s, and 25.2 ml/s, respectively). But otherwise equivalent functional parameter results were further confirmed by the related ameliorations when compared to the initial assessment. Moreover, significantly lower mean PSA levels were found subsequent to the OP and plasma nucleation procedures in comparison to bipolar resection and eventually to plasma vaporization (2.01 ng/ml, 3.11 ng/ml, 0.68 ng/ml, 0.69 ng/ml, respectively). As far as the medium-term complications were concerned (encountered between months 1 and 12 of the follow-up period), equivalent data were established regarding the rates of bladder neck sclerosis and urethral strictures (diagnosed by flexible cystoscopy), as well as urinary incontinence [26].

Zhang et al. compared BTPV versus PlasmaKinetic resection of the prostate with a cutting loop electrode for benign prostate enlargement bigger than 90 ml. There was no statistically significant difference in any baseline characteristic of patients (age, prostate volume, PVR, IPSS, and QOL) between the two groups. Significant differences favoring BTPV were found in operation time (64 minutes and 78 minutes), hemoglobin loss (1.18 g/dl and 1.63 g/dl), serum sodium decrease (2.9 mmol/1 and 4.3 mmol/1), the duration of catheterization (49.3 hours and 78.1 hours), and hospital stay (100.2 hours and 116.2 hours). There were no significant differences in IPSS, QOL, and $Q_{\max}$, and PVR in PVEP compared with PlasmaKinetic resection of the prostate at three-month follow-up [27].

When we compare other complications, in a prospective randomized trial Geavlete et al. found monopolar TURP to have a greater number of capsular perforations (7 of 80 monopolar TURP vs. 1 of 75 BTPV, $P = 0.037$). They also reported clot retention occurred significantly less in BTPV compared to monopolar TURP (1 BTPV vs. 7 monopolar TURP, $P = 0.042$) [16]. Although not statistically significant findings, postoperative complications of urinary tract infections and urge incontinence were seen in fewer patients in the BTPV group in all studies. It also appears that the incidence of erectile dysfunction in both procedures is similar (13% BTPV vs. 12% monopolar TURP) [19]. There were higher rates of dysuria and urinary frequency in BTPV compared to monopolar TURP, although neither was found to be statistically significant in any of the trials [17].

Ozturk used BTPV in the treatment of recurrent vesicoureteral anastomotic stricture following retropubic radical prostatectomy. After 24 months follow-up they reported a success rate 89.2% (25 of 28 patients) for this surgery [28].

## Conclusions

Bipolar TUVP has been shown to be a safe and effective treatment for BPH through several well-performed randomized prospective clinical trials. Clearly, larger multicenter trials are needed with longer term follow-up to assess long-term outcomes, specifically the reoperation rate and rate of urethral stricture occurrence. Certainly there is a role for bipolar TUVP in the toolbox of treatments available for BPH as urologists tackle larger prostate glands endoscopically and operate on sicker patients. Whether bipolar TUVP becomes widely accepted remains to be determined, especially in the face of stiff competition from high-powered lasers (holmium and KTP).

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# 153

# Single Port for Prostate Surgery

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## Introduction

The prostate is a pelvic organ with two main pathologies: benign hyperplasia and cancer. These conditions have been more frequently diagnosed in the past 50 years, and there have been significant advances in the surgical management of prostate pathology.

With the introduction of minimally invasive surgery and the development of modern and novel techniques, there has been continued progress over time from the standard use of trocars, through mini-laparoscopy, to single-port robotic surgery. The search for perfect results, not only cosmetically, but also in terms of reducing the morbidity of the procedures, has manifested itself in the reduction in the number and size of trocars.

Single-port surgery globally has continued to evolve and progress with effective and safe results. These advances by surgeons experienced in laparoscopy and robotics have kept the risk of complications low and helped to set strict criteria for the selection of patients appropriate for this surgical approach, while demonstrating, according to some experts, better postoperative pain control, earlier recovery of intestinal function, and smaller scar length than is achieved with standard techniques [1, 2].

## Access, instruments, and viewing

Technical difficulties that may be identified during single-port minimally invasive surgery include: reduced working space, collision of instruments, restricted movements, and difficulty in the display. However, there have been significant improvements and evolution in four important aspects of this surgical approach: trocars, instruments, optical, and mechanism of retraction [3].

## Simple prostatectomy by single port

Currently, despite advances in endoscopic techniques with the application of new technologies (e.g. bipolar transurethral resection, holmium laser resection, and potassium titanyl phosphate (KTP) laser vaporization) and the emergence of new access devices, open surgery is considered the standard management for prostates of large size in terms of cost-effectiveness for benign hyperplasia.

Over the last decade, with the advent of laparoscopic and robotic surgery, new treatment alternatives have been developed and implemented. In 2002, Mariano et al. described a technique for simple laparoscopic prostatectomy [4], which was reproduced with some modifications and then performed with robotic assistance. The described surgery essentially duplicated the techniques of open surgery, while maintaining a comparable proportion of prostatic tissue extracted as in open surgery, but with the benefits associated with minimally invasive surgery [5, 6].

With the aim of improving cosmetic results and maintaining the good surgical outcomes of laparoscopy, the use of a single point of access into the abdominal cavity through the umbilicus was implemented. This approach was named laparoendoscopic single-site (LESS) surgery, which is the use of endoscopic and laparoscopic techniques through a single hole, using a unique device that enables the introduction of several instruments [7]. We began to explore the possibilities of applying this

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new access method to our technique of laparoscopic simple prostatectomy, initially through the umbilicus and later through a small suprapubic incision to place the port directly into the bladder.

## Single-port transvesical enucleation of the prostate

LESS adenomectomy can be performed by placing a single-port device through the umbilicus using a transperitoneal approach. This is challenging, because the bladder must be dropped and the finger cannot be used to assist with enucleation of the prostate adenoma. In addition, at the end of surgery, the bladder incision must be closed laparoscopically in a watertight manner. With the introduction of the new double-bend instruments, this step has become easier, but can still be technically difficult to complete.

Another option is to place the port directly through the bladder (Figure 153.1). With this approach, the bladder does not need to be dropped, and the finger can be used to assist with the enucleation. At the end of surgery, the bladder closure can be done in a standard open fashion.

Laparoendoscopic transvesical simple prostatectomy is performed through a small incision approximately 2.5–3 cm long, located 3 cm above the pubic symphysis, through which a specialized access device is directly inserted. Through this single access point, multiple instruments can be inserted to complete the operation. The R-port® (Advanced Surgical Concepts, Wicklow, Ireland) was the initial design of this access device, and modifications have led to the development of the TriPort® and QuadPort® (Advanced Surgical Concepts), which each have three and four channels, respectively. This device has two important features: first, it has multiple flexible valves that do not protrude into the cavity and enable the introduction of curved instruments; and second, it has a valve component that is easy to open and does not need to be taken out to be changed – a crucial aspect in intraluminal surgery. Increasing interest in LESS surgery has led to the introduction of new instruments, such as the 5 mm flexible EndoEye videoscope (Olympus, Tokyo, Japan), which provides excellent optics and images, and flexible, curved instruments that permit dissection and laparoscopic intracorporeal suturing [8].

The approach to the surgical management of urinary tract obstructive symptoms secondary to benign growth of the prostate is selected according to the technique used, size of the prostate, and the ability of the surgeon.

### Technique

Current surgical approaches used include endoscopic techniques, such as transurethral resection of the prostate (TURP) (main standard), new trends with laser technology (enucleation with a holmium laser (HoLEP), laser green, among others), open surgery, and laparoscopic and robotic surgery [9].

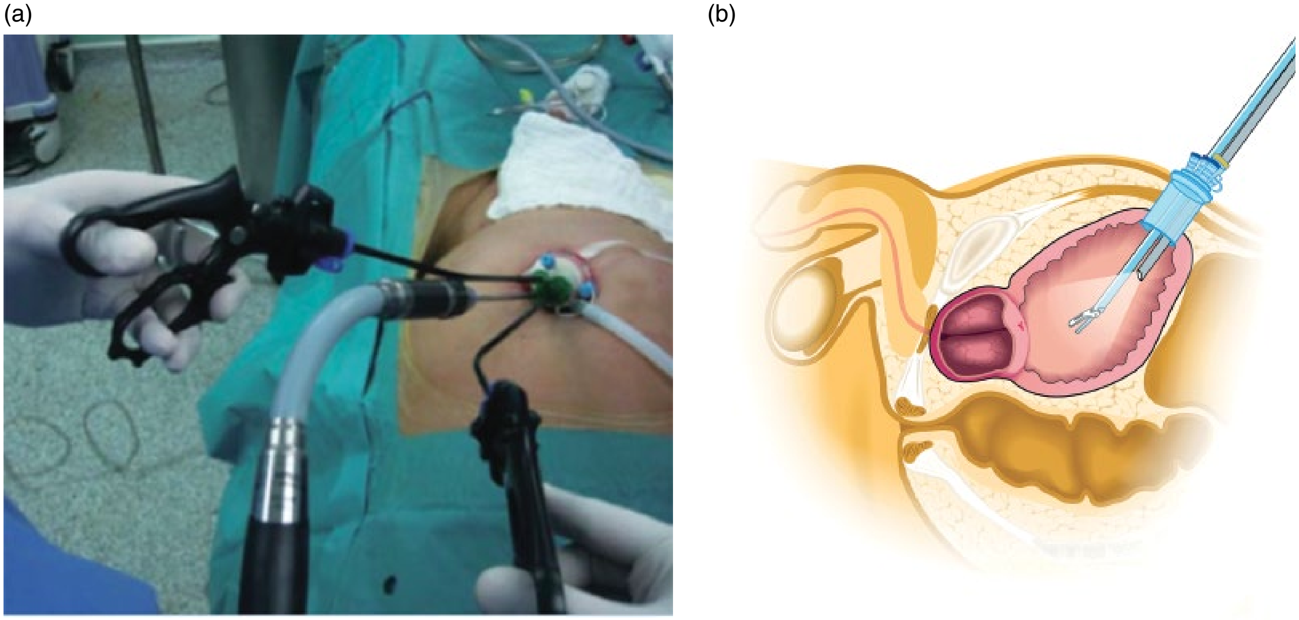

**Figure 153.1** (a, b). Port placement directly through the bladder. Insertion and deployment of the TriPort under cystoscopic guidance.

## Size

Surgery on prostates of less than 80 g should be performed using endoscopic techniques, although there are reports of prostates of larger size (≥120 g) being managed this way. For prostates ≥80 g, open, laparoscopic, and robotic surgery have traditionally been the recommended approaches.

## Ability of the surgeon

The surgeon must resect the greatest amount of tissue in the shortest time possible to avoid complications such as bleeding, irritative symptoms, and postresection syndrome. It is reported that expert hands can achieve a resection rate of 1–1.5 g/min.

Laparoscopic robotic surgery can duplicate the open surgery technique, and demonstrates the same surgical outcomes. It is safe and effective, with less blood loss and a shorter length of hospitalization. It may, however, have a longer operative time. Comparisons of laparoscopic and endoscopic surgery show that the former has the highest percentage of tissue resection and shorter use of a bladder catheter, at the expense of greater bleeding [10, 11].

Simple prostatectomy by single port was initially described in 2008 by Desai et al. [8]. An early experience in three patients with large prostates involved use of the R-port device, which was introduced percutaneously into the bladder through a 2.5 cm infra-umbilical incision under the guidance of cystoscopy (with prior introduction of a hypodermic needle), followed by a U-shaped incision into the bladder neck and adenoma dissection. This direct bladder approach allowed the dissection of the adenoma to be made with assistance of the surgeon's finger, in addition to the apparent advantage of not needing to close the bladder [8]. Sotelo and his group also detailed their technique of simple prostatectomy in 2009 using a multilumen single port through an umbilical incision of 2.5 cm. They described difficulty in developing the prevesical space and subsequent bladder dissection, and after making the cystotomy, had to complete the dissection of the adenoma without the use of additional trocars or percutaneous traction maneuvers [12]. These two groups of researchers have together presented a multi-institutional series of large-scale single-port simple prostatectomies.

## Surgical technique

The equipment and instruments required for single-port transvesical enucleation are listed in Box 153.1. The TriPort is a multiport access device that allows several instruments to pass through simultaneously. It consists of a retractor and a valve. The Choker has an inner ring, two outer rings, and a retractable plastic sleeve. The valve has three openings (two of 5 mm and one of 12 mm) for laparoscopic instruments and a port for inflation. The valve contains a thermoplastic elastomer that enables the proper introduction of the instruments, including needles, with insignificant air loss.

## Surgical steps

The advantages and disadvantages of this procedure are summarized in Box 153.2 and the key points in Box 153.3.

### Patient position and endoscopic evaluation

All procedures are performed under general anesthesia with the patient in a modified low lithotomy position.

**Box 153.1 Equipment and instruments required for single-port transvesical simple prostatectomy.**

**Equipment**

- Laparoscopic video tower (21-inch monitor, EXERA II image processor with light source)
- Video laparoscope: EndoEye (Olympus, Tokyo, Japan), 5 mm, 30° lens
- UHI-3 high-flow $CO_2$ inflator (up to 35 l/min)
- Ultrasonic generator
- Electrosurgical unit (monopolar/bipolar)
- Aspiration–irrigation pump
- Flexible cystoscope

**Instruments to develop the procedure**

- TriPort (Advanced Surgical Concepts, Wicklow, Ireland/Olympus)
- 5 mm flexible articulating instruments: scissors (Cambridge Endo, Framingham, MA, USA)
- 5 mm J hook electrocautery instrument
- Ultrasonic 5 mm shears
- 5 mm suction–irrigation cannula, prebent
- Carter–Thomason device
- Two laparoscopic needle holders
- Silicone three-way 22 Fr and two-way 24 Fr Foley catheters, in case a suprapubic tube is needed
- Sutures: Monocryl 0 with CT-1 needle for adenoma traction, and 2/0 with CT-1 needle for ligature of lateral pedicles and trigonization (the monofilament facilitates the extra-corporeal knotting)
- Sotelo prostatotomy device
- Knot pushers

**Box 153.2 Advantages and disadvantages of single-port transvesical simple prostatectomy.**

**Advantages**

- Pneumovesicum maintains a broad field of work
- Allows the observation of all anatomic details of the bladder, prostate and urethra during each step of the surgery
- Lower risk of intestinal injury and lower likelihood of development of postoperative ileus
- Easy opening of the device enables the extraction of fragments during surgery. Furthermore, it allows the introduction of a finger if necessary to remove the adenoma
- Due to the fact that the adenoma fragments are confined in the bladder and are not released in the abdominal cavity, extraction pouches are not necessary

**Disadvantages**

- Steep learning curve. At first, enucleation is difficult, but the location of the suprapubic incision allows bimanual dissection if necessary. The index finger of the left hand in the rectum elevates the prostatic fossa and the index finger of the right hand through the ring of the TriPort helps the mobilization of the adenoma

**Box 153.3 Key points during the procedure.**

- Placement of a traction suture through the full thickness of the bladder using absorbable material. The same stitch will enable placement of subsequent stitches, which will facilitate introduction of the trocar and the closure of the defect at the end of the case.
- It is important to lubricate the entrance of the TriPort in order to facilitate entry of instruments through the membranes, as well as facilitating the introduction of the videoscope and its rotational movement.
- The incision should be made between the adenoma and the mucosa of the bladder. The surgeon can observe a faint change in color. This serves as a reassuring reference point.
- If problems arise in the traction of the adenoma, the suture can be exteriorized through the abdominal wall with the assistance of a Carter–Thomason device.
- A useful tool designed specifically for prostatic adenomectomy is the Sotelo prostatotomy device. This consists of three parts: a Teflon sleeve, a stainless-steel cylinder body, and a curved shape with sharp edges at the distal end.
- It is important to note that, if necessary, the surgeon can convert the procedure to a standard laparoscopic surgery with the addition of more trocars as necessary.

Initially, cystoscopy is performed and the prostate evaluated endoscopically. The bladder is filled with normal saline solution.

### Insertion and deployment of the TriPort

An approximately 2.5 cm skin incision is carried down to the rectus fascia. The incision is located just above the pubis. The bladder wall is identified and cleared of any prevesical fat. Two stay sutures of 2-0 Vicryl are placed.

The bladder wall is entered sharply between the stay sutures, and the inner ring of the TriPort is inserted into the bladder and deployed with the help of an introducer. The inner and outer rings are approximated by removing the slack on the plastic sleeve, thereby cinching the abdominal and bladder walls between the rings of the TriPort in an airtight seal. The valve of the TriPort is inserted and the bladder insufflated with $CO_2$ to create the pneumovesicum. The insertion and deployment of the TriPort is monitored cystoscopically (Figure 153.2).

The use of absorbable material for stitches in the bladder is important. These pass through its entire thickness, one in front of the other. The stitches serve as the anchor for traction and also facilitate the introduction of the trocar. They are also tied together to close the defect upon completion of the surgery. Care must be taken that the incision in the fascia and the bladder is no more than 2.5 cm, otherwise the inner ring of the TriPort will be dislodged. In Figure 153.2, the inner ring of the TriPort is seen outside of the bladder.

### Mucosal incision and enucleation

A large, bulging median lobe can be retracted anteriorly in an efficacious manner with a figure-of-eight stay stitch. This can be placed with a Keith needle or Carter–Thomason port closure needle device. The two ends of the stay stitch are retrieved and anchored outside of the anterior abdominal wall. A Monocryl suture on a CT-1 needle is placed through the adenoma for retraction purposes (Figure 153.3a). A U-shaped incision is made over the bladder mucosa, immediately overlying the adenoma, from the 3 o'clock to the 9 o'clock position, and through the 6 o'clock position. Typically, a reddish zone of mucosa is seen immediately lateral to the internal meatus. This serves as a reliable guide for creating the mucosal incision. The horizontal limb of the U-incision is made using a hook electrode and cutting current to reach the adenoma. The whitish prostatic adenoma is readily identified. The plane between the surgical capsule and the adenoma is created using a hook and suction cannula. The two limbs of the U-incision are created, followed by completion of the circumferential mucosal incision (Figure 153.3b). Separate excisions of each mobilized lobe of the adenoma provide superior visualization of the remaining part of the adenoma, enabling better hemostasis.

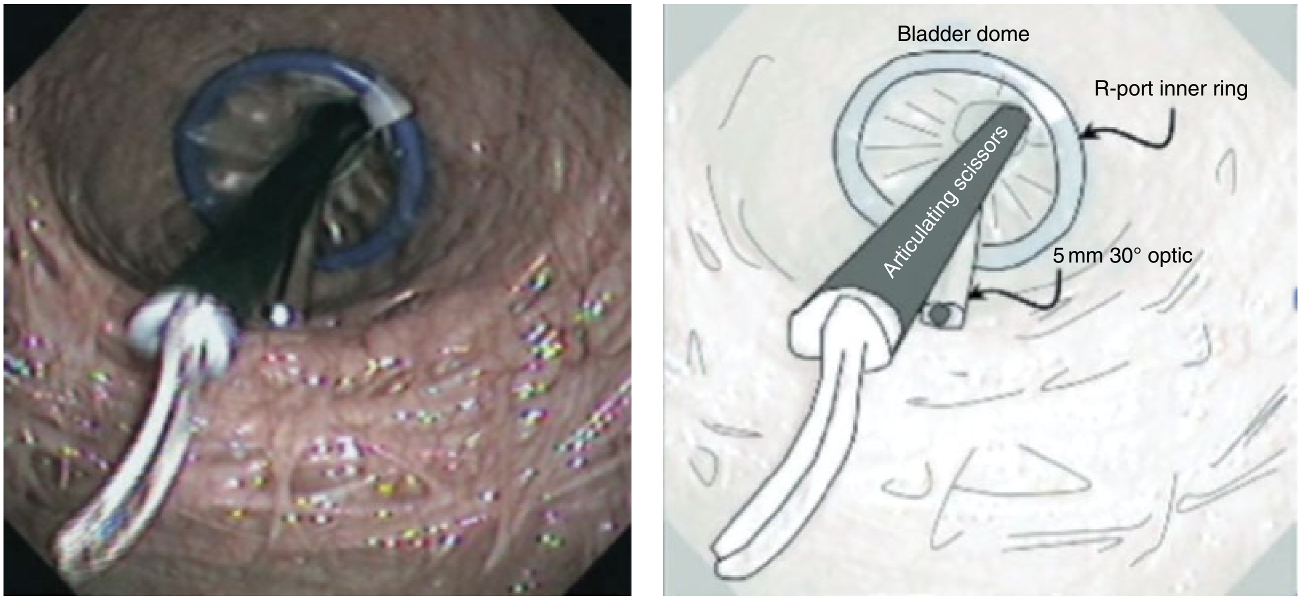
Bladder dome
R-port inner ring
Articulating scissors
5 mm 30° optic

**Figure 153.2** Insertion and deployment of the TriPort under cytoscopic guidance.

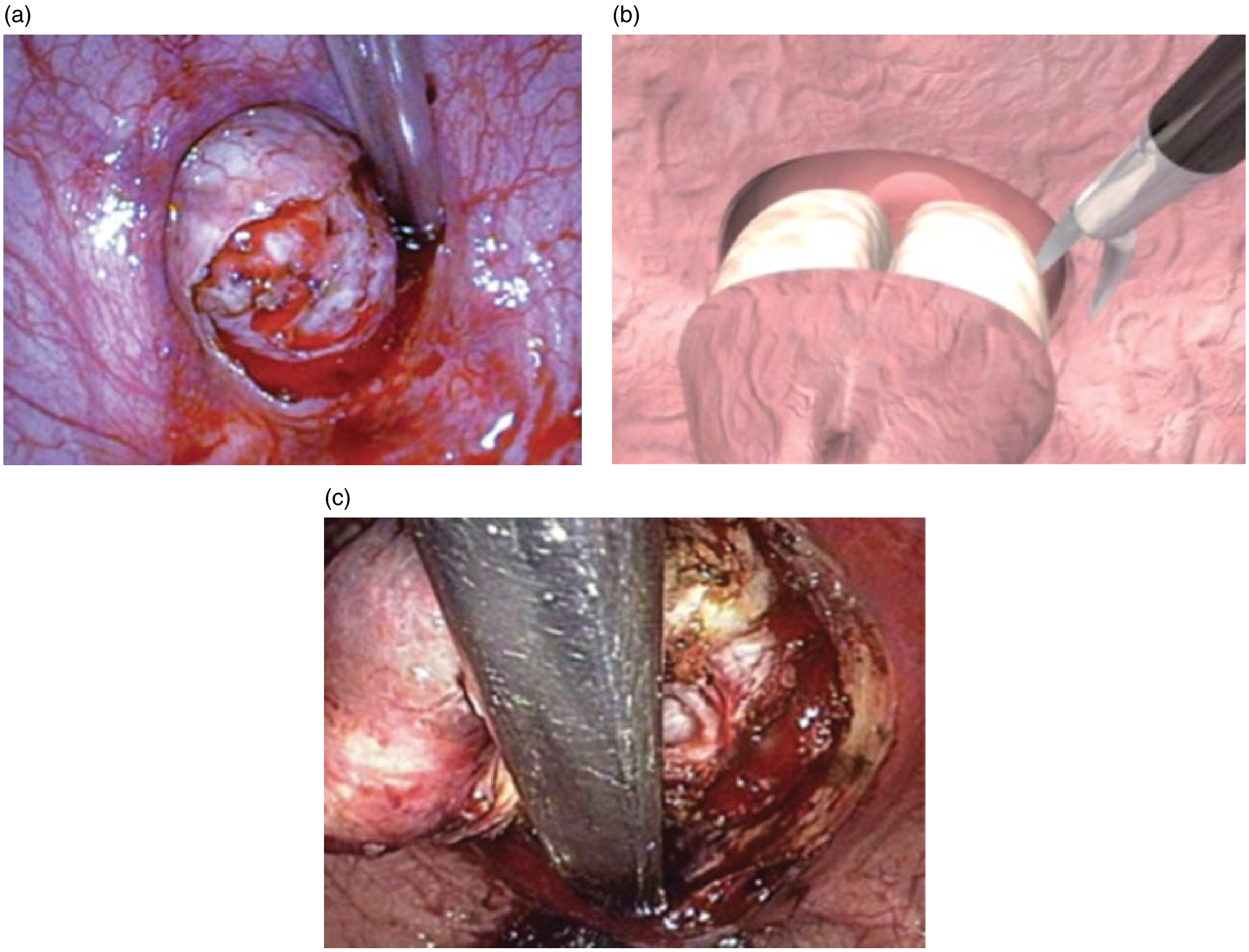

**Figure 153.3** (a) A Monocryl suture on a CT-1 needle is placed through the adenoma for retraction. (b) Mucosal incision and enucleation. (c) Division of prostatic adhesions.

Several maneuvers are used to facilitate the enucleation of the adenoma:

- The valve is removed first and then the right index finger is inserted through the TriPort. This expedites the distal part of the enucleation. The left index finger is placed into the rectum to elevate the prostate. Once the finger dissection has been completed, the TriPort valve is reattached. The pneumovesicum is re-established for incising the urethra at the prostatic apex and completing the procedure.
- Use of the "Sotelo prostatotomy," a device similar to a curette or an osteotome, facilitates enucleation of the adenoma during laparoscopic simple prostatectomy. Its metallic curvilinear tip, with a sharp cold knife on the distal side of the forceps, is used to divide the adhesions between the adenoma and its capsule during circumferential dissection of the gland (Figure 153.3c).
- The urethra is incised with a bipolar resectoscope through the urethra, immediately after the placement of the port and before any dissection from above (Figure 153.4).

#### Hemostasis

After removing the adenoma, hemostatic figure-of-eight sutures are tied down with an extracorporeal knot pusher and must be placed at the 4 and 8 o'clock positions at the prostatic capsule, to control the main prostatic vessels (Figure 153.5).

The lateral pedicles of the prostate should be thoroughly checked and the pneumovesicum pressure decreased to ensure that there is no bleeding. In the event that there is slight bleeding, it can be controlled with a monopolar or bipolar unit. If there is still any doubt, stitches can be made with absorbable sutures and knotted extracorporeally.

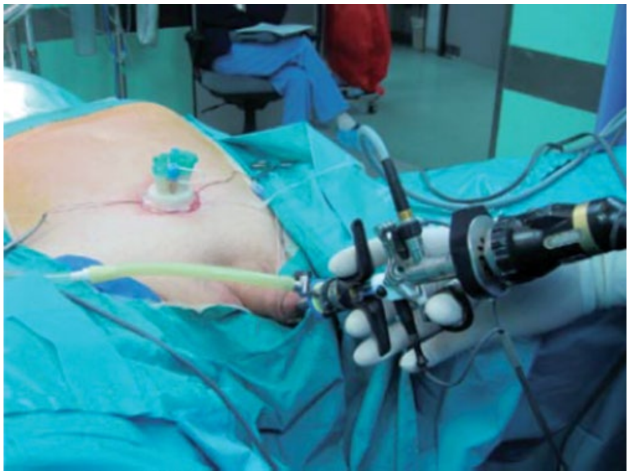

**Figure 153.4** Incision of the urethra with a bipolar resectoscope.

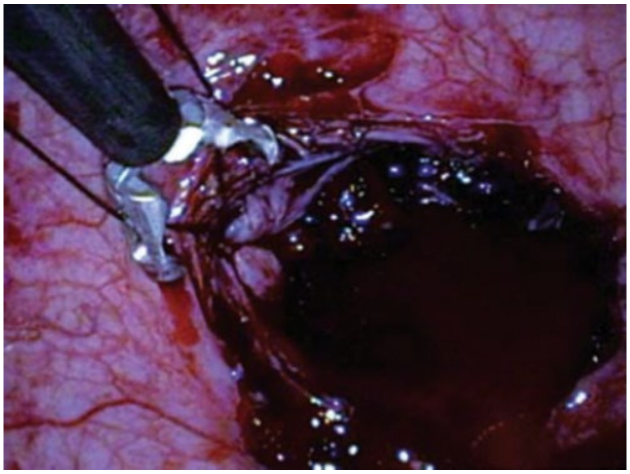

**Figure 153.5** Hemostasis of the main prostatic vessels with figure-of-eight sutures. These are tied down with an extracorporeal knot pusher and must be placed at the 4 and 8 o'clock positions of the prostatic capsule.

#### Specimen extraction

The prostatic adenoma is extracted through the TriPort ring after dividing it into multiple pieces during extraction with Allis forceps (Figure 153.6).

#### Trigonization and closure of the bladder

After removal of the adenoma, trigonization of the prostatic fossa can be performed by suturing the cut end of the posterior bladder neck distally toward the apex of the prostatic fossa. This can be tied down with an extracorporeal knot pusher.

The bladder opening is sutured with 3-0 Vicryl, and the fascia and skin are closed in a standard fashion. Depending on the amount of bleeding, a suprapubic catheter can be inserted through the inner ring of the TriPort (Figure 153.7). The balloon should be inflated before the TriPort is removed. The ring of the TriPort is large enough to pass the distal part of the catheter. In this way, it is easier to ensure that the Foley catheter is inside the bladder (Figure 153.8). Thus, the first Vicryl stay suture, which was previously placed in the bladder, can be tied, along with any additional sutures, to give a watertight closure.

The interest of urologists in single-port surgery has been maintained. When LESS surgery is performed by experienced surgeons, it is considered safe, with rates of conversion and complications similar to those obtained through laparoscopic multiport access (Table 153.1).

Simple prostatectomy by single-port laparoscopy outcomes have been reviewed through large multi-institutional studies at centers where surgeons have greater experience in this technique. These larger studies have strengthened statistics and provided points in favor of re-evaluating at each surgery. Simple prostatectomy by single port is a technically challenging procedure, and for

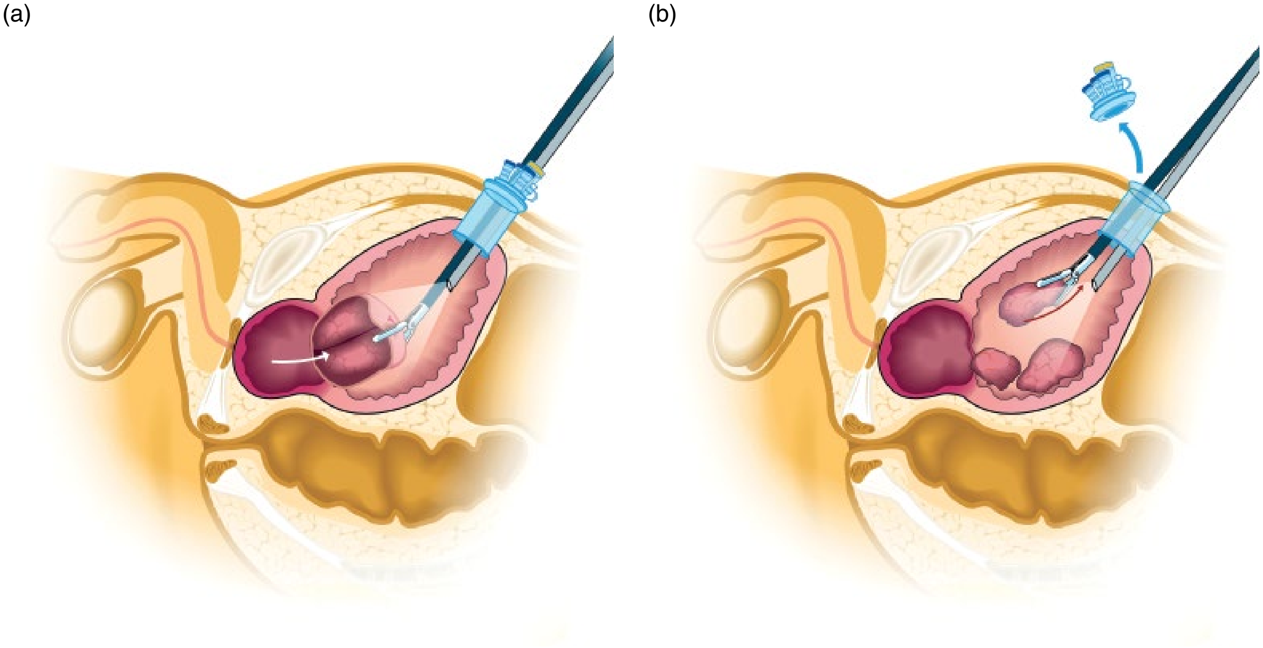

**Figure 153.6** (a, b). Prostatic adenoma is extracted through the TriPort ring after dividing it into multiple pieces during extraction with the Allis forceps.

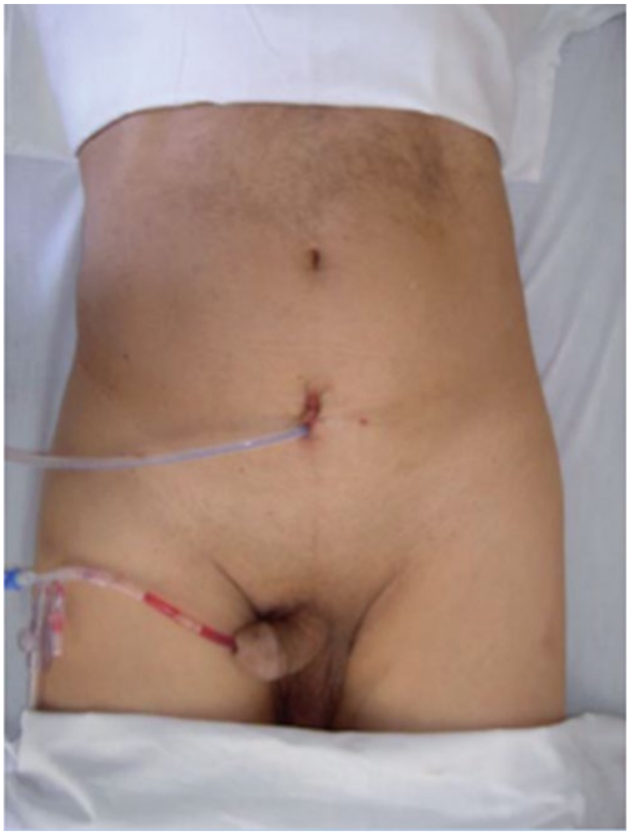

**Figure 153.7** Insertion of a suprapubic catheter through the inner ring of the TriPort.

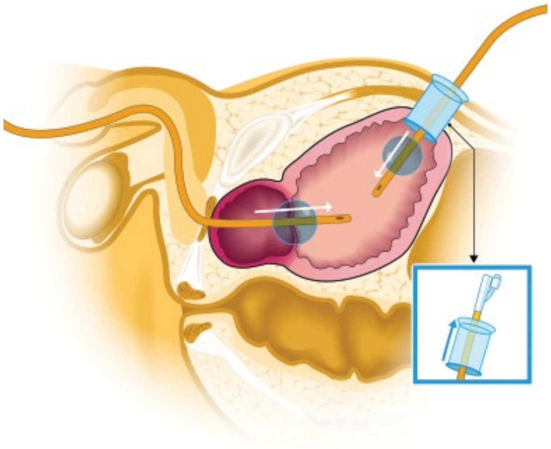

**Figure 153.8** The ring of the TriPort is large enough to pass the distal part of the catheter. This is the easiest way to ensure the Foley catheter is inside the bladder.

this reason it is thought that it will have little relevance and applicability in the future in urology [17]. However, it should be noted, that this technique has been used as the basis for the next generation of pelvic surgery, "radical prostatectomy by single port," which has great potential in the future of global urology.

**Table 153.1** Single-site simple prostatectomy series.

| Authors | Cases (*N*) | Approach | Access device | OR (min) | EBL (ml) | Conversion | Complications Clavien |
|---|---|---|---|---|---|---|---|
| Desai 2010 [13] | 9 | Lap | R-port TriPort | 116 | 460 | 4 to open | Death (1)<br>Bowel injury (1) Hemorrhage (5) Epididymo-orchitis (1) |
| Oktay 2010 [14] | 3 | Lap | Multichannel port | 105 | 190 | – | No |
| Kaouk 2011 [2] | 42 | Lap-Rob | TriPort GelPort | – | – | – | – |
| Fareed 2011 [15] | 9 | Rob | GelPort | 234 | 425 | 1 to open | 2 Hematuria (3b)<br>1 DVT (2)<br>1 UTI (2)<br>1 MI (4a)<br>1 ARF (4a) |
| Vicentini 2012 [16] | 21 | Lap | GelPOINT | 98 | 304 | – | Urinary fistulas (1) Clot retention (2) |

Lap, laparoscopic; Rob, robotic; OR, operative time; EBL, estimated blood loss; DVT, deep vein thrombosis; UTI, urinary tract infection; MI, myocardial infarction; ARF, acute respiratory failure.

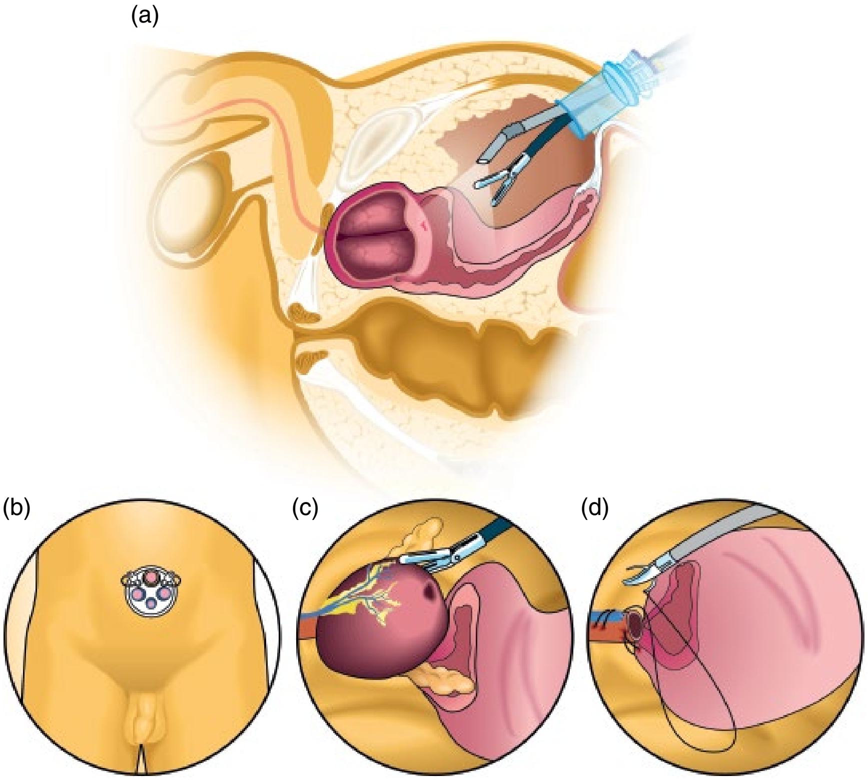

**Figure 153.9** Extraperitoneal laparoendoscopic single-site radical prostatectomy (LESS-RP). (a) Lateral view, (b) umbilical QuadPort, (c) prostate–bladder junction dissection and cut, (d) urethra–bladder anastomosis, reported with separate and continuous stitches.

## Single-port radical prostatectomy by laparoscopy

### Transumbilical approach

In 2008, the first single-port radical prostatectomy by laparoscopy (laparoendoscopic single-site radical prostatectomy, LESS-RP) was carried out in four patients with low-risk prostate cancer. A transabdominal approach was used, with a Uni-X port (Pnavel Systems, Morganville, NJ, USA) (Figure 153.9). The greatest difficulty described by Kaouk et al. occurred with the urethrovesical anastomosis, which was only achieved with suture interrupted with exo-nudos (knots tied on the outside, with a knot pusher). The use of an additional port was not necessary in any of these cases. One complication reported was of a patient who suffered a rectourethral fistula (Clavien grade IIIb), which was resolved with surgical management. From an oncologic viewpoint, half of the patients (2) had positive surgical margins with a detectable prostate specific antigen (PSA) at follow-up, and no reports of erectile function [18]. In another series of 31 cases in 2012, looking at nerve sparing in low-risk tumors (T1c to T2a) and presurgical Sexual Health Infentory for Men (SHIM) score >21, an additional 3.5 mm port was used [19]. These authors reported 32.3% nerve sparing, and 33% of the patients maintained adequate erectile function in the postoperative period (SHIM score in this series >21 points with or without medication).

The main approach used currently for LESS-RP is transperitoneal; however, an extraperitoneal approach has been described. In their first experience, Rabenalt et al. used the TriPort (Advanced Surgical Concepts) device and precurving instruments, achieving an anterograde dissection and 6 points apart in anastomoses in each of the cases [20]. Another group that reported their experience with the extraperitoneal approach described the use of two systems: the QuadPort multichannel (Olympus, Japan) and an artisan multichannel device made with a surgical glove, which used a flexible laparoscope and precurved and flexible instruments [21]. The last series reported was in 2013 by Jiang et al., who performed an extraperitoneal approach in 20 patients with a variable artisan multichannel device made with a surgical glove, along with straight and precurved instruments [22]. All describe the advantage of using precurved tools for LESS-RP.

## Transvesical approach

With applying the concept of transvesical simple prostatectomy by single port described by Desai et al. in 2008 [8], in 2011 Gao et al. published the largest series of transvesical prostatectomy by single port in 20 patients with low-risk prostate cancer (PSA = 10 ng/ml, Gleason <7 and clinical stage T1c or T2a). They began the initial dissection with a retrograde approach, starting by the bladder neck, and subsequently worked in an antegrade manner with dissection of the seminal vesicles and prostate; urethrovesical anastomosis was performed by inserting a foreskin graft with separate points. No additional ports were used and the neurovascular package was preserved in all patients, with reported results of 60% erectile function with 21 points or more on the International Index of Erectile Function (IIEF-5) scale, 100% continence, and 0% positive margins. Two years later, another series of 16 patients from the same author was published. This featured the addition of an innovative way to release tension on the anastomosis by making three incisions near the bladder neck, and completing the anastomosis with continuous barbed suture on each side [23] (Figure 153.10).

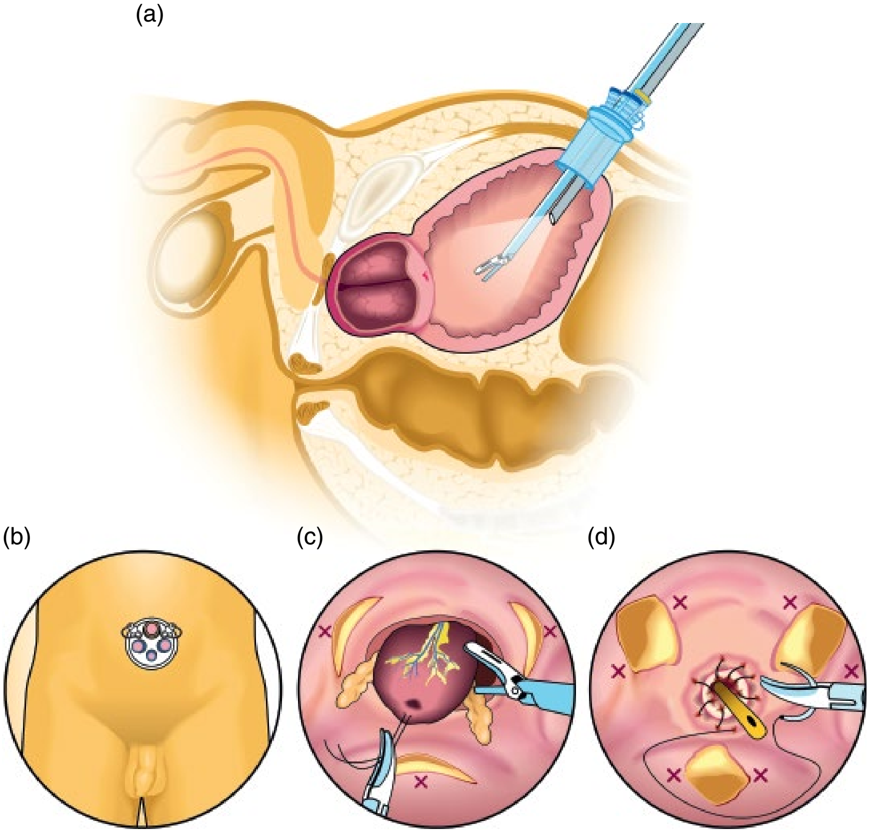

**Figure 153.10** Transvesical laparoendoscopic single-site radical prostatectomy (LESS-RP). (a) Lateral view, (b) umbilical QuadPort, (c) mucosa–muscle incisions between 2 and 4 o'clock, 5 and 7 o'clock, and 8 and 10 o'clock, marked as "X," ease urethra–bladder anastomosis, (d) continuous closure urethra–bladder anastomosis and enlargement of the mucosa–muscle incisions.

## Radical prostatectomy single-port laparoscopy assisted

The well-known advantage of the laparoscopic robot-assisted approach is the mobility of the instruments, which theoretically decreases the likelihood of collision. The da Vinci® (Intuitive Surgical Inc., Sunnyvale, CA, USA) surgical system has been characterized by its size and bulky nature, and it is clear that initial robotic platforms were not developed for LESS procedures. Nevertheless, surgeons and urologists have carried out single-port robot-assisted radical prostatectomies (R-LESS-RP).

### Transumbilical technique

The first two cases of R-LESS-RP were reported by the Montsouris group in 2009. The first case was in a cadaveric model and the second in a living patient [24, 25]. In both cases no single-port device was used, but a single umbilical incision was made with subsequent separate insertion of a trocar; a 12 mm port for the camera was used and two 8 mm robotic ports for the tools with a separation between the ports of approximately 3.5 cm. The dorsal venous complex was closed with a stitch and the urethrovesical anastomosis was performed with six separate points. The main difficulty described by surgeons was the external collision of the robotic arms, with the consequent limitation of movement and progression of surgery. This French technique and its rhomboid configuration of ports has been replicated by other groups trying to make it functional and successful (Figure 153.11).

To date, the most extensive series has been described by White et al. [26], who describe the results of 20 patients undergoing R-LESS-RP. They used two 8 mm robotic ports and one single-incision laparoscopic surgery (SILS) port. The robotic laparoscope was placed through the channel of the SILS, which measured 12 mm. The surgical technical was done in antegrade manner, following the steps of the conventional technique of prostatectomy radically assisted by a robot, with an average operating time of 200 minutes. Out of the 20 patients only 4 had complications. Oncological results revealed positive surgical margins in 24% of the evaluated patients (4/17) and node dissections were carried out in 60% of the patients.

A recent series with 11 patients describes the use of the first prototype of the da Vinci SP® single-port robotics platform, which offers insertion of the camera and instruments through a single port. In general, the patients were young, with a medium prostate, not obese, and of low risk. In this series conversion was reported to be 0% and the complications were mostly minor. The average surgical time was 239 minutes, with 18.2% positive margins, continence to 30 days of 55%, and potency of 63.3% [27].

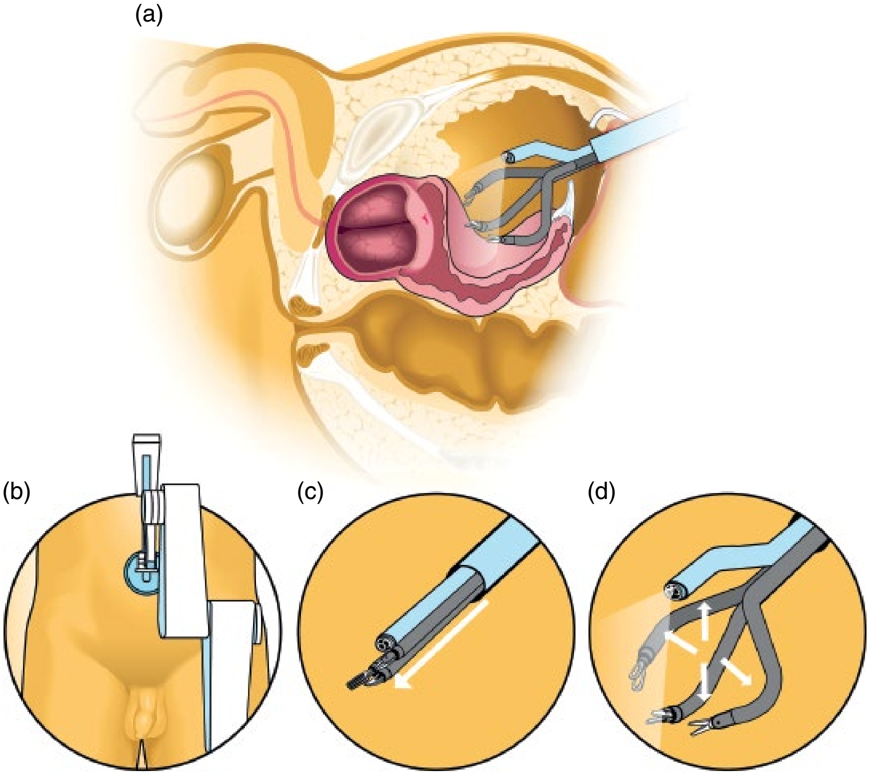

**Figure 153.11** Transperitoneal robot-assisted laparoendoscopic single-site radical prostatectomy (R-LESS-RP). (a) Lateral view, (b) da Vinci SP docking, (c) system elements entry, (d) system components deployment. The "Y" principle is observed.

### Transvesical technique

The first transvesical robotic radical prostatectomy (TRRP) was developed in two cadaveric models in 2008 by Drs. Desai and Sotelo. The first model involves a suprapubic horizontal incision (mini-Pfannenstiel) and includes several trocars through the fascia to the bladder. In the second model a QuadPort system was used. This device showed advantages over the conventional trocars by a single orifice, and from this observation this technique was adapted as a possible way by surgeons to make this intervention [3, 28]. In 2009 they performed the surgery in a 61-year-old patient with prostate cancer while preserving the neurovascular bundles and avoiding the use of additional ports [29] (Figure 153.12).

## The future

The first robotic platform was developed in 2012 and was designed to improve the interface between the surgeon and the patient, to avoid difficulty generating movements in an inverted mirror through a computer on the platform; however, these instruments lacked articulated movement, making some complex movements, such as suturing, more difficult, in addition to collisions of the external arms.

With a completely different concept – a Y-shaped single port – the second single-port robotic platform offered an intracorporeal triangulation with flexible instruments, thereby avoiding any possible collisions. This design is characterized by a straight shaft and two-sided flexible instruments, and a 3D laparoscope with a relatively small and flexible diameter at the tip. The three instruments and optics are introduced through a straight sheath, providing a solid instrument.

This concept of a Y-shaped platform has been used to perfect a new single-port robotic prototype called a "spring plate mechanism," which is characterized by a spring plate that enables the transmission of force and improves the size of the working space.

The da Vinci Single Port (SP) system entered the market in late 2017, after FDA approval, bringing with it the great advantage of being able to perform surgery in a single quadrant with a single incision of 2.5 cm, leading to expectations that it will prove to be a highly successful tool in minimally invasive surgery following its initial promising results [27] (Figure 153.13).

In the field of urology, the first natural orifice transluminal endoscopic surgery (NOTES) procedure described was a transvaginal nephrectomy in a porcine model in 2002. This was followed by a human nephrectomy using a transvaginal port. A pioneer group, Krambeck and

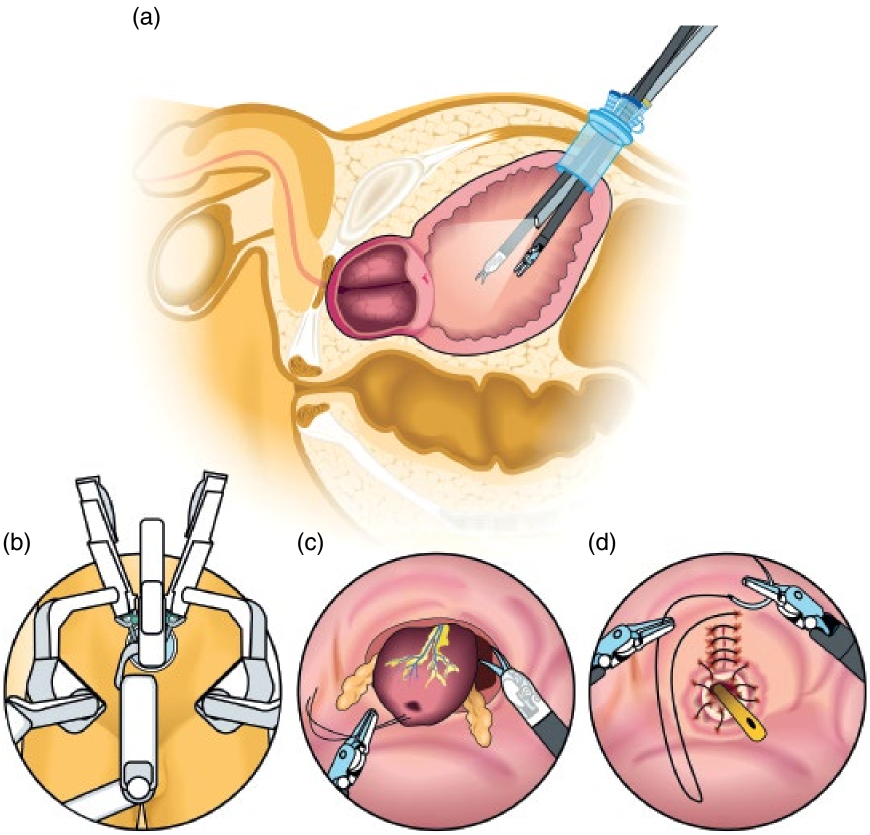

**Figure 153.12** Transperitoneal robot-assisted laparoendoscopic single-site radical prostatectomy (R-LESS-RP). (a) Lateral view, (b) da Vinci Si docking, (c) intravesical dissection of the prostate and seminal vesicles, (d) urethra–bladder anastomosis with anterior plication.

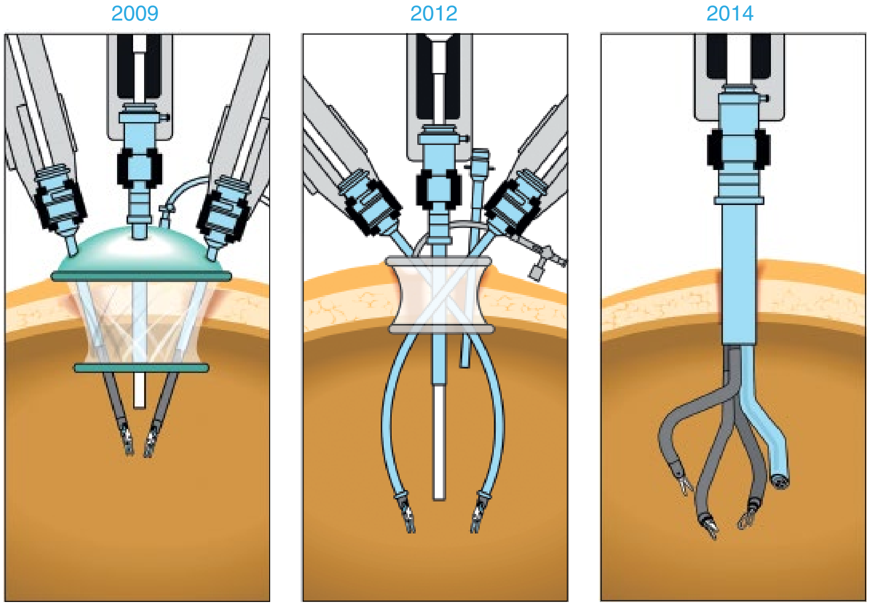

**Figure 153.13** Robotic laparoendoscopic single-site (LESS) prostatectomy: (2009) First radical LESS prostatectomy, rhomboidal configuration; (2012) first platform LESS VesPa (not used for prostate), (2014) second platform LESS, da Vinci SP uses "Y" principle.

Humphreys, demonstrated the feasibility of NOTES-RP (natural orifice transluminal endoscopic surgery – radical prostatectomy) in canine and cadaveric models in 2010 and 2011, respectively, using the urethra as the natural orifice [30, 31]. They used a holmium (Ho:YAG) laser (VersaPulse®, Lumenis Inc., Santa Clara, CA, USA) with a 26 Fr resectoscope to complete the prostate dissection procedure. The prostate sample was liquefied (using a morcellator) and the anastomosis was performed through a urethravesical anastomosis device (LSI Solutions, Victor, NY, USA) with monofilament polydioxanone 3-0.

Laparoscopic surgery depends on visual information since there is a lack of tactile feedback. The RoboSurgeon System® was developed to address this. It incorporates a system with a head-mounted display (HMD) combining a three-dimensional organic electroluminescent HMD unit (HMS-3000MT, Sony Corporation, Tokyo, Japan) with various image modalities, including an endoscope, transrectal ultrasound, and magnetic resonance imaging through interface multiplexers, enabling an improvement in technique and results in real time [32].

These developments demonstrate how quickly surgeons are modifying surgical approaches and designing techniques that are less invasive with the goal of achieving good results.

See accompanying Video 153.1.

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# 154

# Bladder Injections for Refractory Overactive Bladder: Intra- and Transvesical Procedures

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## Introduction

Overactive bladder (OAB), as defined by the International Continence Society, is "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection (UTI) or other obvious pathology" [1]. OAB can be neurogenic (N-OAB) or idiopathic (I-OAB). N-OAB results directly from neurologic disorders, such as multiple sclerosis, myelomeningocele, and spinal cord injury [2], while I-OAB is a clinical diagnosis of exclusion after ruling out alternative sources of symptoms, such as benign prostatic hyperplasia (BPH), UTI, malignancy, or painful bladder syndrome [3, 4]. The worldwide incidence of OAB is estimated to be 11% [5], and the prevalence ranges from 7% to 27% in men and 9–43% in women [3, 5–12]. The primary concern for many OAB patients is reduced quality of life (QOL) [13–17]. I-OAB leads to deterioration in QOL in about 50% of patients, with the proportion increasing to 80% in those with incontinence [17]. The impact on QOL can extend to sexual function, marital satisfaction, and psychosocial functioning with increased rates of depression associated with worsening incontinence symptoms [18–21].

First-line treatment of OAB includes behavioral therapies combined with pharmacologic management when necessary [3, 4]. Behavioral modifications include bladder training, pelvic muscle training, fluid management, and bladder control strategies. Pharmacotherapy may be initiated simultaneously with behavioral therapy or when behavioral therapy is insufficient in managing symptoms. Pharmacologic options are considered second-line interventions and include anticholinergic/antimuscarinic and beta-adrenergic medications. Cholinergic receptors in the bladder, stimulated by acetylcholine released from parasympathetic neurons, are responsible for bladder contraction during voiding [22, 23]. However, such receptors exist elsewhere in the body, including the brain, salivary glands, heart, gastrointestinal tract, and eyes, resulting in side-effects, such as cognitive problems, dry mouth, tachycardia, constipation, and blurred vision [3, 22, 23]. Such side-effects, along with a relative lack of efficacy, have led to discontinuation of anticholinergic medication in >60% of patients at 12 months [24]. Almost half of patients discontinued medication because they felt it "did not work as expected," and almost one-fourth of patients cited the side-effects as their reason [25]. Mirabegron, a beta-adrenoceptor agonist, is an alternative to anticholinergic medications with similar efficacy for treatment of OAB [26] although currently there are relatively few studies. By targeting the sympathetic system, mirabegron can be used in patients with poor tolerance or contraindications to anticholinergic therapy. Mirabegron has been shown to have lower rates of dry mouth and constipation, which may contribute to higher rates of adherence and persistence at 12 months compared to anticholinergics [27].

Patients refractory to first- and second-line treatments may be offered botulinum toxin A (BTX-A) intravesical injections, peripheral tibial nerve stimulation, or sacral neuromodulation. In rare cases, the patient with refractory OAB may be offered indwelling catheterization or surgery, such as bladder augmentation or urinary diversion. This chapter discusses the mechanism, efficacy, technique, and side-effects of endoscopic injections of BTX-A into the detrusor wall of patients with refractory OAB.

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## Mechanism of action

Botulinum toxin is a potent neurotoxin produced by the anaerobic bacterium *Clostridium botulinum*, which can result in severe symptoms including mydriasis and progressive neuromuscular paralysis, producing muscle weakness, dyspnea, and possibly death. These symptoms were first described in the 1820s by the German physician Kerner who observed an outbreak among soldiers suffering "sausage poisoning" from having eaten infected sausages [28]. It was not until 1897 that the microbiologist van Ermengem discovered the culprit bacterium which he termed "bacillus botulinus" (from the Latin word *botulus* meaning sausage) after isolating it from the tissue of several people who died following a funeral dinner as well as from the smoked ham served that day [29]. Botulinum toxin was first used medically in 1977 by the opthalmologist Scott to treat patients with strabismus or blepharospasm, and US Food and Drug Administration (FDA) approval for this application was granted in 1989 [30]. In 1988, Dysktra et al. described the first urologic application of botulinum toxin – injection into the external urinary sphincter to treat detrusor sphincter dyssynergia in spinal cord injury patients [31]. Since that time, the urologic indications for therapy have expanded to include N-OAB, I-OAB, interstitial cystitis/bladder pain syndrome (IC/BPS), chronic pelvic pain syndrome, and detrusor sphincter dyssynergia (DSD).

The pathophysiology of OAB is not fully understood, but may involve lack of inhibition by upper motor neurons in patients with N-OAB, and oversensitivity of sensory fibers and reflex pathways in patients with I-OAB. Botulinum toxin has been shown to block both the afferent and efferent fibers, resulting in a decreased sensation of fullness, and reduced smooth muscle contractility, respectively [32–34]. Different strains of botulinum toxin (A to F) interact uniquely with different SNARE proteins, which are required for the release of acetylcholine from the presynaptic terminals. These interactions inhibit cholinergic neurotransmission at neuromuscular synapses and subsequently decrease or abolish muscle contractions [35]. BTX-A has the longest duration of action and has become the focus of medical applications.

There are five different preparations of BTX-A: onabotulinumtoxinA (Botox™), abobotulinumtoxinA (Dysport™), incobotulinumtoxinA (Xeomin™), Prosigne™, and Purtox™. Studies suggest that 1 unit of onabotulinumtoxinA is roughly equivalent to 3–5 units of abobotulinumtoxinA, 1 unit of Xeomin, and 1 unit of Prosigne, although no randomized control trials comparing dose, efficacy, and safety exist [36]. OnabotulinumtoxinA and abobotulinumtoxinA are the most commonly used preparations. Studies on abobotulinumtoxinA show similar treatment efficacy to onabotulinumtoxinA [36–39]. AbobotulinumtoxinA has been studied at doses of 500, 750, or 1000 U; 500 U resulted in too short a duration of action, while side-effects with 1000 U were too great (reports of temporary generalized weakness) [40]. A study by Jeffery et al. demonstrated a clean intermittent catheterization (CIC) rate at six weeks of 35% for treatment of I-OAB with Dysport 500 U [39]. Revindra et al. also showed abobotulinumtoxinA 500 U had a rate and duration of efficacy similar to that of onabotulinumtoxinA 200 U, but they demonstrated a higher rate of CIC in the abobotulinumtoxinA group (42% vs. 23%) [38]. The majority of evidence on BTX-A therapy in OAB is with onabotulinumtoxinA use. Because of this, the remainder of the discussion will focus solely on onabotulinumtoxinA.

## Results of onabotulinumtoxinA injection

The efficacy of injection of onabotulinumtoxinA into the detrusor smooth muscle of the bladder wall of patients with refractory N-OAB was first demonstrated by Schurch et al. in 2000 [41]. In this study, 21 patients with spinal cord injury who experienced incontinence secondary to neurogenic detrusor overactivity, required CIC to empty, and had failed anticholinergics were treated with onabotulinumtoxinA. Following treatment they demonstrated a significant increase in mean maximum bladder capacity (from 296 to 480 ml, $P < 0.016$) and a significant decrease in mean maximum detrusor voiding pressure (from 65 to 35 $\mathrm{cmH_2O}$, $P < 0.016$). Of the 21 patients, 17 were completely continent at six weeks follow-up and were satisfied with the procedure; improvements in urodynamic parameters and incontinence persisted at 36 weeks in 11 patients [41]. Since that initial description, many studies have demonstrated the utility of onabotulinumtoxinA injection as an appropriate therapy for patients with I-OAB and N-OAB refractory to anticholinergics [3, 4, 36–71].

## Neurogenic overactive bladder

Multiple placebo-controlled studies have demonstrated the efficacy of onabotulinumtoxinA in patients with N-OAB [45–51]. Two recent double-blind, placebo-controlled, Phase 3 studies demonstrating the efficacy of onabotulinumtoxinA in patients with N-OAB provide the strongest evidence for its use [48, 49]. A total of 691 patients with N-OAB secondary to multiple sclerosis (MS) or spinal cord injury (SCI) were included in a pooled analysis [48–50]. Patients were included if they had >14 episodes of urge incontinence per week and had failed a trial of appropriately dosed anticholinergic medication for >one month due to inefficacy or intolerance. Patients were then randomized to receive intradetrusor injections of 30 ml of onabotulinumtoxinA 200 U, 300 U, or placebo. The trigone was spared during injection. Six weeks following treatment statistically significant decreases in weekly urge incontinence episodes were seen in the 200 U (−22.6 MS, −19.6 SCI) and 300 U (−24.0 MS, −18.2 SCI) group compared to placebo (−14.0 MS, −6.4 SCI). In addition, rates of total continence at six weeks increased in both the 200 U (41.5% MS, 30.9% SCI) and 300 U groups (44.2% MS, 35.9% SCI) compared to placebo (10.7% MS, 7.3% SCI). Significant increases in I-QOL scores were seen in both onabotulinumtoxinA groups compared to placebo. Urodynamic studies (UDS) performed at six weeks after injection demonstrated an increase in maximum cystometric capacity (MCC) compared to placebo (151–157 ml, 157.2–168 ml, and 6.5–18 ml). Mangera et al. performed a systematic review of available literature in 2014 supporting these findings. They reported statistically significant improvements in daily incontinence (−63%) as well as multiple UDS parameters, including MCC (+68%) [37].

The FDA-approved starting dose for onabotulinumtoxinA in the treatment of N-OAB is 200 U. Apostolidis et al. showed 200 U to be the most effective dose in a placebo-controlled dose-response study comparing 50, 100, and 200 U onabotulinumtoxinA [51]. In the previously discussed Phase 3 studies the 300 U dose did not add to the clinical efficacy in any subpopulation compared to 200 U [48–50].

## Idiopathic overactive bladder

The American Urological Association (AUA) and Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) released an amendment to the 2012 non-neurogenic OAB guideline statement upgrading the use of onabotulinumtoxinA (100 U) as third-line treatment from an option to standard [3, 4]. This was largely based on updated review of the literature with 27 new studies including five randomized trials with placebo control groups and 2 trials with active controls [4]. Several randomized, double-blind trials were performed demonstrating the efficacy and tolerability of 100 U onabotulinumtoxinA [52–61]. The largest Phase 2 trial was performed by Dmochowski et al. who compared 50 U, 100 U, 150 U, 200 U, and 300 U onabotulinumtoxinA to placebo [52]. They found 100 U to be the optimal dose to improve UI episodes and other OAB symptoms, while doses of 150 U or greater led to a dose-dependent increase in postvoid residual (PVR) without providing additional clinical benefit. Two Phase 3 double-blind, placebo-controlled trials performed by Chapple et al. and Nitti et al. provide the most robust evidence, showing a three- to fourfold decrease in frequency of UI episodes in 100 U onabotulinumtoxinA compared to placebo [62–64]. Pooled analysis of the data included 1097 patients with at least three UI episodes per three days and eight micturitions per day who had failed anticholinergic therapy due to inefficacy or intolerance. Subjects were then randomized to onabotulinumtoxinA 100 U or placebo divided in 20 detrusor injections. The trigone was spared during injection. The onabotulinumtoxinA group demonstrated a significant improvement in UI episodes per day compared to placebo (−2.8 vs. −0.95) at 12 weeks. The onabotulinumtoxinA arm also demonstrated 27.1% rate of total continence compared to 8.4% in the placebo arm. Furthermore, patients who received onabotulinumtoxinA were more likely to report improved frequency and urgency. A systematic review of available literature in 2014 reported statistically significant decrease in daily incontinence (−59%) as well as improvement in multiple UDS parameters including MCC (+58%) [37].

Rovner et al. demonstrated objective improvement in MCC on UDS in patients treated with onabotulinumtoxinA 100 U at 12 weeks compared to placebo (+71.0 ml vs. +49.5 ml), as well as improved compliance at MCC (+63.0 vs. 22.8 ml/cm$H_2O$) [65]. Of note, the presence of detrusor overactivity on baseline UDS did not impact the efficacy of onabotulinumtoxinA injection for patients with I-OAB. Because of this, routine UDS testing is not required prior to treatment with onabotulinumtoxinA for I-OAB [66].

## Pediatric overactive bladder

Pediatric patients with myelomeningocele experience difficulty with bladder function, and many suffer from detrusor overactivity and incontinence. In addition, there is concern for deterioration of their upper tracts as they may have high bladder pressures due to poor or intermediate compliance and vesicoureteral reflux. OnabotulinumtoxinA is not currently approved for use in pediatric OAB, however multiple studies have demonstrated clinical benefit. Mangera et al. performed a systematic review of available literature on onabotulinumtoxinA use in pediatric N-OAB refractory to medical management. OnabotulinumtoxinA treatment was found to improve MCC from 50% to 59% and maximum detrusor pressure decreased from 42% to 50% [37]. In addition, a reduction in the grade of vesicoureteral reflux was noted in one study, potentially as a result of decreasing bladder pressure [66]. Use of onabotulinumtoxinA in pediatric patients is being investigated for treatment of OAB in non-neurogenic patients with positive preliminary data [67, 68]. Urethral external sphincteric injection of onabotulinumtoxinA in children with dysfunctional voiding has been shown to be beneficial as well [69–71].

## Repeat injections

As the effects of onabotulinumtoxinA injection have been shown to last approximately 6–9 months, patients require repeat injections to continue to experience the therapeutic benefits. Initially there were concerns raised regarding the possibility that repeat injections would result in a blunted response over time due to antibody formation to the toxin. Several studies in N-OAB patients have evaluated the efficacy of repeat injections of onabotulinumtoxinA with five to seven injections over a 6- to 8-year period, and have demonstrated that urodynamic and clinical improvements in QOL and decreased medication requirements after the first injection were maintained for a duration of 6–9 months after each subsequent application [72–76]. In addition, it was postulated that repeat injections could result in fibrosis from repeated puncturing of the mucosa; however, several studies have investigated this and found no evidence of it [77–79].

## Adverse outcomes

Adverse outcomes associated with the injection of onabotulinumtoxinA include mild hematuria, dysuria, systemic toxicity, UTIs, and urinary retention requiring CIC. OnabotulinumtoxinA carries a black box warning from the FDA due to risk of toxin spread from the site of injection, which may cause difficulty swallowing or breathing and in very rare instances risk of death. The risk of symptoms is probably greatest in children treated for spasticity but may occur in adults. Additional signs of systemic toxicity include hypoasthenia, impaired vision, extremity weakness, dry mouth, dysphagia, and constipation [65]. Systemic onabotulinumtoxinA toxicity is uncommon after intradetrusor injection and more often associated with higher doses administered for nonurologic reasons by other specialties [80]. Peripheral muscle weakness has also been noted to occur in rare instances, and has been associated with patients receiving a higher dose (1000 U) of abobotulinumtoxinA [40, 72]. When treating adults for one or more indications, the total cumulative dose of abobotulinumtoxinA is not to exceed 400 U over a three-month interval.

Rates of UTI following onabotulinumtoxinA injection range from 3.6% to 54% in the literature [3]. This variability may depend on patient-related factors as well as the indication for onabotulinumtoxinA therapy. In the two Phase 3 trials of onabotulinumtoxinA in N-OAB, patients with SCI had a UTI rate of 44.8%, similar to a rate of 49.5% of patients with SCI who underwent placebo. Patients with MS who underwent onabotulinumtoxinA therapy for N-OAB had a higher rate of UTI compared to placebo (53.5% vs. 29.2%), which is likely explained by higher rates of urinary retention requiring *de novo* CIC in this patient population. A systematic review of onabotulinumtoxinA use in I-OAB found a UTI rate of 21% compared to 7% in the placebo group and a rate of 39% for patients with N-OAB compared to 33% following placebo injections [37].

In general, an increase in PVR can be expected following onabotulinumtoxinA injection; however, the definition of urinary retention and the threshold for initiation of CIC differs among the various studies. Dmochowski et al., who compared 50 U, 100 U, 150 U, 200 U, and 300 U onabotulinumtoxinA to placebo found a dose-related increase in PVR [52]. Phase 3 trial data on onabotulinumtoxinA use for I-OAB reported CIC rates of 6.5% after onabotulinumtoxinA 100 U versus 0.4% in the placebo group [60–64], while a literature review reported a 12% rate of CIC in this population [37]. Phase 3 trial data on onabotulinumtoxinA use for N-OAB with MS reported a posttreatment CIC rate of 40% with onabotulinumtoxinA 200 U and 51% with 300 U, compared to 17% with placebo [48–50]. The need to perform CIC may not be an issue for a patient with N-OAB who has likely had to perform CIC in the past, while the need for *de novo* CIC may prove very bothersome in a patient who has never had to do so. However, the need for postprocedure CIC did not impact patient satisfaction in the N-OAB population [48–50]. While many of our N-OAB patients are already proficient in performing CIC, we prefer to teach all our patients CIC, including the I-OAB patients, prior to treatment.

CIC usually needs to be performed for about 1–3 months until PVR decreases as the effects of the onabotulinumtoxinA wear off. Of note, rates of CIC are significantly increased following repeat injections in patients who experienced retention with a prior injection [81, 82]. Factors that can predict a need for *de novo* CIC are a projected isovolumetric detrusor pressure of less than 50 in women (sensitivity 0.83, specificity 0.7) and a bladder contractility index of less than 120 in men (sensitivity 0.7, specificity 0.79) [82].

## Technical considerations

OnabotulinumtoxinA injection into the bladder wall can be accomplished using either rigid or flexible cystoscopy using local, regional, or general anesthesia [65], although general anesthesia is rarely needed. The technique was originally described by Schurch et al. using a rigid cystoscope and an endoscopic needle to inject 1 mL just beneath the detrusor epithelium at 20–30 sites, sparing the trigone (see Video 154.1) [41]. Later the "Dasgupta technique" was described using a flexible cystoscope: a sheath is passed through the working channel of the cystoscope to protect the scope during passage of a 27G needle and to stabilize the needle during injection [83]. In addition, a minimally invasive sedation-free technique can be performed by instilling 40 ml of 1% lidocaine into the bladder via a catheter 10 minutes prior to cystoscopy [84, 85]. Thus, onabotulinumtoxinA injection can be performed in the operating room or office with either a rigid or flexible cystoscope, depending on surgeon preference. The FDA has approved 100 U of onabotulinumtoxinA for treatment of I-OAB and 200 U of onabotulinumtoxinA for treatment of N-OAB. The onabotulinumtoxinA is diluted in 20 ml of sterile saline for 100 U and 30 ml for 200 U. It is then injected in 0.5–1 ml increments through the detrusor, separated by a distance of 1–1.5 cm. The standard depth of onabotulinumtoxinA injection is to the detrusor layer of the bladder wall, although some research suggests a benefit of suburothelial injections. OnabotulinumtoxinA delivered to the suburothelial space may modulate the release of sensory nerve endings and potentially inhibit detrusor overactivity mediated by sensory nerve dysfunction [86–88]. Studies have shown similar benefits between suburothelial and intradetrusor injections, although suburothelial injections may be associated with higher rates of voiding dysfunction [86–88].

Some controversy exists regarding whether the trigone is included or spared from injection. Many of the initial studies advocated avoiding injection of the trigone as urologists felt it could lead to vesicoureteral reflux; however, this has not been shown to occur in two prospective studies [89, 90]. One study showed a greater effect on reducing urgency sensation in I-OAB [91]. Kuo et al. compared outcomes for 100 U onabotulinumtoxinA injections in the bladder body, bladder body plus trigone, and bladder base plus trigone and found no difference in success rate (70–74%), changes in urgency, or adverse events [92], and a meta-analysis comparing trigonal and extratrigonal injection sites also found no differences in short-term efficacy or adverse events [93]. Studies have also explored injection of the external (striated) sphincter in patients at risk for urinary retention with some positive preliminary results, however the utility of urethral sphincteric onabotulinumtoxinA injection for non-neurogenic voiding dysfunction is unclear [94–96].

## Conclusions

A moderate percentage of patients with OAB, either from idiopathic or neurogenic causes, are refractory to behavioral modification and oral medications. Endoscopic injection of BTX-A into the detrusor wall is well-established as an alternative therapy in these patients as multiple randomized, double-blind trials have demonstrated clinical and urodynamic efficacy, resulting in fewer incontinence episodes, improved QOL, and increases in bladder capacity and decreases in maximum detrusor pressures. These beneficial results last approximately 6–9 months and injections can be repeated as necessary with no apparent tachyphylaxis. In general, this treatment is well tolerated. However, patients can experience increased residual volumes requiring CIC for 1–3 months until spontaneous voiding can resume, and also are at a higher risk for UTIs.

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# 155

# STING Procedure for Reflux

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## Introduction

The endoscopic treatment of vesicoureteral reflux (VUR) involves the injection of a bulking agent at the orifice of an incompetent ureter in order to create a suitable flap–valve mechanism to prevent the retrograde flow of urine during voiding. Many different types of bulking agents have been used in the history of endoscopic reflux therapy, although the perfect agent has been elusive. The ideal substance for endoscopic treatment of reflux should be easily injectable, nonimmunogenic, stable, and safe for human use [1].

## Search for the ideal bulking agent

Matouschek was the first to describe the endoscopic treatment of VUR in 1981 when he described the injection of Teflon® polytetrafluoroethylene (PTFE) at the ureteral orifice to increase resistance to urine back flow [2]. Following the publication of excellent results using the subureteral PTFE (Teflon) injection (the STING technique) by O'Donnell and Pruri, the procedure received general acceptance in Europe, but was not widely used in the United States, where there was concern over implant migration [3]. The numerous reports of PTFE migration to remote areas such as the brain and lung following injection in the urethra and bladder neck sealed the fate of PTFE therapy [4, 5]. In addition to the risk of migration, there was concern over the development of granulomatous reaction around the PTFE, leading to possible calcification and making subsequent reimplant surgery difficult [6].

Once it was clear the future of the endoscopic treatment of reflux would not include PTFE, scientists searched for other agents to be used in the desirable technique. Silicone (Macroplastique; Urpoplasty Inc., Minneapolis, MN, USA) was a very effective agent when used with the STING procedure, correcting reflux in over 80% of ureters, with little morbidity. Unfortunately, silicone can cause a local foreign body reaction, and on the basis of the variable size of its particulates (35–540 μm), has a theoretical potential for migration risk. Also, the difficulty in injecting the viscous solution made the procedure less desirable. Finally, Macroplastique came to light at a time of great concern over systemic collagen disorders arising from silicone implants, and the material never achieved popular use [1, 7]. Recently, however, studies have demonstrated improved results with polydimethylsiloxane as compared to commonly used agents (specifically with high-grade reflux), raising the question as to whether this material should be revisited as a viable alternative [8].

The next agent to be explored for the endoscopic therapy of reflux was glutaraldehyde crosslinked bovine collagen (Contigen; C.R. Bard Inc., Murray Hill, NJ, USA). This substance has several characteristics that limited its widespread use for the STING procedure. First, it has the possibility of an allergic reaction, and therefore demands requisite allergy testing preinjection. Also, as has been noted in other areas of collagen injection (in cosmetic surgery, or the urethra for intrinsic sphincter incontinence), the substance has a limited staying power, and can show significant volume loss over time from the site of injection. Finally, long-term efficacy was not comparable to other, more durable agents [1, 7].

Calcium hydroxylapatite (Coaptite; Boston Scientific Inc., Natick, MA, USA) is a mixture of water and glycerin with 3% methylcellulose gel. It had commendable results in studies on patients with reflux requiring endoscopic correction, but had a higher single injection failure rate when compared to competing agents.

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Companion website: www.wiley.com/go/smith/textbookofendourology

The material is thought to be biocompatible and nonmutagenic, and currently is indicated only for female stress urinary incontinence secondary to intrinsic sphincter deficiency [1].

As research into tissue engineering expanded in the 1990s, one of the first areas investigated for human use involved the growth of chondrocytes for the treatment of VUR in children. Autologous chondrocytes were harvested from the auricular cartilage of patients and six weeks after their harvest and growth in culture, they were suspended in an alginate solution that included calcium chloride and calcium sulfate, which provided a scaffold for cartilage formation. The cells were then injected cystoscopically using the STING technique. The elastic cartilage tissue formed was able to correct VUR without any evidence of obstruction, and represented the first human application of cell-based tissue engineering technology for urologic applications [9].

However, the costs of the technique, as well as the need for a second harvesting procedure, limited the widespread use of the technology. In addition, variable degrees of cell growth appeared to occur, leading to inconsistent success rates [10].

Another novel material for use in the STING procedure was introduced in the late 1990s. Crosslinked dextranomer and hyaluronic acid (Deflux) had been used safely in the body for other indications for years, with no migration and long-term durability. Deflux was thought to have many of the characteristics of an ideal and effective bulking agent, as it is thin enough to allow needle injection, yet viscous enough to maintain its volume, is biocompatible, elicits minimal inflammation, and maintains its periureteral configuration over time [11].

In the first few years after the introduction of Deflux and its acceptance into widespread use, it demonstrated excellent results and durability, and had become the agent of choice. As the experience with the use of Deflux grew, the techniques, methods, and circumstances of use evolved.

As the years have passed, complications have arisen from the use of Deflux as well, with overall success rates only in the 70% range, and reports of the implant causing long-lasting inflammation and the formation of granulomas, and pseudocysts around the Deflux injection site. In many cases the implant has become calcified, mimicking a ureteral calcification on imaging studies, and the incidence of early and obstruction as a result of Deflux injection is increasing [12, 13].

In instances where Deflux is being considered as a treatment option, another dextranomer/hyaluronic acid-based bulking agent (Vurdex; BioScience GmbH, Germany) has been developed, with similar results to Deflux but a significantly lower price [14].

## Technique

The traditional STING procedure involved the injection of bulking material just outside the ureteral orifice at the 6 o'clock position, elevating a mound with the compressed ureteral orifice located at the top of the hillock. Using the traditional STING technique, the success rates with Deflux injection, while variable, were acceptable, but certainly lagged behind those of surgical reimplantation. The Atlanta group pioneered a novel method, termed "HIT" and now "double HIT," which has raised the success levels of Deflux injection above 90% [15, 16]. In this method, the ureter is hydrodistended so that the needle may be placed inside the ureteral tunnel, a few millimeters within the orifice (see Video 155.1). This allows the first injection of the HIT technique to track bulking agent along the ureteral sheath, and more efficiently coapt the ureter (especially larger, dilated ureters). The second hit is similar to the traditional STING injection, but is slightly more cephalad, and coapts the ureteral orifice and elevates a mound of bulking material at the terminal ureter (see Video 155.2 for the complete double HIT technique). This technique creates a "mountain range" of bulking material along the course of the ureter, in contrast to the original simple hillock (Figures 155.1 and 155.2) [17].

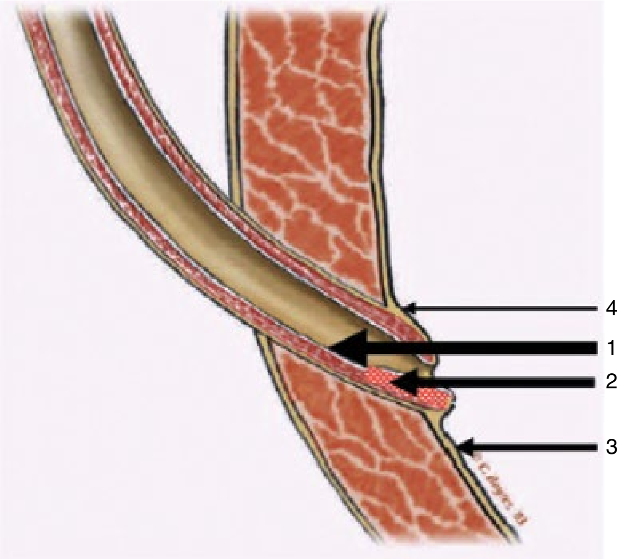


**Figure 155.1** Locations of needle placement for the **1**, intraureteric proximal technique (HIT); **2**, intraureteric distal technique (double HIT); **3**, traditional STING technique; and **4**, superior tunnel. *Source:* Kuipers S, van der Horst EH, Verbeke JI, et al. Prevesical calcification and hydronephrosis in a girl treated for vesicoureteral re-flux. *Glob Pediatr Health* 2016;3:2333794X16652272. Reproduced with permission of Elsevier.

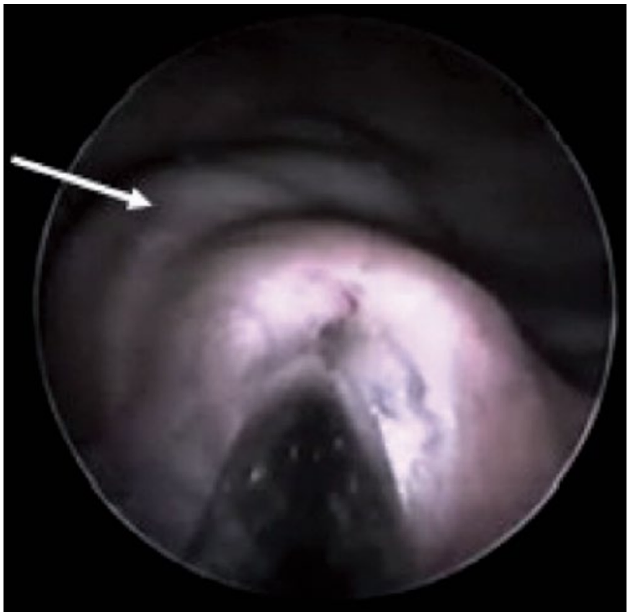


**Figure 155.2** "Mountain range" mound (arrow) produced by the double HIT injection technique. *Source:* Kuipers S, van der Horst EH, Verbeke JI, et al. Prevesical calcification and hydronephrosis in a girl treated for vesicoureteral re-flux. *Glob Pediatr Health* 2016;3:2333794X16652272. Reproduced with permission of Elsevier.

The double HIT method has not only been employed for primary VUR (90% cure), but also for repeat endoscopic injections (90%), VUR associated with paraureteral diverticula (81%), complex cases such as post reimplantation (88%), neurogenic bladders (78%), duplication anomalies (80%), and in adults (88%). Several other studies have supported the use of Deflux in the setting of anatomic variants such as duplex systems as well [17–20].

The experience with the double HIT technique was also important in identifying the need for sometimes large volumes of injectable material for cure. There is considered to be a 20% volume loss over time when using Deflux, so as a matter of technique it is important to use an adequate amount of material so that cure is ensured. Limiting the amount injected in an effort to limit costs often results in increased expenses later as failure rates are higher [21]. Also, failure is usually due to caudal migration of the bleb, so more proximal injection using the double HIT method, as well as the larger volumes, has improved results [17].

The use of hydrodistention in these procedures also led to studies correlating the degree of ureteral distention with reflux. A grading system has been developed for ureteral dilation, which correlates well with grade of reflux. The hydrodistention grading system defines grades of reflux as: H0, no hydrodistention; H1, ureteral orifice open but tunnel not evident; H2, tunnel seen only, and H3, extravesical ureter visualized (Figure 155.3). In studies, VUR and dynamic hydrodistention classification grades correlate significantly ($P < 0.001$), and provide a reliable method of evaluating the presence or absence of VUR. These findings, combined with the studies demonstrating a lack of correlation of intraoperative cystogram and late cure, have allowed surgeons to do away with the postoperative cystogram (at the time of the injection), as lack of hydrodistention can confirm cure [15, 22].

## Follow-up

Follow-up for STING procedures varies. As mentioned, it has been determined that a cystogram is not needed at the time of injection, as ureters that do not hydrodistend are considered cured. Cystography may, however, pick up contralateral unrecognized reflux, which may then be easily treated [23].

Traditionally, patients are observed for approximately three months on prophylactic antibiotics and then studied with renal bladder ultrasound and voiding cystourethrogram (VCUG) following injection therapy. In cases where the expected cure rate is high, the VCUG may be avoided and children do well. There has been some research into the appearance of injected bleb on postoperative ultrasound and cure rate. One study has demonstrated that while there is no difference in the volume of the visible Deflux on postoperative ultrasound in cures and failures, when a greater than expected volume of Deflux is retained (termed mega-implant), the cure rate is much higher than in cases with a less than expected volume remaining (micro-implants) or no visible implant [21]. The same study demonstrated durable implant size over 36 months postoperatively in these patients [21].

The bleb at the site of Deflux injection can persist long term, and this raises issues for future imaging and misinterpretations of the mass. Studies have demonstrated that the blebs can appear as calcifications on computed tomography (CT) scans and be mistaken for ureteral stones, and appear bright on T2-weighted images, but do not enhance on T1 scans [24–26]. It is important to note the history of intervention in these patients, so unnecessary medical interventions are not performed for these findings. The pathologic description of Deflux material has also been well described, so any tissue sent for pathologic evaluation in cases of reimplantation after injection therapy should be readily identifiable [27].

Long-term data regarding Deflux are now available, with some studies demonstrating durable results, while others show declining success rates over the long term, and yet others demonstrating the risk of possible late obstruction. However, it is important to keep in mind that in most cases the patients with late failures had risk factors, such as dysfunctional elimination, which may

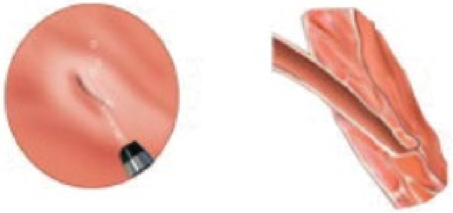
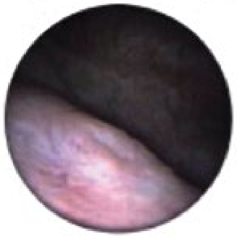
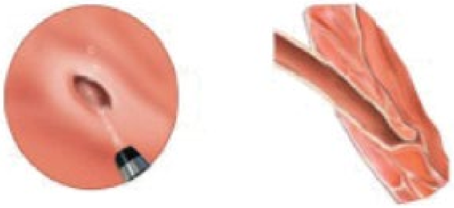
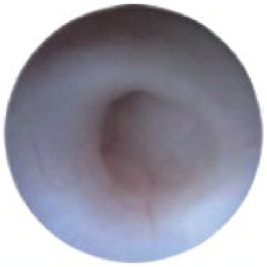
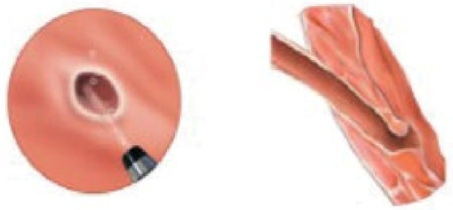
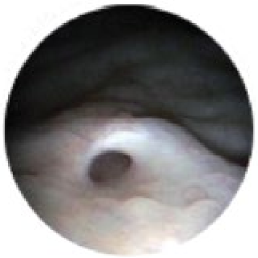
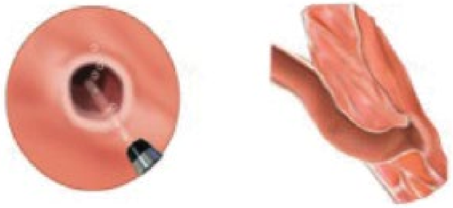
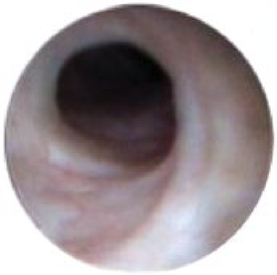
| Hydrodistention grade | Description | Cystoscopic appearance | Example |
|---|---|---|---|
| H0 | No orifice distention evident |  |  |
| H1 | Orifice opens<br>Intramural tunnel not evident |  |  |
| H2 | Orifice opens<br>Intramural tunnel evident<br>Extramural ureter not evident |  |  |
| H3 | Orifice opens<br>Extramural ureter evident or ureter can accept cystoscope |  |  |

**Figure 155.3** Hydrodistention grading system developed by Kirsch et al. *Source:* Williams MA, Giel DW, Colleen Hastings M. Endoscopic Deflux injection for pediatric transplant reflux: a feasible alternative to open ureter-al reimplant. *J Pediatr Urol* 2008;4:341–344. Reproduced with permission of Elsevier.

have contributed to the poor results. It seems prudent to follow these children closely for several years to rule out treatment failures or other complications such as obstruction [28–30].

## Role of the STING procedure

Typical of many areas in pediatric urology, the treatment of VUR is highly controversial. The opinions on STING therapy for reflux vary from religious opposition to overzealous support. The exact role for endoscopic reflux therapy remains to be defined, but it is clear that it is gaining a more prominent position in the armamentarium of the surgeon treating various forms of reflux. Studies have expanded its role from simple refluxing ureters to more complex systems, such as duplicated ureters, ureters associated with diverticula, transplant ureters, and even ureters in neurogenic bladders. The appeal of STING therapy to many is that the procedure poses minimal morbidity with the chance of great reward if a cure results. If cure is not achieved, the grade of reflux is often downgraded to a less clinically significant level, and repeat injections may also be performed. Once STING has failed twice, all experts agree that any surgical intervention needed should then proceed to open reimplantation, and surgery following even repeat injection procedures is only slightly more difficult than virgin surgery. In summary, this procedure may offer a simple cure, while not burning any bridges [31].

There is a concern that Deflux injection, being a relatively simple procedure, will be overutilized to the detriment of patients. As with any technology or procedure, the clinician's judgment is crucial to the success of the methodology chosen, and judicious use of any technique is a must [32]. Some have attempted to push the envelope with mixed results. Deflux has been used in combination with botulinum toxin A injection as a means of total endoscopic management of a noncompliant neurogenic bladder. These combined therapies were able to decrease bladder pressure and the rate of urinary tract infections (UTIs), but is not a likely long-term viable solution to a high pressure neurogenic bladder with secondary reflux [33].

The detractors of STING therapy point to studies expressing low cure rates per ureter, extolling that it is in the best interests of the patient to provide a one-time, highly successful surgery. The proponents rely on the support of studies stating higher cure rates, and the "less is more" philosophy of surgical intervention. It seems that these differences are often philosophical, and depend on the personality, experiences, and training of the surgeon, and all the studies published have done little to sway adherents from either camp to the other side.

A unique benefit of the STING procedure is that it can easily be paired with a positionally instilled cystogram (PIC) as a simple procedure to diagnose and treat VUR. Studies have demonstrated that children with recurrent febrile UTIs with negative VCUG studies may have occult reflux (as VCUGs have a known false-negative rate), and these cases can be diagnosed and treated with PICs followed by Deflux injections. The PIC is performed by using cystoscopy with contrast running as the irrigation fluid and pointing the beak of the cystoscope at the ureteral orifice in a partially filled bladder. Fluoroscopic images of reflux are considered proof positive of occult reflux, and treatment with STING therapy is almost always the next option. Considering the relation of ureteral hydrodistention and reflux grade, it may be debatable as to whether contrast instillation is necessary in an obviously distended system (grade 3), but documentation of the pathology is always helpful in justifying the therapy [34, 35].

Another interesting area of research into the uses of the STING procedure for reflux therapy has been the push by proponents of the technique to use it as a first-line therapy for reflux. These authors point to the low patient compliance with prophylactic antibiotics, claiming that first-line injection therapy would be a more inexpensive, simpler option for families, with little morbidity. For example, Hensle et al. noted that only 17% of patients with VUR on prophylaxis are compliant and that 58% had a diagnosis of UTI within 1 year of treatment [36]. Elder et al. demonstrated that treatment with Deflux in children with reflux resulted in fewer UTIs than management with prophylactic antibiotics, and concluded that Deflux should be considered first-line therapy [37]. Koyle and Caldamone made a case that misuse of antibiotics has spread resistance, and thus should be replaced by first-line Deflux therapy in appropriate patients [38].

There has historically been a general lack of controlled studies regarding prophylaxis for vesicoureteral reflux, although the RIVUR study (Randomized Intervention in Children with Vesicoureteral Reflux) demonstrated that antimicrobial prophylaxis was associated with a reduced risk of recurrent UTIs [39]. In general, compliance is low with antibiotic prophylaxis, but that does not mean that the therapy is ineffective or not worthwhile. When given appropriately, prophylaxis does prevent infections, and does not have a large impact on microbial resistance [40]. All parents should have all options discussed with them on visits with their child's pediatric urologists (from open surgery to prophylaxis), and prophylaxis remains standard first-line therapy. New innovations, including injection therapy, should be closely studied and offered in an unbiased fashion.

With the availability of minimally invasive techniques, such as extravesical ureteral reimplantation, mini-ureteroneocystostomy, and extravesical and intravesical laparoscopic and robot-assisted procedures, there has been a push by some surgeons to prove that traditional ureteral reimplantation can be performed with new techniques and technology in an outpatient setting, with comparable morbidity and higher cure rates than with endoscopic procedures. Some studies have also demonstrated decreased total cost with these procedures. It is clear that as minimally invasive surgical technology advances, there will be pressure on the endoscopic options of therapy to maintain high cure rates to compete with these increasingly inexpensive and benign procedures [41–43].

The choice of therapy for VUR remains controversial. The main goal of preventing renal scars and infection in these young children must be kept in mind, and we are fortunate to have a multitude of excellent options to choose from to achieve this goal. In the hands of a trained pediatric urologist, with close follow-up of their patients, all three options of antibiotic prophylaxis, STING therapy, and open surgery can be used wisely in an effort to maintain urologic health.

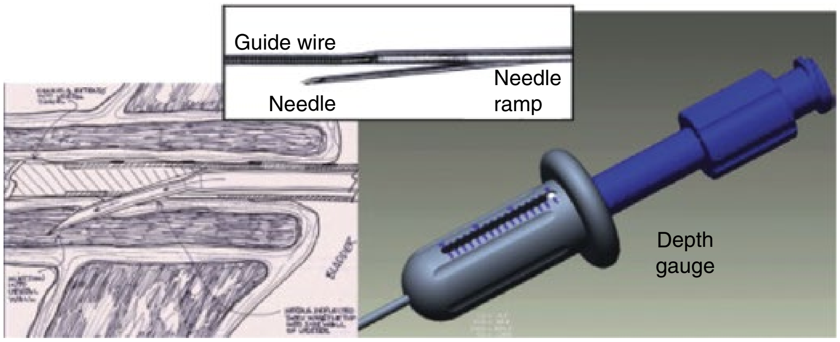


**Figure 155.4** Cook Injekt VUR Injection needle. The device has a filiform tip with markings to help physicians achieve proper needle position and depth relative to the ureteral orifice for precise placement of the bulking agent. *Source:* Kuipers S, van der Horst EH, Verbeke JI, et al. Prevesical calcification and hydronephrosis in a girl treated for vesicoureteral re-flux. *Glob Pediatr Health* 2016;3:2333794X16652272. Reproduced with permission of Elsevier.

## Dysfunctional elimination

It is our opinion that as the identification and treatment of dysfunctional elimination improves, the rates of resolution of refluxing ureters will also improve (as well as the success rates of STING procedures), obviating the need for open surgery in most children [40]. In fact, the Atlanta group currently reserves open surgery only for patients who fail injection therapy (two injections), have high-grade reflux or megaureters (that require tapering), and if this is the preference of the parents [17].

Results have been published showing that the treatment of dysfunctional elimination does not affect the success of endoscopic therapy of reflux, but the definition of dysfunctional voiding and the documentation of its successful treatment are not always well documented or proven [17, 44, 45]. Our center has unpublished data showing that the incidence and severity of dysfunctional elimination is widely underestimated, and that a focus on biofeedback and constipation therapy may greatly reduce the incidence and severity of reflux in children.

## Conclusions

The introduction of Deflux into the realm of endoscopic reflux therapy has provided surgeons with an almost ideal bulking agent, and allowed for the expansion of the STING procedure. The techniques have improved, as well as the results, and endoscopic therapy has become a reasonable option for almost all children with reflux, and in some circumstances a good first option. As the treatment of dysfunctional elimination becomes more codified and widespread, the need for open surgery will likely wane, while the numbers of endoscopic cases will continue to expand. The growing experience among practicing urologists, standardization of techniques, and introduction of new tools that help the consistency and accuracy of needle placement (Figure 155.4) will help ensure reproducibly high success rates for endoscopic therapy in the future.

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# 156

# Minimally Invasive Therapy for Bladder Pain Syndrome (Interstitial Cystitis)

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## Introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic pain syndrome affecting both men and women and characterized by irritative voiding symptoms (urinary frequency, urgency, dysuria, nocturia), and pelvic organ pain exacerbated by bladder filling [1]. The clinical diagnosis of BPS is challenging, as patients may present with a myriad of symptoms resembling other urologic, gynecologic, or gastrointestinal conditions. As such, BPS is a diagnosis of exclusion that requires a multimodal treatment approach. This chapter will review IC/BPS with a focus on minimally invasive treatment options.

## Definition/nomenclature

IC/BPS is a clinical syndrome where patients report "an unpleasant sensation" (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes [2]. Once considered a disease related only to the bladder, it is becoming increasingly evident that this syndrome is associated with other pain syndromes and medical conditions affecting multiple organ systems [3].

Patients can be categorized into two separate subtypes of IC/BPS, and management can vary depending upon the clinical findings. "Classical" IC/BPS is characterized by the presence of erythematous patches in the bladder mucosa known as Hunner's lesions, which were described nearly 100 years ago by Guy Hunner [4] (Figure 156.1). In addition to erythematous mucosa, Hunner's lesions contain a central scar and can be associated with glomerulations that may bleed as the bladder empties [5]. Only cystoscopy can accurately determine if inflammatory disease is present, and only 30% of IC/BPS patients demonstrate abnormalities on urinalysis that would prompt cystoscopic evaluation [6]. Thus the true incidence of Hunner's lesions in IC/BPS patients is unknown and incidence ranges between 5% and 50% [7]. Alternatively, patients with "nonclassical" disease are characterized by a normal cystoscopic examination in the face of typical symptoms and normal cystoscopic findings.

## Epidemiology

Considering the difficulty of establishing an accepted definition, collected data have been difficult to interpret, leading to variations in the reported prevalence internationally. In a large study from Finland, the estimated prevalence in women was 230 per 100 000, and a study of urban females in Vienna, Austria gave an overall estimate of 306 per 100 000 women, with the highest prevalence (464 per 100 000) among middle-aged females (40–59 years old) [8, 9]. Similarly, a population-based study in the United States found the prevalence to be 197 per 100 000 women and 41 per 100 000 men [10]. In a recent population-based prevalence study, the Rand Corporation contacted a random sample of 146 231 homes via telephone. Using a case definition with high specificity for IC/BPS, nearly 3% met criteria for IC/BPS. According to the study, approximately 3.3 million women in the United States met criteria for IC/BPS [11]. Screening and data collection based on symptoms rather than diagnosis show the prevalence to be much higher. A primary care office survey screening patients for symptoms of IC/BPS estimated the prevalence to be 12 600 per 100 000 women [12]. Studies by Parsons et al. suggest that IC is highly prevalent in young women

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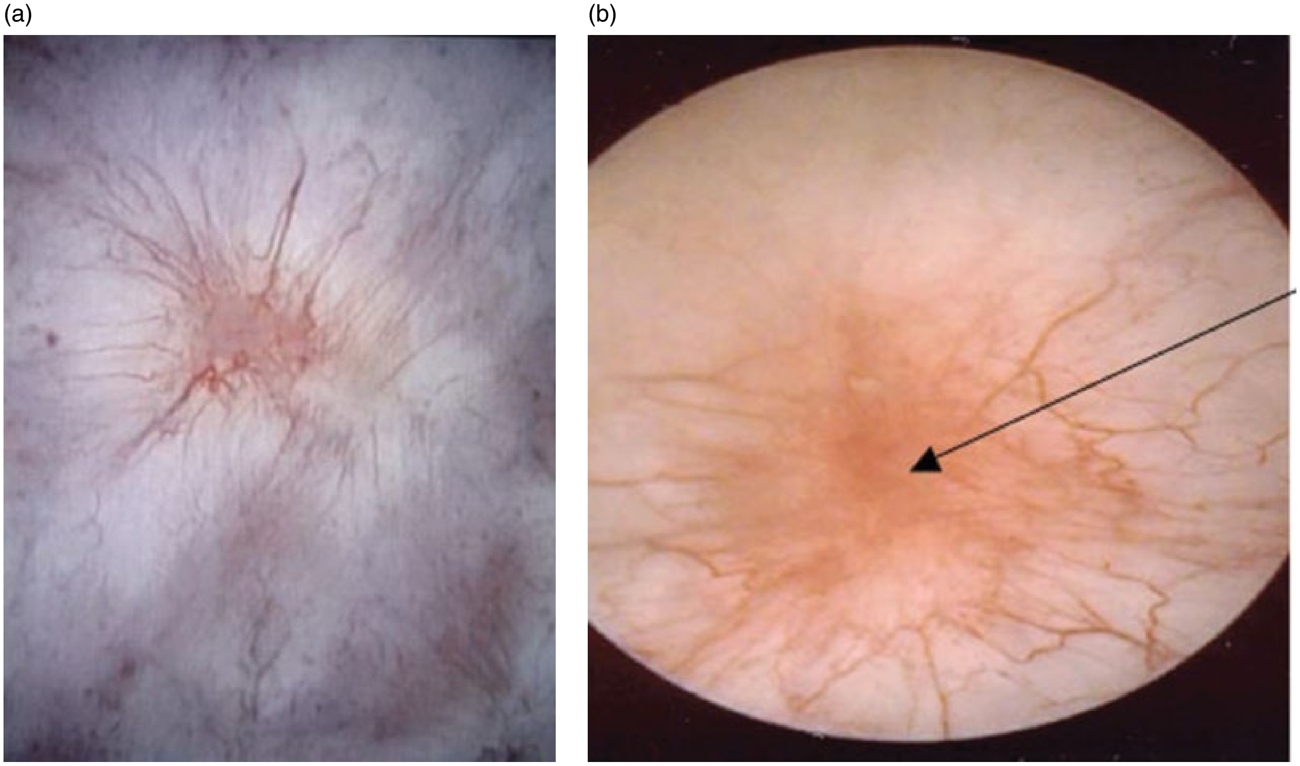

**Figure 156.1** Hunner's lesions: erythematous patches typically found in extratrigonal position in interstitial cystitis/bladder pain syndrome (IC/BPS) patients (a), the arrow indicates the central scar often seen in these lesions (b).

and may affect as many as one in four [13, 14]. The estimated female-to-male ratio is estimated to be 5:1 or higher [9, 15]. Furthermore, men tend to present at an older age and based on prior reports have a higher incidence of Hunner's lesions [16, 17].

Most patients diagnosed with IC/BPS are adults, but the condition has been reported in children and young adults [18, 19]. A history of pediatric voiding dysfunction, such as dysfunctional voiding or enuresis, is reported to be 10 times higher in IC/BPS patients versus the general population.

IC/BPS is a chronic condition and unfortunately has a profoundly negative impact on patient's quality of life [15]. In addition to affecting overall mental health and sexual function, IC/BPS often coexists with depression, chronic pain syndromes (fibromyalgia, temporomandibular disorder, and chronic fatigue syndromes), and irritable bowel syndrome [15, 20–22].

## Etiology

Numerous explanations and etiologies for IC/BPS have been proposed, suggesting that the disease is the manifestation of multifactorial causes working through numerous pathways. Existing data also supports the theory that IC/BPS may be a systemic disorder, with bladder symptoms and pelvic pain being the primary manifestation [23, 24]. Evidence exists for a genetic component to IC/BPS. Adult female first-degree relatives of patients with IC/BPS are reported to have a prevalence 17 times that found in the general population [25]. In a study including >25 000 twins born between 1959 and 1985, less than one-third of female twins had genetic factors playing into susceptibility of BPS [26]. In addition, there is a greater concordance of IC/BPS among monozygotic than dizygotic twin pairs, strengthening the evidence for genetic susceptibility to IC/BPS [27].

An infectious etiology for IC/BPS has been proposed to explain the initial insult in the pathogenesis of IC/BPS. Various pathogens, including bacteria, viruses, and fungal organisms, have been investigated. However, highly sensitive and specific molecular methods for identifying infectious agents by detection of DNA or RNA were unable to demonstrate any particular microorganism responsible for the development of IC/BPS. Another infection-related theory is that pathogens subvert host defense mechanisms, leading to frequent clinical or subclinical infections. These repeated infections subsequently activate neuroimmune pathways which lead to the development of IC/BPS symptoms [28, 29]. At this time there is no conclusive evidence to support an

**Table 156.1** Potential mechanisms involved in the pathogenesis of interstitial cystitis.

| Mechanism | Pathophysiologic effect |
|---|---|
| Bladder lining abnormalities | Damage to the bladder protective glycosaminoglycan layer |
| Abnormalities of descending inhibitory pain pathways | Dysfunction in brain centers (or the pathways from these centers) that normally downregulate pain signaling in the spinal cord |
| Neurogenic inflammation | Increased bladder neuropeptide containing nerve endings juxtaposed to increased and activated mast cells, increased urine interleukin (IL) 6 |
| Neurohormonal dysregulation | Dysfunction in the hypothalamic–pituitary–adrenal axis, including higher bladder expression of corticotropin-releasing hormone (CRH) |
| Decreased urothelial repair | Increased secretion of antiproliferative factor (APF) shown to inhibit urothelial cell growth *in vitro* |
| Comorbid conditions | Mechanism unknown; increased rate of psychiatric comorbid conditions, including depression, anxiety, posttraumatic stress, and somatization, as well as allergies, chronic fatigue syndrome, endometriosis, fibromyalgia, irritable bowel syndrome, and inflammatory bowel disease [16, 33] |

Adapted from Theoharides et al. [23].

infectious etiology to IC/BPS, however active infection must be ruled out to make a diagnosis of this condition.

Several other nonmutually exclusive theories that may explain the pathogenesis of IC/BPS have been described in detail and are summarized in Table 156.1. Briefly, immune/neuroimmune mechanisms may have an important role in pathogenesis, including excessive release of neurotransmitters, mast cell-mediated inflammation and morphologic changes in the nerves innervating the bladder. Currently there is no clear evidence of IC/BPS being an autoimmune disease, or being the main etiology for the disease. However, following the recognition of mast cells within the bladder wall of patients with IC/BPS, numerous studies have been published suggesting their role in pathogenesis. Mast cells play a primary role in allergic reactions and acute inflammatory response by recruiting leukocytes, which in turn activate mast cell degranulation [30]. These cells are also involved in angiogenesis, wound healing, bone remodeling, atherosclerosis, and reaction to neoplasm. Multiple components including endocrine, immune, and neurologic pathways are thought to play a role in the pathogenesis of IC/BPS. Activated mast cells play a central role in the activation and signaling of these pathways, linking these cells to the disease process [31]. Although the presence of mast cells and their production of histamine (which causes pain and hyperemia) may provide a reasonable explanation for the disease process, mast cells can be found in the bladder wall of patients without IC/BPS as well as patients with overactive bladder [32].

The bladder epithelium is lined by bladder surface mucin, a continuous layer of proteoglycans and glycosaminoglycans (GAGs). This layer is thought to provide both a permeability barrier to noxious solutes in the urine and a host defense against bacterial adherence. Injury or destruction of the protective layer leads to increased epithelial permeability and susceptibility to infection. Increased mucosal permeability is nonspecific and can be a consequence of bladder inflammation, injury or chemical cystitis, and it may be part of the normal process of aging. Parsons and Hurst hypothesized the concept that IC/BPS in a subset of patients is the result of a defect in the epithelial permeability barrier of the bladder surface GAG [33]. Multiple investigators have demonstrated a link between increased mucosal permeability and GAG layer damage, but whether this represents a primary cause of IC/BPS or merely reflects a secondary event is unclear [33–36]. Furthermore, urothelial dysfunction can also be affected by altered cell adhesions and tight junction proteins [37]. Arguments against the "GAG theory" state that injury to the GAG layer with various invasive treatments including bladder fulguration, bladder hydrodistention, or the intravesical administration of clorpactin or the organic solvent dimethyl sulfoxide (DMSO) may improve bladder symptoms. On the other hand, treatments aimed at "restoring" the GAG layer have a role in the treatment of IC/BPS and will be discussed later in the chapter.

Inflammation, especially if repeated or chronic, can alter tissue innervation, central pain processing mechanisms and tissue response. Neuropeptides present in the spinal cord have an important role in the mediation of nociceptive input, which under pathologic conditions such as inflammation can be altered, leading to functional consequences. Activation of pain fibers can trigger neurogenic inflammation through release of neuropeptides and subsequently increase vascular permeability. Furthermore, mast cell degranulation can be stimulated by neuropeptide mediators, exacerbating inflammation, injury, and increased epithelial permeability. Numerous studies also indicated increased sympathetic activity in patients with IC/BPS [38–40].

Investigation by Keay et al. into the role of certain cytotoxins involved in epithelial cell damage seen in IC/BPS led to the discovery of antiproliferative factor (APF) [41]. In subsequent studies, the presence of this factor in urine samples was found to be a sensitive and specific biomarker for IC/BPS [42]. The presence of APF significantly decreases levels of heparin-binding epidermal growth factor-like growth factor (HB-EGF), and at the same time upregulates the levels of epidermal growth factor (EGF), which leads to inhibition of primary urothelial cell proliferation [43]. Urine levels of APF, HB-EGF, and EGF reliably distinguish patients with IC/BPS from controls [42]. The presence of APF can also be used to distinguish between men with IC/BPS and those with chronic pelvic pain syndrome/chronic prostatitis [44]. Currently these tests are not commercially available.

## Signs/symptoms and diagnosis

IC/BPS is a clinical diagnosis of exclusion based upon chronic (more than six weeks duration) unpleasant symptoms including pain, pressure, and discomfort perceived to be related to the bladder and associated with lower urinary tract symptoms [2]. The pain usually varies with the degree of bladder distention; hence, urgency and frequency of urination are usually present in an attempt to minimize discomfort [45]. Patients may also complain of pain or pressure throughout other pelvic structures, including the vagina, rectum, and vulva. Urinary tract infection and other potential treatable causes must be ruled out and treated if clinically warranted. Median age of presentation is 40–45 years. According to reports from the interstitial cystitis database, the most common baseline pain sites are lower abdominal pain (80%), urethral (74%), and lower back (65%). Most patients describe intermittent pain of moderate intensity and there have been reports of links between pain sites, urinary symptoms, and worse quality of life [46, 47]. More specifically, suprapubic pain exacerbated by bladder filling has been reported to be a symptom shared by most men and women with IC/BPS [47]. According to a recent study from the MAPP research network the most bothersome single symptom in a cohort of 424 patients with IC/BPS was suprapubic/bladder pain. The women in this cohort did have significantly more bladder-focused symptoms (58%) compared with men (34%) [48]. According to recent prevalence data, between 1.9% and 4.2% of the male population in the United States are estimated to have IC/BPS [49]. There is significant overlap in the symptomatology of IC/BPS and chronic bacterial prostatitis, including suprapubic pain and perineal pain. Sexual dysfunction is also an associated finding, including erectile dysfunction and painful ejaculation.

There is no evidence to suggest that IC/BPS poses a risk of future bladder malignancy; however, it is important to consider underlying malignancy or carcinoma *in situ* in patients over 40 years of age with a smoking history. Other rare conditions, such as eosinophilic cystitis, malacoplakia, scleroderma, schistosomiasis, and detrusor endometriosis, must also be considered. In women, gynecologic problems including endometriosis, pelvic congestion syndrome, and salpingitis can mimic the IC/BPS symptom complex and careful evaluation to rule out any correctable condition should be undertaken. Patients with IC/BPS may also report urinary urgency when queried about whether they normally feel a sudden desire to void. Although these patients may also have simultaneous voiding dysfunction, the urgency felt by IC/BPS is considered to be secondary to pain rather than an impending loss of urinary control [50]. A large-scale survey of individuals diagnosed with IC/BPS showed an unexplained association with other chronic disease and pain syndromes. Allergies, irritable bowel syndrome, and sensitive skin were the most common associated conditions [51]. Furthermore, pain and urgency exacerbations have been documented to occur in small observational reports, especially in periods of high stress [52].

For patients undergoing an initial evaluation, a thorough medical history and evaluation of pain and voiding complaints should be obtained. Pertinent medical history including a description of allergies, history of gastrointestinal, gynecologic, autoimmune, and musculoskeletal disease should be addressed. Symptoms can be evaluated using several validated questionnaires, all of which are designed to assess severity of symptoms. Symptoms scales available include the O'Leary-Sant Symptom and Problem Index, the University of Wisconsin Symptom Instrument, the Global Response Assessment, and the Pelvic Pain and Urgency/Frequency Scale. Although these questionnaires are useful to investigate the severity of symptoms, they do not possess strong diagnostic utility [53]. In addition to characterizing the patient's lower urinary tract symptoms baseline pain symptoms, a physical exam should be performed should be performed including an evaluation of the pelvic floor. Although a presumptive diagnosis can be made based on history and physical examination, further evaluation is necessary to rule out other treatable causes. The 2011 American Urological Association guideline for diagnosis and treatment of IC/BPS provides a comprehensive diagnostic algorithm [1] (Figure 156.2). In addition to indicated laboratory tests, cystoscopy may be performed, however it can be omitted in uncomplicated cases. When indicated, cystoscopy may be used to identify patients with Hunner's lesions, or ulcerative mucosal lesions seen on the bladder urothelium. Biopsies of this area must be performed, as these lesions may resemble carcinoma *in situ* of the bladder. Glomerulations are an additional cystoscopic finding classically described during bladder hydrodistention. Glomerulations are described as submucosal petechiae that have the tendency to bleed once the bladder is emptied after hydrodistention.

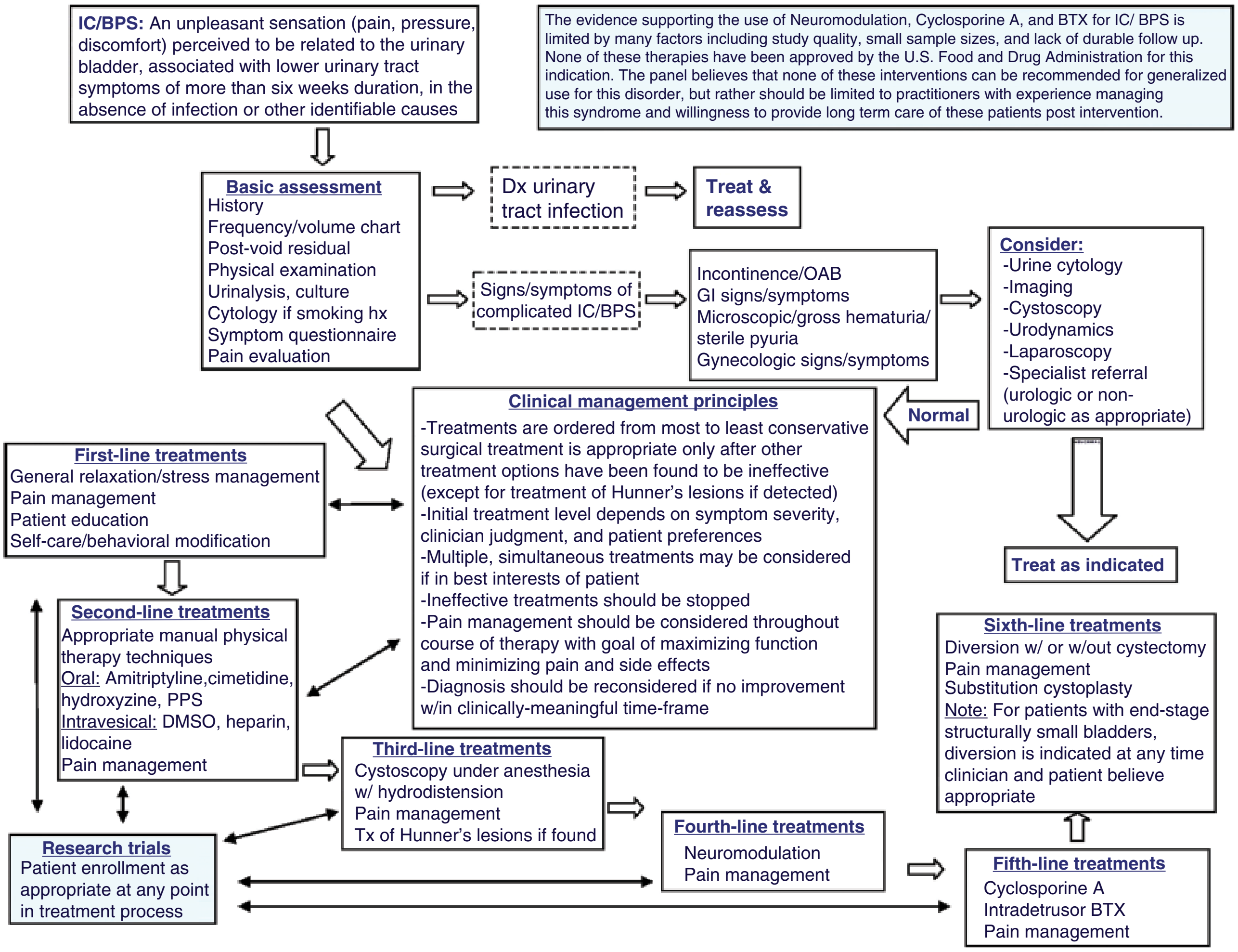
IC/BPS: An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes
The evidence supporting the use of Neuromodulation, Cyclosporine A, and BTX for IC/ BPS is limited by many factors including study quality, small sample sizes, and lack of durable follow up. None of these therapies have been approved by the U.S. Food and Drug Administration for this indication. The panel believes that none of these interventions can be recommended for generalized use for this disorder, but rather should be limited to practitioners with experience managing this syndrome and willingness to provide long term care of these patients post intervention.
Basic assessment
History
Frequency/volume chart
Post-void residual
Physical examination
Urinalysis, culture
Cytology if smoking hx
Symptom questionnaire
Pain evaluation
Dx urinary tract infection
Treat & reassess
Signs/symptoms of complicated IC/BPS
Incontinence/OAB
GI signs/symptoms
Microscopic/gross hematuria/ sterile pyuria
Gynecologic signs/symptoms
Consider:
-Urine cytology
-Imaging
-Cystoscopy
-Urodynamics
-Laparoscopy
-Specialist referral (urologic or non-urologic as appropriate)
Normal
Treat as indicated
Clinical management principles
-Treatments are ordered from most to least conservative surgical treatment is appropriate only after other treatment options have been found to be ineffective (except for treatment of Hunner's lesions if detected)
-Initial treatment level depends on symptom severity, clinician judgment, and patient preferences
-Multiple, simultaneous treatments may be considered if in best interests of patient
-Ineffective treatments should be stopped
-Pain management should be considered throughout course of therapy with goal of maximizing function and minimizing pain and side effects
-Diagnosis should be reconsidered if no improvement w/in clinically-meaningful time-frame
First-line treatments
General relaxation/stress management
Pain management
Patient education
Self-care/behavioral modification
Second-line treatments
Appropriate manual physical therapy techniques
Oral: Amitriptyline,cimetidine, hydroxyzine, PPS
Intravesical: DMSO, heparin, lidocaine
Pain management
Third-line treatments
Cystoscopy under anesthesia w/ hydrodistension
Pain management
Tx of Hunner's lesions if found
Fourth-line treatments
Neuromodulation
Pain management
Fifth-line treatments
Cyclosporine A
Intradetrusor BTX
Pain management
Sixth-line treatments
Diversion w/ or w/out cystectomy
Pain management
Substitution cystoplasty
Note: For patients with end-stage structurally small bladders, diversion is indicated at any time clinician and patient believe appropriate
Research trials
Patient enrollment as appropriate at any point in treatment process

**Figure 156.2** Algorithm for the treatment and diagnosis of interstitial cystitis/bladder pain syndrome (IC/BPS) of the American Urological Association. *Source:* Hanno PM, Burks DA, Clemens JQ et al. AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. *J Urol* 2011;185(6):2162–2170. Reproduced with permission of Elsevier.

Hydrodistention is not recommended as a diagnostic or therapeutic procedure because of its adverse effects and low diagnostic yield (low sensitivity and specificity).

Intravesical administration of concentrated potassium chloride, known as the potassium sensitivity test, is still used by some physicians to distinguish the source of pain in women with chronic pelvic pain and possible IC/BPS. The test can be easily performed in the office setting, but may provoke pain and has a low diagnostic value (75% sensitivity) [54]. Another office-based test is the "anesthetic challenge." It is especially useful in patients presenting with acute pelvic pain exacerbations and involves installation of an intravesical anesthetic [55]. Although there is no documentation about sensitivity and specificity, this test is reasonable and can yield useful information about likelihood of bladder-based pain, especially in patients who have a positive response.

## Management

IC/BPS is a complex disease that poses a therapeutic challenge to practioners in various specialties. Even when urinary symptoms are addressed, many patients experience debilitating pelvic pain that is difficult to treat. Recognizing that the etiology of IC/BPS is likely multifactorial, patients are now treated with multimodal and multispecialty approaches to address the different pain components. Lifestyle modifications, pharmacologic therapy, physical therapy, and surgical treatment options are available and often used in sequence or combination to offer patients the best symptom control possible [56].

Patient counseling and education are paramount in the initial treatment of IC/BPS. Patients should be reassured that their symptoms, although bothersome, are not life threatening and that multiple therapies are available.

Behavioral therapy should be introduced to the patient initially as first-line therapy. Pelvic floor retraining, diary keeping, and controlled fluid intake can be utilized in patients with IC/BPS, especially in those with predominant frequency. Expert opinion suggests that maintaining a normal lifestyle and increasing the quality of life for patients with IC/BPS can be achieved with stress reduction, meditation, exercise, massage, and warm tub baths [57]. Numerous complementary and alternative medical therapies have been used in patients with IC/BPS [58]. One randomized controlled study used guided imagery created specifically for IC/BPS patients and compared their pain and urinary symptoms to controls. More than 45% of the treatment group responded with marked improvement on the Global Response Assessment (GRA) and also noted decreased pain and urinary urgency [59]. Acupuncture has been used in patients with IC/BPS and other chronic pain syndromes. Limited evidence exists that it is more effective than placebo and overall results with acupuncture have failed to show long-term efficacy [60, 61].

Dietary modification is another method that can be used to ameliorate symptoms of IC/BPS. Many patients report symptom flares coinciding with intake of certain foods and drinks. Spicy foods and beverages such as alcohol, coffee, and soda are often credited with the onset of symptoms. A recent questionnaire-based study suggested that approximately 90% of IC/BPS patients have food sensitivities [62, 63].

Pelvic floor physical therapy is also a recognized nonpharmacologic treatment for IC/BPS. Physiotherapists guide therapy sessions by applying manual pressure to stretch and compress bundles of muscle fiber, as well as engaging patients in relaxation exercises. When conducted by experienced physiotherapists, pelvic floor myofascial release can achieve up to 70% improvement in symptoms for patients with IC/BPS [64].

Pharmacologic therapy with oral agents often begins with amitriptyline, pentosanpolysulfate sodium, cimetidine, and hydroxyzine [65]. Amitriptyline is a tricyclic antidepressant that has been shown to ameliorate symptoms of IC/BPS when administered in small doses. It has four pharmacologic actions useful for the treatment of IC/BPS: (i) it blocks active transport at presynaptic nerve endings, affecting reuptake of serotonin and norepinephrine, (ii) it has central and peripheral anticholinergic actions; (iii) it blocks H1 receptors and can therefore stabilize mast cells, (iv) it is a sedative. The success rate of amitriptyline is 40–60%, based on small nonrandomized studies. In one large multicenter randomized controlled trial, Foster et al. showed that amitriptyline in conjunction with behavioral modification was not equivalent to placebo when given to amitriptyline-naive patients with IC/BPS. In a subgroup analysis it was demonstrated that patients who achieved and tolerated 50 mg daily had improvements in symptoms [66]. Dose-limiting side-effects include weight gain, constipation, urinary retention, dry mouth, and palpitations.

Pentosanpolysulfate (Elmiron™) is the only US Food and Drug Administration (FDA)-approved agent for the treatment of IC/BPS. The drug is a synthetic sulfated polysaccharide similar to the heparan sulfate analog. Heparan sulfate is one of the GAGs normally found coating the bladder mucosa [67]. Pentosanpolysulfate is thought to be effective in replenishing the defective GAG layer and it has been shown to be a potent inhibitor of allergic and nonimmune mast cell stimulation [67, 68]. Sant et al. conducted a clinical trial to evaluate the safety and efficacy of pentosanpolysulfate. No clinical benefit was observed when pentosanpolysulfate was compared to placebo. In regards to adverse effects, most were noted to be minor and included reversible alopecia, diarrhea, liver enzyme abnormalities, and skin rash. Although this study demonstrated the drug's safety, it was underpowered to make conclusions about efficacy [69]. Parsons et al. performed a randomized controlled trial and found that 32% of the patients treated with pentosanpolysulfate reported significant improvement in comparison to placebo [70]. pentosanpolysulfate was also found to be beneficial in a meta-analysis by Hwang et al., which showed the drug to be more efficacious than placebo in the treatment of pain, urgency, and frequency associated with IC/BPS [71]. The duration of therapy appears to be more important than the dosing. Nickel et al. demonstrated an overall response rate of 50% in dosages ranging between 300 mg and 900 mg at 32 weeks; however, the recommended dosing is 100 mg three times daily for 12 months [72].

Histamine H1 (hydroxyzine) and H2 (cimetidine) antagonists have shown modest therapeutic benefit in the treatment of IC/BPS. H1 receptor blockers are used for their ability to inhibit neuronal activation of mast cells and suppress degranulation. Evidence for the efficacy of hydroxyzine is limited and the maximum benefit demonstrated was a 40% reduction in symptoms [73]. Other trials have found no clinical benefit in symptom improvement [69]. Cimetidine's mechanism of action in IC/BPS is unclear and promising results were found in approximately 66% of patients in one early study [74]. However, follow-up studies showing improvement in suprapubic pain and voiding symptoms were limited by small sample size and lack of histologic evidence to note qualitative change [75].

## Minimally invasive procedures for IC/BPS

### Intravesical agents

The installation of intravesical agents provides an alternative or adjunct to oral therapies as well as a nonsurgical option for patients refractory to conservative treatments. Several agents are available including DMSO, pentosanpolysulfate, chondroitin sulfate, hyaluronan, heparin, and anesthetic agents (lidocaine and bupivacaine). Although the use of intravesical agents is widespread, evidence supporting their efficacy is limited and largely composed of uncontrolled trials [76].

DMSO, a lignin derivative, is the only intravesical agent with FDA approval for the treatment of IC/BPS. DMSO acts as an anti-inflammatory, analgesic, and muscle relaxant [77, 78]. As with many intravesical agents, DMSO is administered weekly for six weeks as a single agent, or as a "cocktail" of several instravesical medications. Reported response rates range from 50% to 90%; however, patients may experience an acute flare-up of pain and irritative voiding symptoms with the initiation of treatment [78, 79]. Common agents used concurrently with DMSO for patients that fail monotherapy include heparin sodium, a steroid (triamcinolone is used in our institution), an antibiotic (gentamicin in our institution), and sodium bicarbonate. Despite the routine use of adjunctive agents, data are limited to support improved patient tolerability and clinical benefit [80]. Side-effects from DMSO include a self-limiting garlic-like odor and taste. The drug is also not recommended for use during pregnancy.

Pentosanpolysulfate, when used as an oral agent, achieves a low bladder concentration, resulting in a long lag time (3–6 months) before clinical improvement can be observed [81]. Davis et al. investigated the drug's safety and efficacy as an intravesical formulation in a randomized trial comparing oral therapy to a combination of oral and intravesical pentosanpolysulfate [82]. Patients who received the combined regimen had a twofold reduction in the severity of IC/BPS symptoms compared with those receiving oral therapy only ($P = 0.4$). Overall quality of life was significantly improved in the combination group, making it a suitable option for moderate to severe IC/BPS. The incidence of adverse events was comparable in both groups.

Intravesical anesthetic agents have an important role in the minimally invasive management of IC/BPS. Local anesthetics are weak bases and therefore absorption is limited in the urinary bladder. Higson et al. first described alkalinization of intravesical lidocaine by administering 40 ml of 1% lidocaine with 40 ml of 8.4% sodium bicarbonate [83]. Henry et al. later showed that alkalinization of urine in the bladder provides safe and predictable lidocaine absorption as well as enhanced anesthetic action, leading to decreased pain scores in patients with IC/BPS [55]. In addition to the well-known action as a local sodium channel blocker, local anesthetics also prevent histamine release from mast cells and function as anti-inflammatory agents. Inflammatory responses are dampened by decreasing the level of certain mediators such as interleukin 1, interleukin 8, and various cytokines [84–86]. The effect of intravesical alkalinized lidocaine was investigated in a randomized trial by Nickel et al. [87]. The multi-institutional study included 102 patients with a diagnosis of IC/BPS. Preliminary results showed the agent to be effective, providing short-term amelioration of symptoms in the majority of patients. The effects lasted beyond the treatment period and no significant adverse effects were reported.

## Endoscopic procedures for IC/BPS

Endoscopic procedures may be indicated during the evaluation and/or treatment of patients with IC/BPS. For patients where cystoscopy is indicated for other reasons (gross, microscopic hematuria) or when initial management steps have been unsuccessful, cystoscopy with bladder hydrodistention may be a useful diagnostic tool. Bladder hydrodistention was first performed in 1922 and eventually became the gold standard to diagnose IC by the 1970s [88]. Findings consistent with interstitial cystitis included reduced anesthetic bladder capacity, presence of Hunner's lesions, and the presence of glomerulations along the bladder mucosa. Hunner's lesions can be distinguished from glomerulations during hydrodistention, as glomerulations become apparent as the bladder is filled. Although these diagnostic criteria still apply today, the utility of hydrodistention has been called into question as a result of studies such as the one performed by Waxman et al., which demonstrated almost half of asymptomatic women in the cohort had cystoscopic findings consistent with IC following hydrodistention [89]. Furthermore, the mechanism for symptom relief is unknown, but theorized to be due to an increased elaboration of bladder surface mucin or a result of temporary nerve injury resulting in incomplete sensory impairment [90]. In our practice, cystoscopy without hydrodistention is performed when there is a concern for Hunner's lesions or if other etiologies have not been excluded.

Bladder hydrodistention is usually performed under general or regional anesthesia. Distension is performed under direct cystoscopic vision to avoid overdistension and mucosal tearing. Distention is limited to short duration intervals of 2–4 minutes at a pressure ranging from 60 to 80 $\mathrm{cmH_2O}$. Glomerulations can often be seen after hydrodistention as punctate submucosal hemorrhages (Figure 156.3). In patients with Hunner's lesions, a biopsy and fulguration should be performed to rule out the presence of malignancy (Figure 156.4). Once a biopsy is performed, bladder hydrodistention is not recommended in the same setting to avoid complications related to bladder perforation and hemorrhage. Finally, consideration should be given to instillation of 20–30 ml of a short-acting anesthetic agent (1% lidocaine), to aid in decreased pain following hydrodistention. For patients

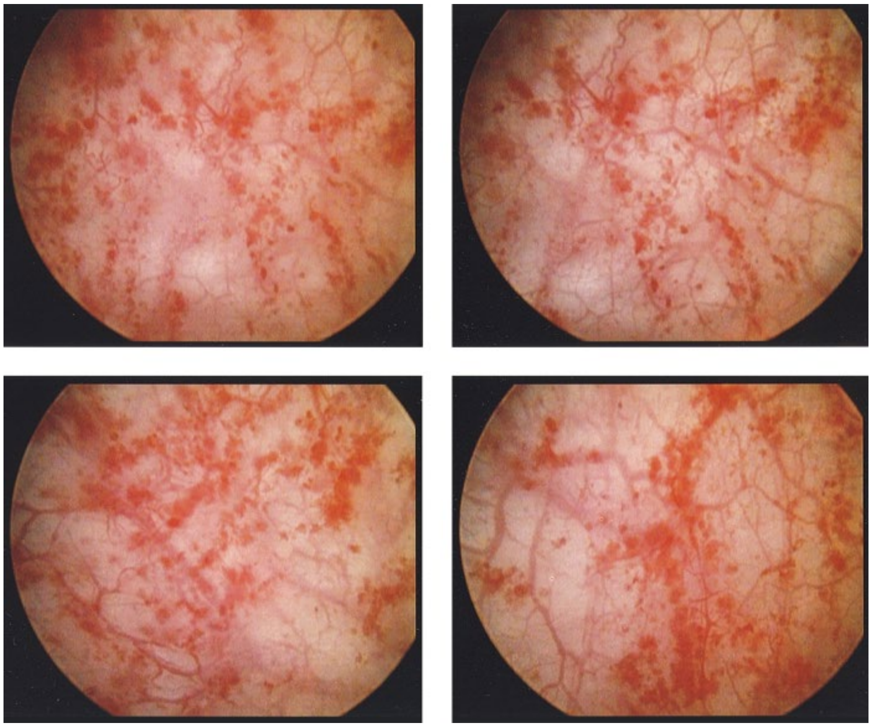

**Figure 156.3** Glomerulations: submucosal hemorrhages seen in interstitial cystitis/bladder pain syndromepatients after hydrodistention.

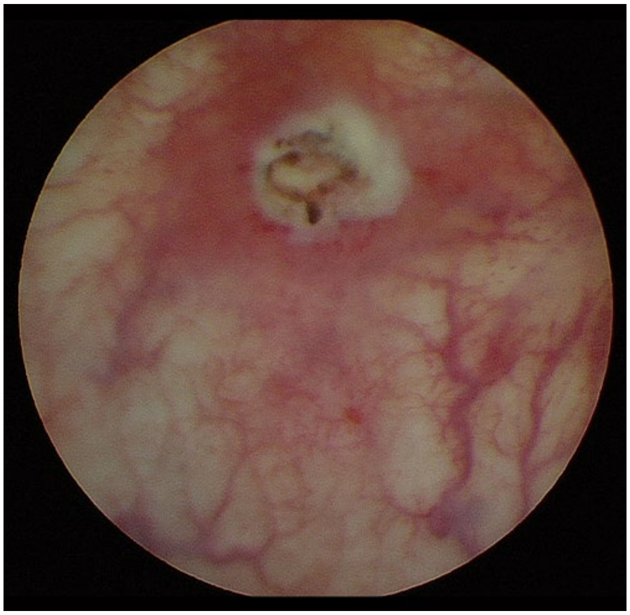

**Figure 156.4** Hunner's lesion after endoscopic fulguration. Note the intense inflammatory tissue reaction that develops upon application of electrocautery.

with severe IC/BPS and small bladder capacity, intravesical installation of hyaluronic acid can prolong the effect of bladder hydrodistention. The number of mean voids per day and bladder capacity were significantly improved for up to nine months in patients receiving hyaluronic acid compared with hydrodistention only or hydrodistention with installation of heparin [41]. Intradetrusor injection with botulinum toxin A (reviewed below) has been reported in setting of hydrodistention, with a 25% reduction in urinary frequency and overall response rate found to be 74% [91].

Intradetrusor injections with botulinum toxin type A (BTX-A) and submucosal injection of triamcinolone acetonide represent the most invasive of the intravesical agents used in IC/BPS. In general, BTX-A is used for the treatment of muscle overactivity and spasticity of various diseases. With regard to urologic disease, BTX-A is FDA approved for neurogenic detrusor overactivity and overactive bladder. BTX-A has also been used off-label in the treatment of IC/BPS, owing largely to its analgesic properties that have been shown to impede the release of neuronal signals such as substance P and glutamate [92]. Giannantoni et al. showed that intravesical injection is effective for the short-term management of refractory painful bladder syndrome [93]. Patients received 200 U of BTX-A diluted in 20 ml of 0.9% sodium chloride, using a rigid cystoscope and a flexible needle. A total of 10 U were given per injection site and injections were administered to the lateral wall and trigone. This group demonstrated significant improvements in daytime and night-time frequency, and improved bladder capacity was noted on follow-up cystometry. However, a significant number of patients required clean intermittent catheterization to manage short-term detrusor hypocontractility. Others have reported satisfactory efficacy; with injections of 100 U of BTX divided into 10 sites in the trigone no patients experienced voiding dysfunction [94]. Furthermore, Smith et al. reported their experience with BTX for IC/BPS patients, with 71% of patients having significant improvement in Cystitis Symptom Index score [95]. BTX has been used in the setting of bladder hydrodistention to reduce postprocedure pain. Liu and Kuo treated patients with 100–200 U of intravesical BTX followed by hydrodistention [91]. Treatment was considered successful if patients reported an improved quality-of-life index, complete resolution of bladder pain, and absence of voiding dysfunction. Partial response was recorded for patients with improved quality-of-life index, reduced pain (reduction of >2 points on the pain scale), and a greater than 25% reduction in urinary frequency. Patients reported symptomatic improvement at three months and the overall response rate was 74%. In addition to intradetrusor injections, BTX injections of the pelvic floor have been used in patients with a significant pelvic pain component secondary to myofascial dysfunction [96].

### Endoscopic management of Hunner's lesions

Hunner's lesions are found in approximately 5–10% of patients with IC/BPS. Patients in this subgroup tend to experience greater urinary frequency and are found to have smaller bladder capacities. Although these patients present with severe symptoms refractory to conservative management, endoscopic management using fulguration or resection techniques offers a durable therapeutic option. In the setting of a new diagnosis of a Hunner's lesion, a biopsy is recommended in order to rule out carcinoma *in situ* of the bladder.

Transurethral resection of Hunner's lesions and surrounding mucosa has been investigated by several retrospective studies. Peeker et al. reported an analysis of 103 patients with Hunner's lesions who underwent a total of 259 transurethral resections of visible lesions. Ninety-two patients reported improvement of symptoms, and 40% of this group had a durable response lasting beyond 3 years. In addition, they found that patients with a diminished bladder capacity demonstrated the poorest response to treatment [97]. Although transurethral resection has been shown to be safe and effective, there remains the theoretical risk of bladder perforation and scarring. As a result, fulguration of Hunner's lesions has become the preferred method of endoscopically managing Hunner's lesions. Fulguration can be performed using a Bugbee electrode, rollerball, or monopolar or bipolar loop. In our institution we prefer to use the Bugbee electrode, set at 30 V. Endoscopic fulguration has been shown to be an effective procedure, but many patients may require repeat interventions to achieve a durable response. Hillelsohn et al. found that 45.8% of patients required repeat fulguration within 4 years of treatment [98]. Despite a high reintervention rate, bladder fulguration is still a reasonable therapeutic option. In a recent study, Chennamsetty et al. retrospectively analyzed a cohort of 76 patients who underwent 214 endoscopic fulgurations, where 89% of patients noted some degree of improvement in symptoms and 98% would undergo the procedure again [99]. Furthermore, they found that bladder capacity was not significantly decreased by undergoing multiple procedures.

Laser ablation of Hunner's lesions is an endoscopic alternative to fulguration; however, there are no clinical trials available to compare the efficacy of each method. In one early study using a neodymium:YAG (Nd:YAG) laser over half of the cohort reported a therapeutic benefit. However, two small bowel perforations occurred during the study, thus limiting its widespread use. Laser ablation was revisited by Rofeim et al., who performed a prospective study in a cohort of 24 patients and a follow-up of 23 months [100]. Low-energy (10–15 W) settings were used to ablate visible lesions and limit the depth of penetration to 5 mm. Within 2–3 days of the procedure, patients reported a decrease in pain, frequency, and urgency. Fifty percent of patients required only one treatment and had a mean response of 19 months. There were no significant complications, including bladder perforation or bowel injury, likely due to attempts to avoid bladder distension.

Endoscopic steroid injection of Hunner's lesions can serve as an alternative to fulguration techniques in the management of Hunner's lesions. The theoretical advantage of steroid injections is the potential of successfully managing Hunner's lesions without the associated complications, resulting in scarring or bladder perforation. Cox et al. performed a prospective study utilizing triamcinolone acetonide injections directly into Hunner's lesions [101]. They performed injections under general anesthesia, and injected 10 ml of triamcinolone acetonide (40 mg/ml) divided into 0.5 mL injections per site (Figure 156.5). Their results showed that 28/30 (93%) of patients reported improvement in urinary symptoms, while 21 (70%) reported much improvement. In our institution we utilize doses as low as 30 mg with similar results with regard to irritative urinary symptoms related to Hunner's lesions.

## Conclusions

The diagnosis and management of IC/BPS remains challenging for both patients and practitioners. For most patients, medical management remains the cornerstone of the treatment plan. However, for patients who fail medical management or those who have predominantly

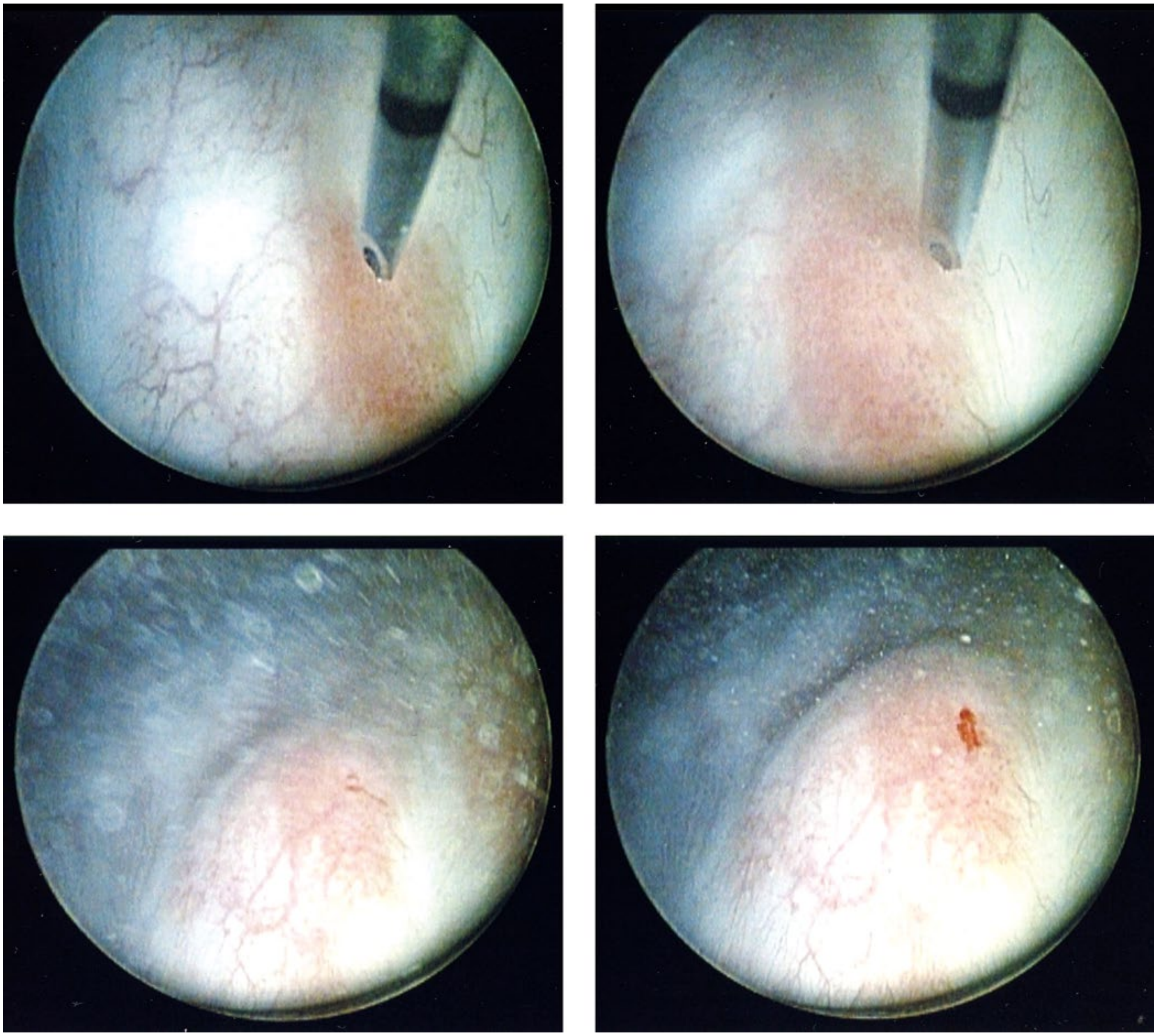

**Figure 156.5** Submucosal triamcinolone acetonide injection. Note how the needle bevel is positioned towards the bladder lumen so that a submucosal wheal is formed.

bladder pain symptoms, minimally invasive techniques are a safe and effective way to manage IC/BPS. Future directions to better characterize symptoms and effectively treat patients with IC/BPS are being investigated and will surely fill a void in this urologic condition.

See accompanying Video 156.1.

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## 157

# New Techniques for Resecting Bladder Tumors

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## Introduction

Bladder cancer is the second most commonly diagnosed urological malignancy. The incidence and prevalence of bladder cancer in western as well as in developing countries continue to rise [1]. Although it is not the most frequent malignancy, bladder cancer's high recurrence and progression rates, as well as its long disease-specific survival rate, makes the treatment for bladder cancer far more costly than that for other cancers, such as rectum, lung, and prostate [1]. In addition, because of the high recurrence rates, follow-up procedures such as cystoscopies with biopsies and intravesical chemotherapy also contribute to the high costs [1]. Thus the primary aim of surgical and nonsurgical treatment strategies are to optimize the outcomes and reduce the secondary interventions.

The majority of patients with bladder cancer are diagnosed with a nonmuscle-invasive bladder cancer (NMIBC). Most of these are candidates for transurethral resection of bladder tumor (TURBT), with conventional monopolar transurethral resection of the bladder being the gold standard for this operation. Complete and radical tumor removal during TURBT is essential for initial diagnosis and follow-up strategy planning [2].

There are diagnostic, surgical, and oncologic limitations to the contemporary technology and techniques used for conventional TURBT. The main diagnostic issue is the absence of the detrusor layer in the pathology after TURBT. Without the presence of the muscle layer, pathologists are often unable to correctly define pT stages of bladder cancer. The second most common diagnostic issue is thermal damage to the specimens, which can significantly affect pathological results. As a result of these drawbacks, low-quality pathologies may require a second-opinion pathologist consultation, and additional costly immunohistochemical investigations [3]. Surgical disadvantages of conventional TURBT include bladder perforation, obturator nerve stimulation, bleeding, and ureteral ostium injury during or after the surgery. Although the complication rate of monopolar TURBT is low, for high-risk patients there could be surgical and safety issues.

The oncological outcomes for any cancer procedure are major limitations. Piecemeal resection of the lesion ignores the parameter of negative surgical margins, leaving behind positive margins and viable cancer cells with potential for recurrence and metastasis. This approach also allows tumor cells to migrate into the irrigation fluid, which facilitates their implantation and early recurrence. Another issue is the possibility that tumor cells may disseminate into paravesical fat in the case of perforation [3].

In order to improve conventional TURBT, a "non-piecemeal-resection" endoscopic technique was developed with the aim of optimizing treatment results. The technique consists of entire (*en bloc*) tumor endoscopic removal by means of a loop and hook-shaped or J-shaped electrode. Initially, this technique did not gain widespread popularity because of the technical limitations of endoscopes and monopolar generators. However, with recent improvements and developments in monopolar and bipolar electrosurgery, the introduction of vaportrodes, holmium laser devices, and water jet technology, the *en bloc* tumor removal technique has been revisited.

The purpose of this chapter is to provide an overview of the current state of the *en bloc* technique, the surgical technique and technology used, patient selection

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strategies, indications and contraindications for the *en bloc* procedure, the feasibility of immediate intravesical chemotherapy, and postoperative follow-up and catheterization time.

## Technique of *en bloc* bladder tumor removal (see Video 157.1)

The procedure is initiated with induction of general anesthesia and positioning the patient in dorsal lithotomy position.

### Step 1

The bladder is thoroughly and systematically inspected by rigid or flexible cystoscope, using bladder mapping. If the technology is available, photodynamic diagnosis, narrow band imaging, or computer virtual chromoendoscopy will significantly enhance tumor size detection and facilitate the identification of satellite sessile tumors [4, 5].

### Step 2

Once the tumor has been detected and evaluated, the bladder mucosa, submucosal layer, and muscle layer are dissected (all at the distance of 0.5–1 cm) around the tumor base, with monopolar (bipolar) loops, a hook-shaped (J-shaped "sand-wedge," Figure 157.1) electrode, or an end-firing laser fiber. All visible bleeding blood vessels are simultaneously coagulated. The tumor is circumferentially resected together with the base and separated from the bladder wall. The separation technique is different. When "frontal energy" is used (hook or J-shaped electrodes, end-firing laser fibers) the separation movement are like axe cuts; when "circular energy" is applied (circle or bent loops, Figure 157.2), the movements are similar to those used when sawing a tree.

Next, electrocautery (laser energy) is used to burn and seal the blood vessels.

Water jet technology has an additional step. A flexible hole probe (hybrid knife) penetrates the mucosa around the tumor base into the level of the resection margin. Water is pumped through the probe under the tumor base to elevate the tumor, and then the tumor is carefully resected in one piece with the base by the same instrument (Figure 157.3).

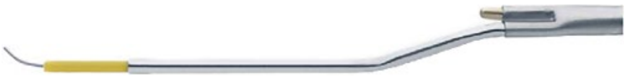

**Figure 157.1** Sand-wedge electrode.

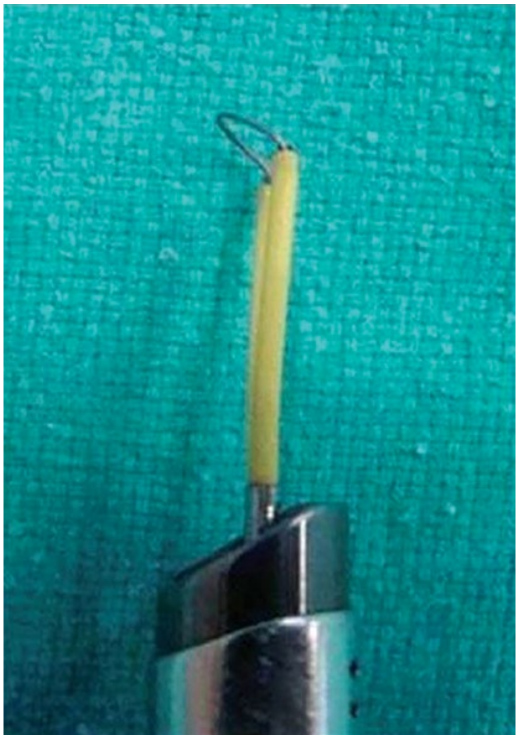

**Figure 157.2** Bent loop.

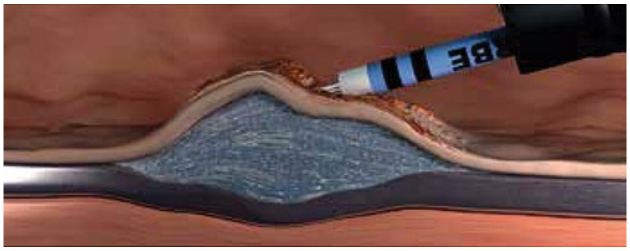

**Figure 157.3** Waterjet hybrid knife tissue elevation and dissection.

### Step 3

Following resection of the tumor, resected specimens are actively aspirated through the sheath. Alternatively, tumor pieces can be removed using different forceps (baskets, extractors, etc.) (Figure 157.4). When large tumors are presented, specimens can be divided into smaller sections by conventional resectoscope loop and then removed.

### Step 4

Once the tumor has been removed, the resected area is checked for bleeding, possible perforations, or residual tumors. Photodynamic diagnosis, narrow band imaging, or chromoendoscopy can be used to enhance intraoperative visualization of the resection margin and detect tiny satellite papillary tumors.

### Step 5

The final step of endoscopic operation for bladder cancer is postoperative chemotherapy instillation. If there is no severe bleeding or perforations, chemotherapeutic drugs can be instilled via a catheter immediately after instrument removal from the bladder.

Energy sources that are used for *en bloc* resection are listed in Table 157.1.

## Discussion

Ukai et al. from Japan reported using a J-shaped needle electrode to remove bladder tumors and Kawada et al. reported the use of *en bloc* resection for a 2.5 cm papillary tumor in 1997 [3, 6]. Three years later, in 2000, Ukai and authors published their own experience of *en bloc* resection, using a J-shaped needle monopolar electrode to make a circumferential incision around the tumor that also included a 5 mm safety margin [3]. The first step of the procedure was to make a blunt dissection from the line of incision. After the tumor was detached, it was removed using either a syringe or, in the case of large pieces, a laparoscopic retrieval bag [7]. The technique of cold-cup biopsies to insure complete tumor removal was also described by some authors [8–10].

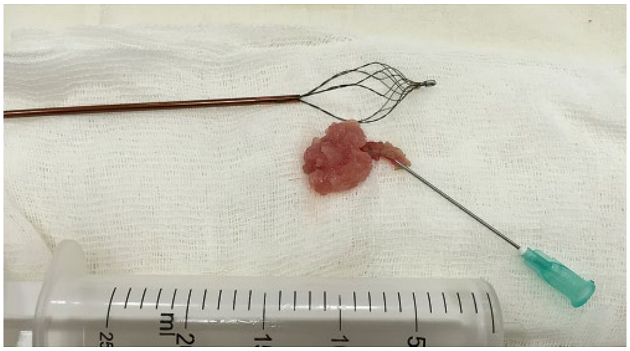

**Figure 157.4** Extractor and removed tumor.

The use of holmium:YAG (Ho:YAG) laser for transurethral *en bloc* resection of bladder cancer was first published by Saito, who concluded that it was a safe and useful technique for pathological evaluation [8]. Wolters et al. published a paper using a thulium laser for *en bloc* tumor resection. They were able to demonstrate detrusor muscle in all six cases, showing that it was possible to achieve exact staging at the time of primary transurethral operation [9]. Nagele et al. proved the feasibility of waterjet-induced resection to safely remove bladder tumors [10] and Fritsche et al. presented the first prospective clinical trial of waterjet-induced resection [11]. In addition to finding the application to be safe and applicable for *en bloc* dissection, they also reported feasibility in tumor sizes up to 7.5 cm. These authors [10, 11] first injected saline into the submucosal layer under the tumor base. After the tumor was elevated from the bladder wall, it was then safe to use *en bloc* resection. The results of numerous published data are shown in Table 157.2.

The data in Table 157.2 clearly show that the ideal tumor size for *en bloc* removal ranges from 2 to 4 cm, and the recurrence rate varies between 15% and 37%.

**Table 157.1** Instrumentation for *en bloc* transurethral bladder resection.

| Energy source | Resection device | Pro | Cons |
|---|---|---|---|
| Monopolar | Angled or flat loop<br>Hook electrode<br>Sand-wedge (J-shaped) electrode | Easily switched to transurethral resection<br>No additional costs<br>Many urologists are familiar | Obturator reflex<br>High perforation risk<br>Transurethral resection syndrome<br>Thermal pathology injury |
| Bipolar | Rectangular longitudinal loop<br>Hook electrode<br>Button (mushroom) electrode | Patients with pacemakers, metal prosthesis<br>No transurethral resection syndrome<br>Less thermal pathology damage | Urethral stricture? |
| Waterjet (hybrid) | Hybrid knife | No or diminished perforation risk<br>Good quality of pathology | Need for additional instruments for biopsy<br>Relatively new technique |
| Ho:YAG | Laser fiber | Bloodless technology<br>No pathology injury<br>No obturator reflex<br>Diminished perforation risk | High cost<br>Time-consuming technique |
| Tm:YAG | Laser fiber | The same as Ho:YAG<br>Faster than Ho:YAG | High cost<br>No long-term data |

**Table 157.2** Results of *en bloc* tumor resection.

| Authors, year | No. of patients | Tumor size (mm) | Follow-up (mo) | Recurrences (%) |
|---|---|---|---|---|
| **Electrosurgery** | | | | |
| Ukai, 2010 [12] | 97 | >20 | 3–84 (27) | 37 |
| Hurle, 2016 [13] | 87 | <30 | 24 | 15 |
| **Hybrid knife** | | | | |
| Fritsche, 2011 [11] | 17 | 4–75 | 4–14 | 23.5 |
| **Ho:YAG laser** | | | | |
| Xishuang, 2010 [14] | 64 | 5–36 | 24 | 31.7 |
| **Tm:YAG laser** | | | | |
| Muto, 2014 [15] | 55 | 20–40 | 8–25 (16) | 14.5 |

Although many papers have looked at the efficacy and safety of *en bloc* resection, only a few publications have relatively large samples. Kramer et al. is currently the largest study in this particular field, with 221 patients enrolled at six academic hospitals in this European multicenter study [16]. Using monopolar/bipolar current or holmium/thulium laser energy, the results of this study found that *en bloc* resection of bladder tumor is a safe and reliable procedure, and provides high-quality resections for tumors >1 cm.

### Laser *en bloc* resection

Zhu et al. compared holmium laser resection with standard TURBT in nonmuscle-invasive bladder cancer [17]. The results revealed no difference in recurrence-free survival between the techniques. The laser group had fewer perioperative complications, and was deemed better in terms of safety and pathology quality. Xishuang et al. further evaluated the safety and efficacy of holmium laser transurethral bladder resection, comparing it with conventional monopolar and plasmakinetic techniques [14]. They found that the complication rate, catheterization, and hospitalization times were superior in both bipolar and holmium laser arms; recurrence rates were equal in all groups.

Another type of laser in *en bloc* resection is the thulium laser (Tm:YAG), a 2 μm laser used for nonmuscle-invasive bladder tumor treatment. A study done by Zhong et al. evaluated the safety and efficacy of a 2 μm continuous wave laser compared with holmium laser and standard transurethral resection. The retrospective study, which included 97 patients, found there was less hemoglobin drop in the 2 μm laser groups; the recurrence rate of all groups showed no statistical significance [18].

In contrast with electrosurgery, which uses a 26 Fr resectoscope, laser resection with a flexible cystoscope is more feasible. Laser resection may be a preferable option in patients with hip joint ankylosis who cannot be placed in lithotomy position. Ho:YAG and Tm:YAG lasers have wavelengths of 2100 and 2013 nm, respectively, and both use water as chromophore. Both these lasers also provide fast and high-power tissue vaporization, and obtain excellent hemostasis. However, the thulium laser produces a smoother cutting line and provides more precise incision than the holmium laser. Zhong et al. advocated that thulium laser resection is superior over electrosurgical techniques in cases when the tumor is located in the bladder neck, or in the bladder dome due to lower perforation risk [18]. Another clinical advantage of laser *en bloc* technique is the absence of obturator nerve stimulation; thus there is no risk of bladder perforation while performing resection on the lateral wall.

## Pathologic considerations

Ukai et al. demonstrated that transurethral resection in one piece (TURBO) can act as an accurate pathological staging tool for bladder cancer [12]. Seven (7%) patients with tumors with deep resection margins positive for carcinoma were assigned an ambiguous pathological stage ("pT1 or higher" or "pT2 or higher"). Five of those patients had tumors with muscle invasion, which can provide a potential reason for the use of therapeutic decision-making, such as performing a radical cystectomy. The remaining two cases have tumors staged as pT1 or higher due to the absence of the muscularis propria. This might represent a limitation of the *en bloc* technique. However, a major advantage of this technique is that urologists can obtain good-quality tumor specimen, which would ultimately lead to superior histopathological diagnosis and accurate pathological staging.

Using the *en bloc* technique, the step-sectioned strips of the entire tumor specimen are amenable to precise histological evaluation of the entire *en face* sections, and the complete interface between the tumor base and the lamina propria. This allows much easier and more definitive discrimination between pTa and pT1 stages. In addition, pathologists can reliably estimate the distance between the invasive front and the resection margin, which can be a potential indicator of histologically proven complete resection. In certain cases with divisional resection, accurate pathological staging was possible when the tumor's topography was exactly reconstructed before resection, though the accuracy of the staging might be lower than for tumors resected in an *en bloc* manner. An important aim of TURBT is to obtain high-quality tumor specimens. It is important to note that those obtained by conventional transurethral resection are inevitable fragmented and poorly oriented.

In assessing the depth of invasion, the only reasonable statement is "stage T1 at least" in the case with lamina propria invasion, or "stageT2 at least" in the case with muscle invasion [19]. The use of clinical staging (Ta or T1) instead of pathological staging (pTa or pT1) is recommended when conventional transurethral resection is performed [20]. In this regard, *en bloc* resection provides tissue specimens adequate for pT categorization because the tumor and surrounding structures are mostly preserved. The presence of the musclaris propria in tumor specimens is crucial for accurately discriminating between stages pT1 and pT2 [21].

In a substantial number of cases, transurethral resection specimens lack the muscularis propria. Herr and Donat showed that 40% of T1 tumors did not have muscularis propria in the specimens [19], while Maruiniak et al. reported the absence of the muscularis propria in 51% of cases [20]. The lack of the muscularis propria in TURBT specimens is more likely to lead to understaging, resulting in misled therapeutic decisions. In the study by Ukai et al., the *en bloc* specimens included the muscularis propria beneath the tumor base in 82% of the cases [12]. *En bloc* technique then might have an additional advantage because we used a technique involving dissection, primarily into normal-appearing tissues under direct vision. Of the 17 patients (18%) whose tumor specimens did not include any obvious muscle issues, 15 patients had tumors that were staged as either pTa or pT1 when negative resection margins were present. Thus, pathological stages were assigned to the tumors in 93% of the patients undergoing *en bloc* resection.

In order to overcome the limitations of TURBT, several authors recommend a second-look transurethral resection for all T1 tumors, multiple high-grade Ta tumors, and all cases including carcinoma *in situ* [22]. Kolozsy reported that 36% of T1 tumors are incompletely resected and that the most common site of residual tumor (26%) was the floor of the resection [23]. Grimm et al. showed that residual tumor was found in 33% of all repeat resection cases, and in 81% of the cases at the initial resection site [24]. Although repeated transurethral resection does not completely eliminate the risk of residual tumor, Ukai et al. found that the *en bloc* technique is a potential tool to replace or even surpass the role of repeated resections [12]. Their follow-up results showed that the overall 5-year recurrence-free rate was 55%, with only one patient (1.2%) having progression to muscle-invasive disease [12]. These high positive results following *en bloc* resection might be attributed to the possibility of residual tumors at the resection floor, even though superficial recurrences from invisible residual tumor might occur at the border of the resection area or elsewhere. Often, it is arduous to entirely remove a poorly demarcated tumor even with *en bloc* technique, especially in cases with associated carcinoma *in situ*. Extreme caution is then needed in evaluating the usefulness of *en bloc* resection, considering there was a selection bias in Ukai et al. study, and a medium follow-up of 27 months is too short to draw any conclusions regarding tumor recurrence and progression [12].

## Limitations

*En bloc* methods also have some limitations. First, there are some technical difficulties compared with conventional resection, such as more resection time, depending on the size, volume, location, and multiplicity of the tumor. Ukai et al. assumed that tumors that are visible and can be completely resected by traditional resection, can also be successfully resected by one piece [12]. Second, Naselli et al. [7] had to divide a large tumor into smaller portions in order to collect it through a resectoscope sheath. Occasionally, it might be difficult to collect a tumor specimen whose largest dimension is substantially larger than the caliber of the resectoscope sheath. The tumor is subject to divisional resection, not because it cannot be resected *en bloc*, but because it is required to be retrieved through the resectoscope sheath. The divisional resection deteriorates the quality of the specimen to varying degrees, but even divided tumor specimens might be better material for pathological evaluation than fragmented chips after resection. Finally, pathologists cannot histologically confirm the completeness of the resection, even though visually complete resection was performed. A resection can be qualified as histologically complete when all margins, including deep and lateral, are negative for carcinoma (Figures 157.5 and 157.6). However, the assessment of every lateral margin in all stepped sections is not always possible, due to denudation of the crush and thermal artifacts of the circumferential epithelium [12]. To overcome these limitations,

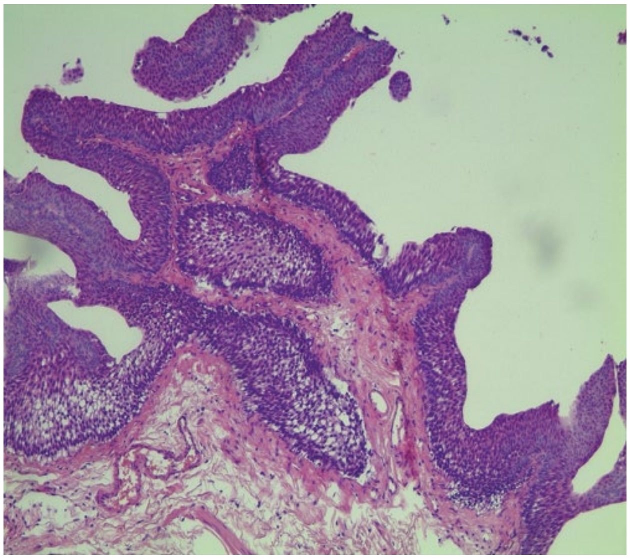

**Figure 157.5** Tumor margin can be clearly seen.

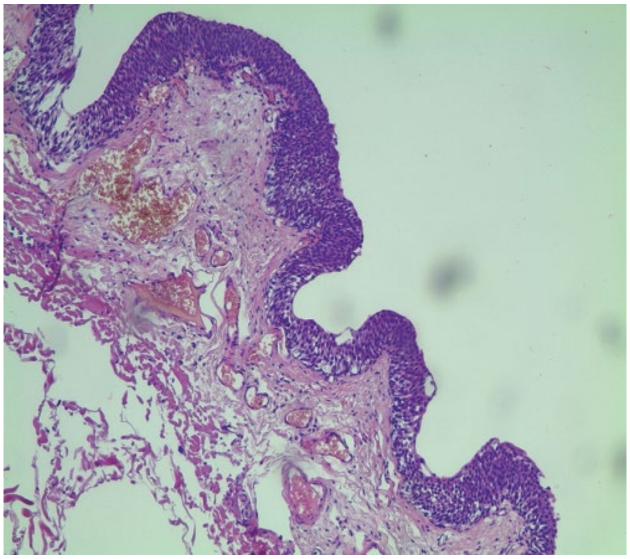

**Figure 157.6** Negative surgical margin (normal urothelium).

improved methods of one-piece resection and collection, yielding high-quality specimens (with a high success rate) should be further studied.

## Complications

The complications rate for *en bloc* resection is low, as the complications for the procedure are similar to those of conventional transurethral resection. All available data concerning possible complications of *en bloc* resection are listed in Table 157.3. In addition to describing the complications, all recent publications classified them according to the Clavien–Dindo system, which focuses on the morbidity and influence of treatment results. Possible explanations for the relatively low complications rate include: (i) *en bloc* technique was performed by only experienced endourologists, while routine transurethral resection was usually done by young, inexperienced residents; (ii) indications for *en bloc* technique include solitary or multiple (less than 4) tumors between 2 and 4 cm in size, which are normally free of complications; and (iii) laser and waterjet technologies have fewer complications than conventional electrosurgery.

**Table 157.3** Complications of *en bloc* resection.

| Series, year | No. of patients | Tumor size (mm) | Complications |
|---|---|---|---|
| Lodde, 2003 [25] | 37 | <25 | Bladder perforation – 1 |
| Saito, 2001 [8] | 35 | <25 | No complications |
| Nagele, 2011 [10] | 5 | <20 | No complications |
| Fritsche, 2011 [11] | 17 | 4–75 | No complications |
| Zhu, 2008 [17] | 96 | <20 | Bladder perforation – 1 |
| Xishuang, 2010 [14] | 64 | <36 | Ureteral orifice stricture – 1 |
| Zhong, 2010 [18] | 55 | <30 | No complications |
| Yang, 2009 [26] | 9 | <30 | Bladder perforation – 1 |
| Gao, 2009 [27] | 32 | <30 | No complications |
| EBRUC, 2015 [16] | 221 | <50 | Clavien ≥3, $n = 6$ |
| Martov, 2016 [28] | 106 | <30 | Clavien ≥3, $n = 2$ |

The low complications rate of the *en bloc* technique in all cases guarantees the option to do immediate chemotherapy instillation, which drastically improves treatment results.

## Oncological efficacy/influence on progression and recurrence

Data from various *en bloc* studies concerning recurrence and progression rates are shown in Table 157.4.

The recurrence rate of nonmuscle-invasive bladder cancer after *en bloc* tumor removal is approximately 30–40%, while the progression rate is 16%. Two monopolar studies have compared *en bloc* tumor removal with conventional transurethral technique. In the first, Lodde et al. reported 36.4% recurrences for transurethral resection [25], and in the second, Ukai et al. reported 37% recurrences [12]. Tumor progression was observed in six cases (16%) in Lodde's study, and there were no data on adjuvant intravesical chemotherapy. Postoperative

**Table 157.4** Recurrence and progression rates of bladder cancer after en bloc resection.

| Authors, year | Stage T | Grade G | Follow-up, months | Recurrence/progress | Instillation chemotherapy |
|---|---|---|---|---|---|
| Lodde, 2003 [25] | Ta = 51,<br>T1 = 11 | G1 = 43<br>G2 = 10<br>G3 = 9 | 10–24 (14) | 12 (36%)/<br>6 (16%) | No data |
| Ukai, 2010 [12] | Ta = 30<br>T1 = 58<br>T2 = 2 | G1 = 3<br>G2 = 46<br>G3 = 48 | Up to 84, medium 27 | Rec 30 (37%) | 46%, then 27% BCG |
| Xishuang, 2010 [14] | Ta = 36<br>T1 = 23<br>CIS = 5 | G1 = 22<br>G2 = 35<br>G3 = 7 | 24 | Rec 20 (31.7%) | Mitomycin in all cases |
| Zhong, 2010 (Ho:YAG arm) [18] | Ta = 19<br>T1 = 5<br>CIS = 1 | G1 = 10<br>G2 = 15<br>G3 = 0 | 24 | Rec 6 (24%) | Epirubicin in all cases |
| Zhong, 2010 (Tm:YAG arm) [18] | Ta = 23<br>T1 = 5<br>CIS = 2 | G1 = 6<br>G2 = 24<br>G3 = 0 | 24 | Rec 8 (26.7%) | Epirubicin in all cases |

chemotherapy was used in 46% cases of transurethral resection and, in cases of recurrence after chemotherapy, was followed in 27% cases by BCG immunotherapy. In Ukai's group, there was no difference in recurrence risks between pTa and pT1 arms [12]. The medium follow-up time was 27 (3–84) months, which was twice as long as in Lodde's study. The recurrence-free time was 77% after 1 year, 63% after 3 years, and 55% after 5 years [29]. The authors marked pT1G3 with the presence of carcinoma *in situ* at the re-evaluation of the initial pathology in one patient whose disease progressed.

Fritsche et al. evaluated recurrence and progrssion rates in waterjet *en bloc* tumor removal [11]. The study included 13 patients with nonmuscle-invasive bladder tumors, in 3 (23%) of which recurrences were found and in 1 case tumor progression. Maximum follow-up was 14 months.

The recent holmium laser technique is described in the works of Zhu et al. [17] and Xishuang et al. [14]. Zhu's group compared holmium laser *en bloc* resection with conventional transurethral resection, and they found similar recurrence rates after both techniques. The average follow-up time was 34 (18–43) months. Xishuang et al. conducted the same study design, and their results between the techniques were statistically insignificant, aligning with the data from Zhu et al. [14]. Zhong et al. conducted a three-arm study comparing conventional bladder resection with thulium and holmium bladder *en bloc* resection [18]. They found the recurrence rates to be 30.95%, 26.67%, and 24.00%, respectively; however, differences were also statistically insignificant. In another study, Wolters et al. showed no pathological recurrences in second-look transurethral bladder resection six weeks after initial thulium *en bloc* bladder removal (4 patients) [9]. The study done by Gao et al. revealed 3 recurrences out of 9 at the area of previous surgery in a group of 32 patients. The overall accumulated recurrence rates were 9% at three months, 22% at six months, and 28% at 12 months. There was no stratification on pT criteria in this study [27].

In a recent study by Muto et al., out of the 55 patients who underwent thulium *en bloc* resection, only one patient had progression with initial pT1G3 [15]. The recurrence rate was 14.5%, with the average follow-up being 16 months (8–25). Second-look cystoscopy was performed in 30–90 weeks for all cases. The authors also noted that all recurrences were found outside the place of previous resection [15].

In the En Bloc Resection of Urothelium Carcinoma of the Bladder (EBRUC) trial, 148 patients were followed for 12 months, and 33 (22.3%) had recurrences. Of those recurrences, 63.6% occurred outside of the *en bloc* resection field, and no statistical difference was noticed between electrosurgical and laser arms [16]. In our recent study, the recurrence rate was 21% (18/86 patients), and all cases were outside the previous surgery site; there were no cases of tumor progression [28].

Based on the results of the current literature, clearly there is a need to evaluate the potential oncologic benefits of the *en bloc* technique. This supports the notion that further examination of this technique is needed, with methods adhering to ubiquitous oncologic principles not followed by the conventional transurethral bladder procedure.

## Conclusions

Approximately 75–85% of bladder cancer patients present with disease confined to the mucosa (pTa, carcinoma *in situ*) or submucosa (pT1). The absence of detrusor muscle in the pathology is associated with higher risk of residual disease and early recurrence. The exact pathological staging of bladder cancer is crucial for the strategy in disease treatment, and complete and accurate removal is essential to achieve good prognosis in the disease management. TURBT with conventional wire loop is still the gold standard treatment for nonmuscle-invasive bladder cancer. Despite several clinical and diagnostic drawbacks, the most important are the oncological disadvantages (tumor resection instead of *en bloc* removal) of the conventional transurethral technique.

Recent advances in endourology have led to the introduction of a range of novel *en bloc* methods that allow bladder tumor to be removed in one piece. For example, different shaped loops and electrodes have been created to facilitate tumor removal, and many new techniques have been evaluated to safely and promptly remove detached tumors from the bladder. These include, but are not limited to, monopolar, waterjet, bipolar, holmium and thulium laser techniques, and every year, more new clinical advancements are announced. This reflects the strong clinical importance of this issue. Although there is a surge of interest pertaining to *en bloc* methods, there is a lack of statistically significant data from properly designed studies. Because of this, these techniques are still under evaluation from clinical and oncological points of view.

Well-established advantages of *en bloc* bladder tumor removal include good-quality pathology specimen with the possibility of macroscopic tumor description, the possibility to evaluate surgical margins, and the presence of both the detrusor muscle and lamina propria muscularis. These advantages allow pathologists to better detect pT and G. Last but not least, an advantage of the *en bloc* technique is the ability to substratify pT1 into pT1a, pT1b, and pT1c due to the presence not only of the detrusor layer but also the lamina propria muscularis of the mucosal layer. Thermal damage to the specimen occurs less often compared to conventional piecemeal tumor resection because the resection area is smaller.

The typical size for *en bloc* resection is between 1 and 3 cm. If the tumor is smaller, it could be easily resected in one cut with conventional wire loop, though many authors advocate the *en bloc* technique in such cases because of the high probability of tumor thermal damage during resection. The upper limit of 3 cm for *en bloc* tumor removal is linked to the difficulty of tumor removal from the bladder in case of larger pieces. Despite the existence of several techniques and tricks to overcome these difficulties, it is much easier to resect larger tumors according to conventional resection rules. However, in some series, the upper limit for *en bloc* removal is 5 or even 7.5 cm. The additional advantages of staying within the limits of 1–3 cm tumor size are the use of existing equipment, no additional operation costs for tumor removal devices, and the increase in patient's safety.

The ideal locations for the *en bloc* technique are the bladder floor and lateral walls, but not near the ureteral ostium. The development of laser techniques greatly increased the safety of bladder tumor removal at the level of the lateral walls due to the absence of obturator nerve stimulation and predictable small penetration lengths. Waterjet technology has also been introduced into real-life clinically practice. The water in the space of the submucosa layer protects the bladder wall from inadvertent perforations, and facilitates tumor *en bloc* removal. Due to the small sample population in waterjet studies, however, this technique is still under evaluation. Laser technology permits the removal of one-piece bladder tumors located in the anterior wall or in the trigonum. The bladder apex is still the most challenging tumor location, and it is relatively contraindicated for *en bloc* removal due to the high risk of intra-abdominal perforation. Another well-established contraindication for *en bloc* removal is tumors in the bladder diverticula, due to the absence of detrusor muscle in the diverticula wall.

*En bloc* bladder tumor removal appears to be a simple and reliable method that offers many advantages over traditional TURBT:

- It diminishes complications, such as obturator nerve reflex and bleeding.
- It overcomes the incise and scatter problem that conventional resection technique has.
- It preserves the architecture of the tumor and allows optimal staging and grading.
- It seems to reduce the risk of local recurrence due to possibility of negative surgical margin. This may reduce the need for second-look bladder resection.

See accompanying Video 157.1.

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# 158

# Incision: Endoscopic Management of Urethral Stenoses

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## Introduction

Endoscopic management of anterior urethral strictures and posterior urethral stenoses takes many forms. Urethral dilation and incision with cold knife or laser urethrotomy are techniques familiar to all practicing urologists. The use of and indications for urethral stents are sometimes misunderstood. Although these procedures have their role in the treatment of urethral disorders, their use should be predicated upon a thorough understanding of urethral anatomy, etiology of disease, and goals of treatment.

Herein, we review urethral anatomy with special attention to the difference in stricture processes that occur in each segment. The types of available endoscopic techniques are discussed and outcomes in each selected process are reviewed. A stepwise approach to evaluating patients with urethral strictures/stenosis is suggested so that the practitioner can gain an adequate understanding of the disease process prior to initiating treatment.

It is imperative that one understands the differences in urethral processes and expected outcomes based on endoscopic treatment techniques prior to undertaking a course of treatment. Both practitioner and patient should agree upon the expected outcomes of intervention prior to treatment. In only a selected few processes will endoscopic management be expected to be durably successful and because of this, open urethral reconstruction remains the gold standard for many conditions in which the patient's goals are cure of the process.

## Urethral anatomy

An understanding of the urethral anatomy is imperative for the urologist performing endoscopic surgery on the urethra. The anatomic relationships of the urethra and corpus spongiosum must precede discussion of the endoscopic techniques.

The surfaces of the corpus spongiosum is the third erectile body of the penis and lies in the ventral groove between the two corpora cavernosa (Figure 158.1). It is surrounded by the tunica albuginea, which is thinner than the tunica albuginea of the corpora cavernosa. The urethra transverses the length of the penis within the corpus spongiosum and at the distal end, the erectile tissue expands to form the glans penis. The bulbous urethra is eccentrically placed in relation to the corpus spongiosum and is much closer to the dorsum of the penile structures. Distally, the penile urethra is more centrally placed within the corpus spongiosum. The meatus is slit-like in configuration with a vertical axis and is on the ventral aspect of the tip of the glans penis (Figure 158.2).

At the World Health Organization conference in Stockholm the consensus opinion was to subdivide the urethra into six separate distinct areas (Figure 158.3):

- The *Meatus fossa navicularis*, contained within the spongy erectile tissue of the glans penis, terminates at the junction of the urethral epithelium with the skin of the glans. This portion of the urethra is lined with stratified squamous epithelium.
- The *penile or pendulous urethra* lies distal to the investment of the ischiocavernosus musculature but is invested by the corpus spongiosum. This section of the urethra maintains a constant lumen size roughly centered in the corpus spongiosum. It is lined with simple squamous epithelium.
- The *bulbous urethra* is covered by the midline fusion of the ischiocavernosus musculature and is invested by the bulbospongiosus of the corpus spongiosum. It becomes larger and lies closer to the dorsal aspect of the corpus spongiosum, exiting from its dorsal surface

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before the posterior attachment of the bulbospongiosus to the perineal body. The bulbous urethra is lined distally with squamous epithelium that gradually changes to the transitional epithelium found in the membranous urethra as it swings upward [1].

- The *membranous urethra* is the portion that traverses the perineal pouch and is surrounded by the external urethral sphincter. This segment of the urethra is unattached to fixed structures and has the distinction of being the only portion of the male urethra that is not invested by another structure. It is lined with a delicate transitional epithelium.
- The *prostatic urethra*, in common use, is the portion of the urethra that lies proximal to the membranous urethra and is mostly surrounded by the prostatic stromal and glandular tissue. Its epithelium is continuous with that of the trigone and bladder.
- The *bladder neck* is the location of the bladder neck musculature, variably surrounded by intravesical protrusion of the prostate. Its epithelium is also contiguous with that of the trigone and bladder.

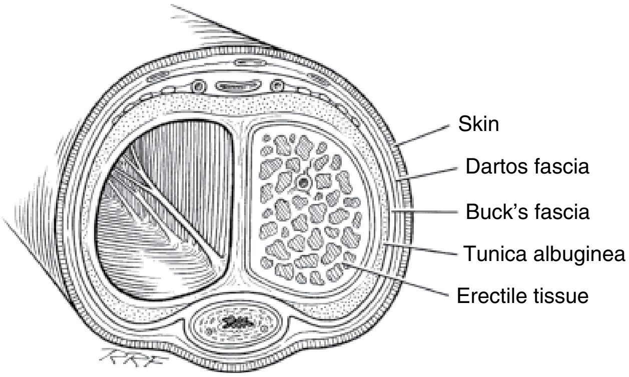

**Figure 158.1** Anatomy of the penis. The fibers of the septum are attached to the inner layer of the tunica albuginea of the corpa cavernosa along the dorsal and ventral midlines. *Source:* Devine CJ and Angermeier, KW. Anatomy of the penis and male perineum. *J Urol* 1994;8(11). Reproduced with permission of Elsevier.

## Urethral stricture disease

The term urethral stricture refers to anterior urethral disease, a scarring process involving the spongy erectile tissue of the corpus spongiosum also referred to as spongiofibrosis (Figure 158.4). Under the urethral epithelium lies the spongy erectile tissue of the corpus spongiosum and, in some cases, scarring can extend through the tissues of the corpus spongiosum and into adjacent tissues. As the scar contracts, it reduces the diameter of the

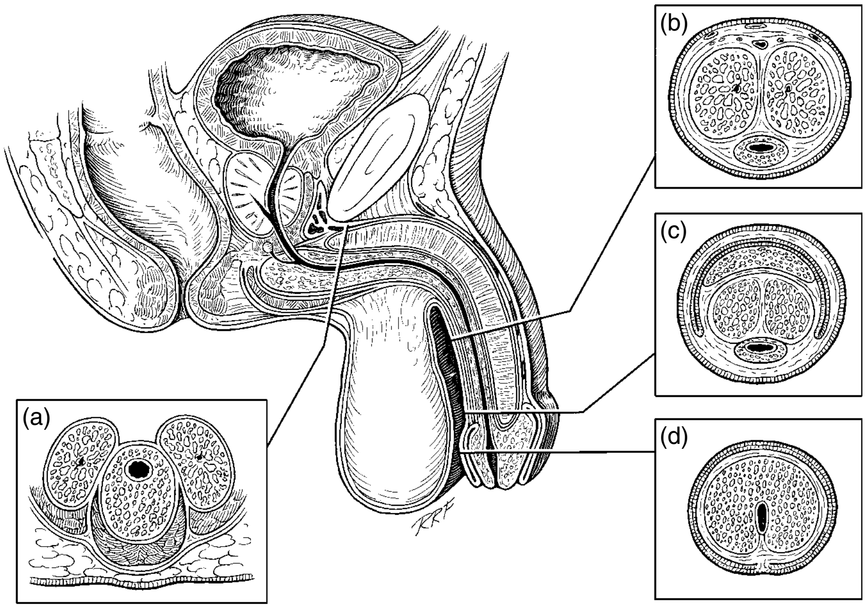

**Figure 158.2** Cross-sections of the anterior urethra. (a) Bulbous urethra. The urethra is eccentrically placed in the corpus spongiosum. Proximally, the corpora cavernosa have split into individual crura, with the urethra lying against the triangular ligament. (b) In the shaft of the penis, the urethra is more centrally placed in relation to the corpus spongiosum, and the corpora cavernosa are intimately fused, separated only by septal fibers. (c) At the coronal margin, the urethra remains relatively centrally placed, and the corpora cavernosa are fused, again separated by septal fibers. The spongy tissue of the corpus spongiosum has become incorporated as the deep tissues of the glans. (d) The fossa navicularis widens somewhat in caliber and is totally surrounded by the spongy erectile tissue of the glans penis. The urethra here is relatively ventrally placed in relation to the body of the corpus spongiosum. *Source:* Carson C, ed. *Topics in Clinical Urology: Complications of Interventional Techniques*. New York: Igaku-Shoin, 1996, pp. 86–94.

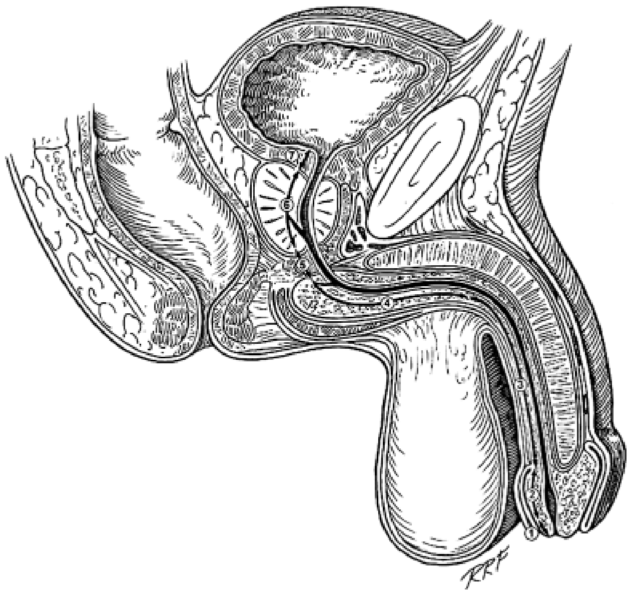

**Figure 158.3** Sagittal section of the pelvis. The urethra is subdivided into the following sections: meatus; fossa navicularis; pendulous or penile urethra; bulbous urethra; membranous urethra; prostatic urethra; and bladder neck. By common usage, the divisions of the meatus, fossa navicularis, pendulous urethra, and bulbous urethra compose the anterior urethra; and the divisions of the membranous urethra, prostatic urethra, and bladder neck compose the posterior urethra. *Source:* Devine CJ and Angermeier, KW. Anatomy of the penis and male perineum. *J Urol* 1994;8(11). Reproduced with permission of Elsevier.

urethral lumen. The normal urethra measures 30 Fr, and its diameter is approximately 10 mm. The calculated luminal area is approximately 78 $mm^2$. If scarring has resulted in a urethra that measures 15 Fr, the lumen is only 55 $mm^2$, or 29% reduced. Scar contraction caused by anterior urethral stricture disease can be markedly asymptomatic early in the process, but as the scarring process and contracture continues and the urethral lumen is further reduced, marked voiding symptoms can develop. This process may occur anywhere within the anterior urethra.

Posterior urethral "strictures" are, in fact, not referred to as strictures at all. By consensus of the World Health Organization conference, the term stricture is limited to the anterior urethra, while distraction defects are those processes of the membranous urethra associated with pelvic fracture and other narrowing of the posterior urethra, urethral contractures, or stenosis [2]. These processes do not involve spongiofibrosis and are thus commonly referred to as stenoses instead of strictures. As with anterior urethral strictures, posterior urethral stenosis is an obliterative process that has resulted in fibrosis and luminal narrowing. This process has usually been initiated by a distraction injury, whether due to trauma or surgical manipulation. Although in some cases these stenoses can be lengthy, the actual process involving the tissues of the urethra is usually well confined. Conditions that result in posterior urethral stenosis include membranous urethral stenosis, prostatic urethral stenosis, bladder neck contracture, vesicourethral distraction, and posterior urethral distraction defects.

## Etiology

Any process that injures the urethral epithelium and/or the underlying corpus spongiosum to the point that healing results in a scar causes a urethral stricture or stenosis. Anterior urethral strictures most commonly result from trauma, infection, inflammatory conditions, or urethral manipulation. In many cases, the inciting event goes unrecognized by the patient until they present with obstructive voiding symptoms.

Traumatic injuries such as straddle injuries are a common example. Penetrating injuries, such as gunshot or stab wounds, may be appropriately treated initially and still lead to development of delayed stricture disease. Iatrogenic trauma is a known etiology of urethral strictures, but with the development of smaller scopes and the recognition of the importance of careful technique, fewer of these cases are now being seen.

The inflammatory dermatosis lichen sclerosus is a commonly seen disease process in patients with anterior urethral strictures. This condition behaves differently from traumatic strictures, recurring quite readily, and thus requires special consideration when contemplating treatment options. Typically, the initial presentation is that of meatal stenosis associated with skin inflammation of the glans penis and prepuce. The inflammation then progresses proximally, perhaps due to distal obstruction, high pressure voiding, and subsequent microextravasation of urine into the corpus spongiosum and glands of Littre.

Infectious strictures associated with gonorrhea, which were commonly seen in the past, are now much less common. With the advent of more effective antibiotics and widely available medical care, gonococcal urethritis today rarely progresses to urethral stricture disease. As we understand the processes currently, nonspecific urethritis due to *Chlamydia* or other organisms does not lead to urethral strictures. The condition of idiopathic urethrorrhagia has in the past been felt to be related to urethral stricture because children were endoscoped for diagnosis. In years past, before the minification of endoscopes, it was felt that those stricture were iatrogenic. However, now there is accumulating evidence that the entity itself can cause proximal bulbous urethral stricture disease [3].

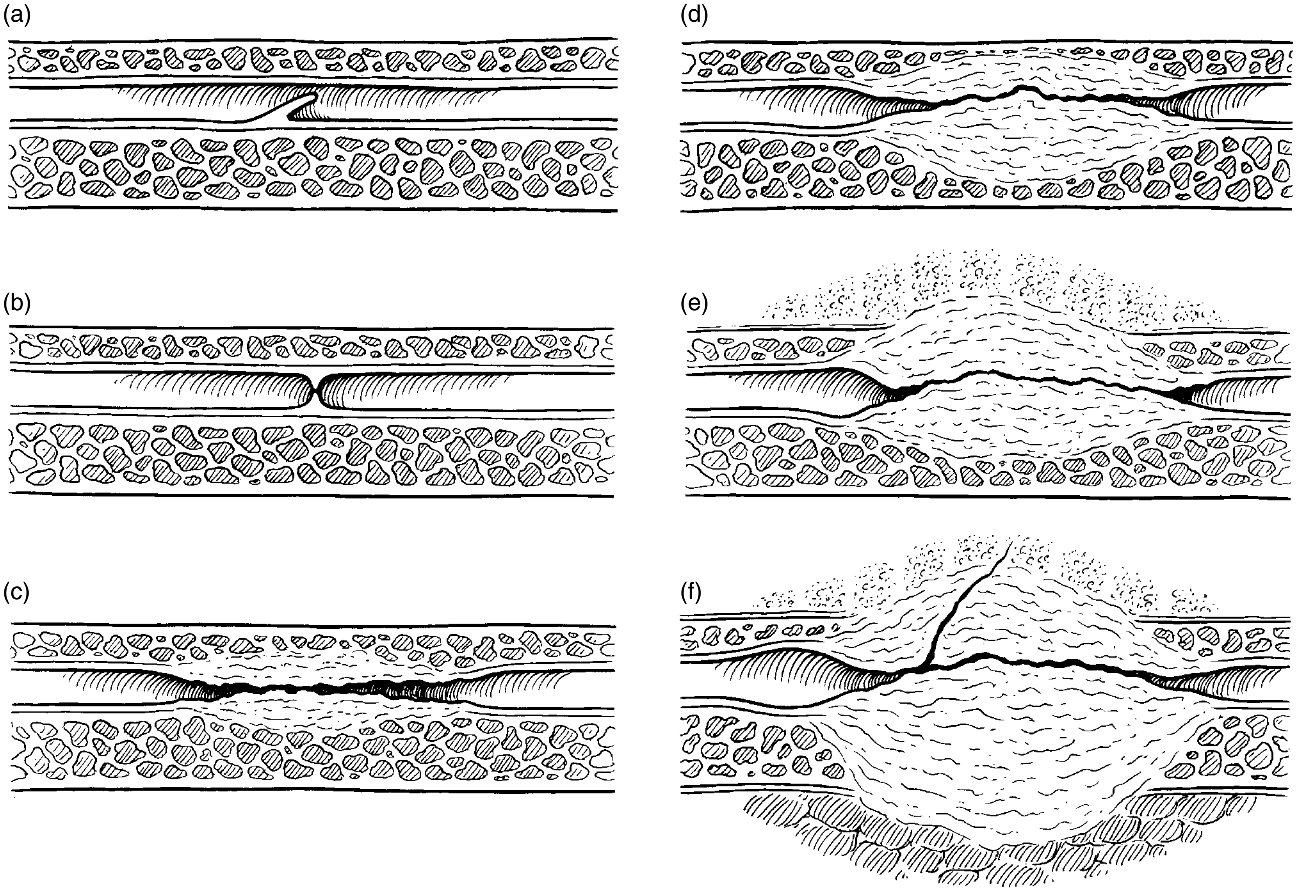

**Figure 158.4** Anatomy of anterior urethral strictures includes, in most cases, underlying spongiofibrosis. (a) Mucosal fold; (b) iris constriction; (c) full-thickness involvement with minimal fibrosis in the spongy tissue; (d) full-thickness spongiofibrosis; (e) inflammation and fibrosis involving tissues outside the corpus spongiosum; (f) complex stricture complicated by a fistula. *Source:* Jordan GH. Management of anterior urethral stricture disease. *Probl Urol* 1987;1:199–225. Reproduced with permission of Wolters Kluwer.

Finally, there are so-called congenital strictures. These strictures occur in infants, are short in length, noninflammatory, and not associated with potential for traumatic etiology. They are the rarest of all strictures.

Posterior urethral stenoses and anterior urethral strictures have many similar causes, although there are also several etiologies specific to the posterior urethra. Membranous strictures may result from urethral manipulation or radiation. Larger French resectoscopes, such as are used for transurethral resection procedures, may cause tearing of the membranous urethra as it departs the corpus spongiosum. Brachytherapy seeds placed distal to the apex of the prostate can lead to radiation damage to this portion of the urethra as well. Prostatic urethral stenosis is rarely encountered, although when seen it may result from iatrogenic endoscopic manipulation of the prostate. Bladder neck stenosis is seen commonly after transurethral resection or radical prostatectomy. It is usually manifest as a short-length stenosis of varying caliber at the junction of the urethra and bladder. In some instances, endoscopic procedures for prostatic enlargement (whether traditional transurethral resection or laser prostatectomy) are performed when there is an unrecognized underlying element of voiding dysfunction. In these cases, the symptoms that prompted treatment will certainly recur. Bladder neck stenosis typically responds well to endoscopic management, by gentle dilation or incision using cold knife, electrocautery, or laser techniques. A more severe form of bladder neck stenosis termed vesicourethral distraction stenosis can be a devastating consequence of radical prostatectomy. It occurs when the vesicourethral anastomosis is disrupted and leads to a longer defect that is quite resistant to endoscopic treatment. Posterior urethral distraction defects are commonly seen with anterior pelvic arch fractures. It has been classically taught that these fractures cause the prostatic apex to separate from the membranous urethra in the manner in which one would remove the stalk from an apple. Newer data, however, shows that these injuries typically occur more distally than the level of the prostatic apex. The level of the distraction defect is usually found just proximal to the departure of the membranous urethra from the corpus spongiosum and thus spares the external urinary sphincter. As in a vesicourethral distraction, this injury leads to extensive fibrosis interposed between the two distracted ends of urethra and is resistant to endoscopic management.

## Diagnosis and evaluation

Patients who have urethral strictures most often present with obstructive voiding symptoms, urinary tract infections, hematuria, dysuria, or urinary retention. Compensatory hypertrophy of the detrusor may initially allow patients to void through a narrowed urethral lumen with few symptoms. In addition, some degree of decreased urethral caliber may not significantly affect the flow dynamics. Patients may not develop significant symptoms until a reduced urethral caliber of 10–12 Fr is reached. Many of these patients will relate an insidious onset of voiding symptoms before progressing to obstructive symptoms or complete obstruction.

First, it is important to question the patient as to history of trauma, especially straddle trauma. A history of urethral infection, previous urethral, prostate or bladder surgeries, and previous catheterizations should be noted. A thorough genital exam should also be performed. Stigmata of hypospadias, lichen sclerosis, previous surgical interventions, and spongiofibrosis may be found. These clues revealed by history and physical exam may give the practitioner additional information as to the etiology of the disease process. This is important to know, as strictures of different etiologies may behave differently when treated.

Prior to any invasive manipulation or investigation, the presence of microorganisms in the urine should be assessed if possible. When the patient is in retention, this may not be feasible and broad-spectrum antibiotic coverage should be given prior to attempt at catheterization, endoscopy, or retrograde urethrography. Urine should be sent for culture when obtained. If it is a nonemergent situation, care should be taken to sterilize the urine prior to proceeding with investigation. In cases of colonization, such as exists in patients with chronic indwelling suprapubic cystostomy catheters, prophylactic doses of culture-specific antibiotics should be given. This is done not with the intent to eradicate colonization, but rather to prevent septicemia during the manipulation.

Passing a urethral catheter is commonly attempted when a patient cannot void. If the catheter does not pass, the nature of the obstruction is determined by dynamic retrograde urethrography. Many cases are managed with acute dilation, but this may not be in the best interest of the patient. When there is doubt, the nature of the stricture should be determined. A suprapubic cystostomy catheter can be used to treat the acute retention and give time to plan more appropriate treatment. Blind passage of filiforms or blind dilation is no longer considered acceptable. The anatomy of the stricture must be determined either through advanced imaging or flexible endoscopy, which at the least, allows the stricture to be visualized and a guidewire to be passed under direct vision through the lumen. In this manner, dilation is not done “blindly,” but with the wire to direct the dilators into the true lumen.

In addition to etiology, the location, length, depth, and density of the stricture (spongiofibrosis) or stenosis must be accurately determined in order to develop a workable treatment plan. The length and location of the stricture can be determined with traditional radiography, urethroscopy, and/or ultrasonography. Some feel that the absolute length of spongiofibrosis may not be evident by ultrasound evaluation alone. Contrast-enhanced studies may be further complemented by the addition of ultrasound studies and together are accurate in determining the length of narrow-caliber annularity [4]. Contrast studies of the urethra are best carried out by or under the direct supervision of the surgeon responsible for treatment of the patient. The depth and density of the scar in the spongy tissue are difficult to determine, but are subjectively best evaluated by physical exam, contrast-enhanced studies that show the appearance of the urethra, and elasticity and appearance of the mucosa by endoscopy. Although magnetic resonance imaging and ultrasonography have been used to help characterize the degree of spongiofibrosis and location of the defect, we find these studies rarely influence the treatment plan developed with traditional radiography and endoscopy.

At our center, imaging includes retrograde urethrography as well as voiding cystourethrography. The patient is placed in a steep lateral oblique position as anteroposterior images often miss lesions or misrepresent their length. Even with gentle technique, extravasation during retrograde urethrography is possible in patients in whom the urethra is markedly inflamed. For this reason, contrast studies should be carried out with contrast material that is suitable for intravenous injection and used either directly from the bottle or diluted according to the manufacturer’s guidelines. It should also be understood that during contrast-enhanced urethrography, more than one projection may be necessary to visualize the stricture. Real-time ultrasound evaluation of the urethra after it has been filled with a lubricating jelly or saline has been described by Morey and McAninch [4, 5]. It is a misconception, however, that ultrasonography always directly visualizes the spongiofibrosis. Morey and McAninch believe that ultrasonography of the bulbous urethra possibly more accurately determines the length of the stricture, which is important in considering an anastomotic repair [4, 5].

An initial endoscopic examination with flexible cystoscope may be necessary after the contrast studies to evaluate the urothelium and assess the degree of spongiofibrosis. A rigid pediatric scope is a very useful tool to help traverse an area of narrow-caliber disease without having to dilate it, as dilation may not be ultimately beneficial. Care should be taken to avoid inciting inflammation of a particularly narrow stricture by passage of the pediatric endoscope. This may cause temporary edema and lead to an episode of acute retention. In the patient who cannot void and has a suprapubic tube, combined contrast studies with endoscopy are helpful in defining the stricture anatomy (Figure 158.5). This evaluation allows delineation of the proximal point of the stricture by endoscopy, and the distal point by retrograde urethrography done simultaneously.

In selected patients, where longstanding outlet obstruction is suspected or where the degree of urethral obstruction does not correlate with symptoms, urodynamic studies may be warranted prior to treatment. Compensatory detrusor hypertrophy in cases of longstanding outlet obstruction may lead to myogenic detrusor failure. In this case, the patient may not void despite correction of the obstructive process. Correction may facilitate intermittent catheterization and thus may be appropriate, but this is an outcome that should be clearly understood by the patient prior to treatment. Likewise, when the degree of symptoms is more severe than would be expected from the degree of luminal narrowing, suspicion is raised for bladder dysfunction or concomitant prostatic obstruction. Video urodynamics maybe helpful to elucidate the level of obstruction, especially if

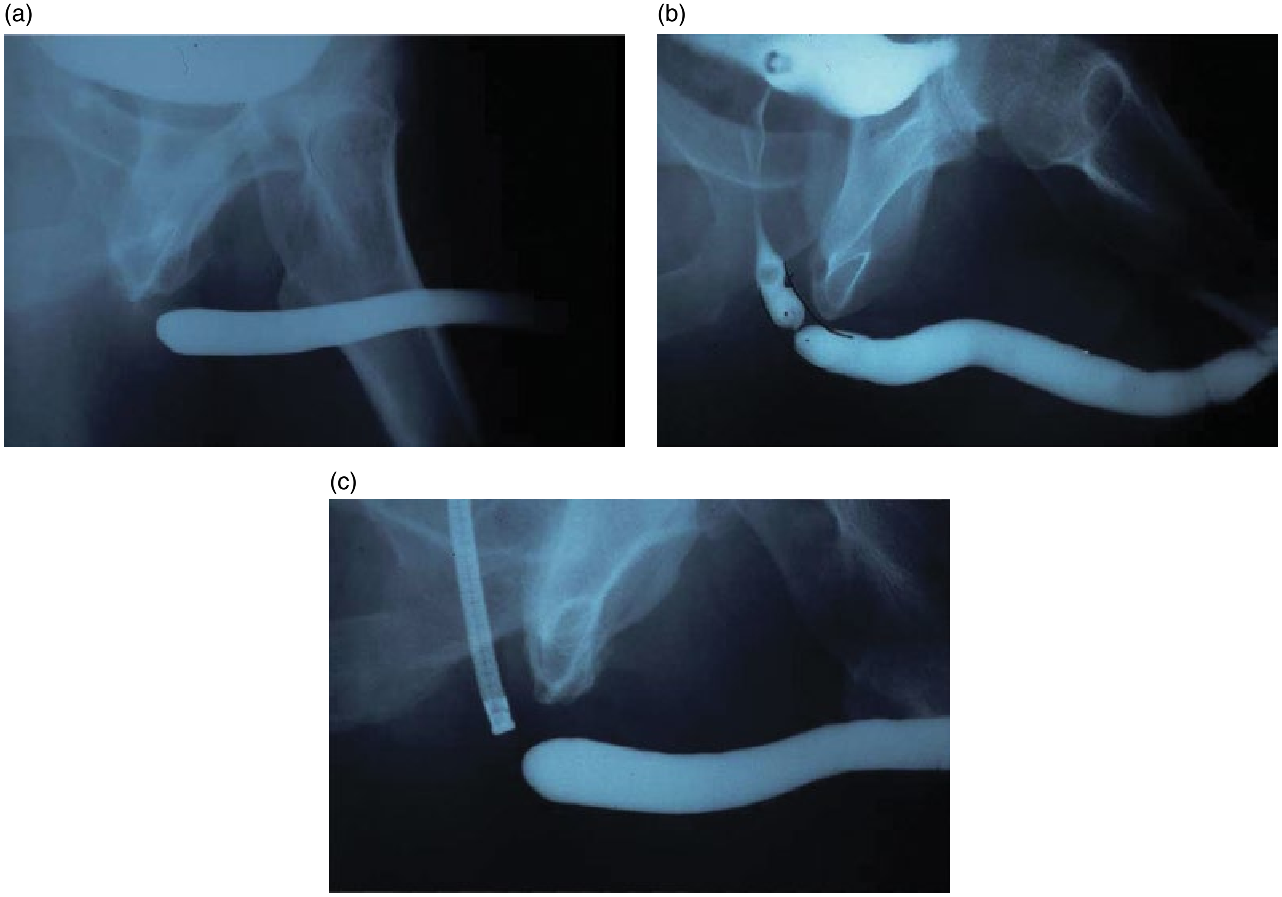

**Figure 158.5** Series of radiographs demonstrating the usefulness of the combination of contrast enhancement with endoscopy. (a) A retrograde urethrogram shows a totally obliterative process involving the proximal bulbous urethra. (b) The patient was successful in relaxing to void; however, there is a suggestion of a wide-caliber annular area proximal to the obliterative process of the bulbous urethra. (c) Endoscopy through the suprapubic cystostomy tube clarifies the anatomy of the proximal urethra and demonstrates the length of the obliterative process. *Source:* Devine CJ and Angermeier, KW. Anatomy of the penis and male perineum. *J Urol* 1994;8(11). Reproduced with permission of Elsevier.

prostatic or bladder neck hypertrophy is present. In these cases, treatment of the urethral narrowing alone may not alleviate obstructive symptoms. In addition, medical treatment of the prostate or bladder neck may decrease or resolve obstructive symptoms without need for treatment of the urethral pathology.

## Treatment

Both the patient and the physician must have a good understanding of the goal of treatment before the treatment choice is made. To this end, treatment options should be discussed with the patient, with care taken to emphasize the anticipated outcome with regard to palliation versus cure. Some patients may prefer palliative stricture management and choose to have periodic dilations in the office, at home, or in the hospital rather than undergo technically detailed open surgery. Others may have cure as a goal and choose open surgical management. The information gained in the evaluation of the stricture is imperative in discussing treatments and expected outcomes with the patient. A thorough knowledge of the etiology of the process is also needed in counseling on risk of recurrence. Many well-described reconstructive procedures utilized today have long-term success rates in excess of 90% and may be used to repair many common types of strictures.

### Dilation

Urethral dilation is the oldest and simplest treatment for urethral stricture disease. It is rarely curative unless the scarring only involves the superficial urethral epithelium. The goal of dilation is to stretch the urethra without tearing it. If bleeding occurs during the dilation, likely the urothelium has been torn rather than stretched and this will produce further scarring.

Filiform dilators have been used for years. The filiform leader is passed initially through the stricture. If the straight tip does not pass, there are spiral tips that may allow passage. The safest way to pass the filiform leader is under direct vision. Also available are a myriad of metal and plastic dilators that may be passed in a similar fashion. Again, blind dilation should be discouraged.

The least traumatic method would be soft dilation techniques over multiple treatment sessions. We believe the safest method currently available is the use of urethral balloon dilation. These catheters may be attached to a filiform tip or passed over a guidewire with an integral coudé tip. For the patient's initial dilation we prefer cystoscopy under anesthesia to allow for placement of a wire which facilitates safe passage of the balloon. In this setting the stricture is truly dilated. A home balloon obturation protocol can then be performed by the patient with the goal of maintaining the operative dilation. This minimizes the amount of repetitive trauma to the urethra and allows the healing process to stabilize while being periodically opposed by the home balloon protocol. We prefer to have the patient use a steroid cream as lubricant for the balloon to decrease urethral inflammation. In addition, oral antibiotic therapy may be used as an anti-inflammatory agent. Initially, the patient starts the obturations several times daily, then daily, then weekly and steadily decreases the frequency as the process allows. This protocol allows for treatment of most types of urethral stricture/stenosis, although as previously stated, distraction defects of the posterior urethra are very difficult to manage in this fashion.

Meatal dilation in cases of meatal stenosis secondary to lichen sclerosis has also been proven to be an effective management strategy. It is easy for patients to perform home dilations using a graduated dilator lubricated with steroid cream. The patients must be thoroughly counseled on proper technique and the goals of dilation if this is to be successful. Frequent nonaggressive episodes of dilation are favored over periodic forceful episodes. In addition to limiting trauma, the patients will usually find dilation to be more comfortable, as very little pain and no bleeding should be encountered. By limiting the amount of distal obstruction, proximal dilation and extravasation should also be minimized, thus decreasing proximal inflammation and possibly stricture formation. With initial persistence and patience, many patients find that eventually the meatal process stabilizes and only infrequent interventions are needed.

Dilation has been shown to be equal to direct-vision internal urethrotomy (DVIU). Steenkamp et al. performed a randomized prospective trial comparing DVIU to filiform dilation in 210 men with urethral strictures [6]. Their results show a 16% greater recurrence rate at 36 months in the dilation group compared to the DVIU group and a 10% higher recurrence rate at 48 months. Stormont et al., in a retrospective review of 199 nonrandomized patients with short bulbar strictures treated with dilation or DVIU, showed that the success rates were equal [7]. At 3 years success rates for the dilation group was 65% compared to 68% for the DVIU group. Because this was a nonrandomized retrospective review there was some selection bias which cannot be excluded.

Complications associated with urethral dilations include cystitis, epididymitis, hemorrhage, recurrent urethral stricture, and false passage.

### Internal urethrotomy

Internal urethrotomy refers to a procedure that opens the stricture by incising it transurethrally. The procedure involves incising through the scar to healthy tissue to allow the scar to expand the lumen with a goal that it will heal with larger caliber. The process of incision essentially sets off a race between epithelialization and wound contracture. If the incised areas epithelialize (i.e. heal by secondary intent) before the wound contracts then the area will stay open. If not, then the stricture has recurred. As with dilation, the goal is to minimize trauma to the unaffected adjacent tissues.

The technique of a cold knife urethrotomy is relatively simple procedure using a 0 or 12° scope with a 19 or 21 Fr sheath. It is important to use isotonic fluid, usually normal saline, to limit the risk of hyponatremia if there is extravasation and possibly the isotonic fluid effect on the tissues during the procedure may be less injurious. A glidewire or ureteral catheter should first be passed through the stricture into the bladder. Something should always be passed through the area before incision to maintain identification of the true lumen. Many surgeons will make the incision at the 12 o'clock position, although we question this because of the location of the urethra within the corpus spongiosum (see Figure 158.2). On cross-section of the corpus spongiosum the thinnest portion is the anterior aspect between 10 o'clock and 2 o'clock. Therefore a deep incision could penetrate through the corpus spongiosum into the intracrural space or corpus spongiosum if the incision is further distal. These incisions into the corpora cavernosa have been associated with erectile dysfunction, likely due to veno-occlusive dysfunction. If it is felt that the spongiofibrosis is deep, an internal urethrotomy will not be curative. We prefer using multiple small radial incisions at 10, 2, and 6 o'clock without cutting too deep into the corpus spongiosum.

Cure rates following DVIU initially were felt to be 80% or above and at first this caused an increase in the use of internal urethrotomy. In addition, many practitioners were more familiar with this type of management than with open urethral reconstruction. The idea of a "reconstructive ladder" was thus popularized. Many felt that it was appropriate to perform multiple endoscopic procedures on recurrent strictures in lieu of opting for open reconstruction. This has since been proven to be faulty logic. Subsequent studies have borne out the issues of endoscopic success and the effect of multiple endoscopic treatments on open reconstruction. Success rates following DVIU have been shown to vary between 35% and 90%. This variation may be dependent on length of stricture, previous treatments, and length of follow-up assessed.

The nature of the strictures being treated with internal urethrotomy has been poorly reported and with various endpoint parameters. This makes comparative assessment difficult because the literature is not clear as to the goal of internal urethrotomy. For many, internal urethrotomy is considered successful if it offers temporary relief. Santucci and McAninch reported curative success rates to be approximately 20% using actuarial techniques [8]. Pansadoro and Emiliozzi as well as others have showed that DVIU is curative in 30–35% [9]. Their study did not show any long-term success for strictures outside of the bulbar urethra. Data show that strictures in the bulbar urethra that are less than 1.5 cm in length not associated with dense, deep spongiofibrosis can be managed with internal urethrotomy with 74% success rates. It has been shown in multiple studies that success of urethral reconstruction is diminished by multiple prior urethral dilations or internal urethrotomies [10–12] (L. Boccon-Gibod, 2005, personal communication). Some have shown a single internal urethrotomy prior to an open urethral reconstruction to be cost effective [13]. Others have refuted this finding and found urethrotomy to lengthen the stricture and make subsequent reconstruction more difficult [14]. In any event, a single attempt at urethrotomy is probably warranted if all of the available criteria favor the chance of success. Otherwise, it may not be cost-effective or of any benefit to the patient if these criteria are not met.

Recurrence of the stricture is the most common complication associated with internal urethrotomy. Complication rates following internal urethrotomy range from 8% to 27%. Complications associated with internal urethrotomy include dysuria, urinary tract infection, septicemia, minor bleeding, retention, scrotal abscess, extravasation, urinary sepsis, and epididymo-orchitis. Erectile dysfunction has also been reported as a complication after internal urethrotomy in up to 11% of patients. Possible causes could be fibrosis after extravasation with infection or injury to the cavernous nerves with deep incision. Other more uncommon complications include urethral–internal pudendal artery fistula leading to high-flow priapism, severe hemorrhage, and urosepticemia. These complications are unusual and are usually associated with aggressive internal urethrotomy.

Since the success rate with internal urethrotomy is so poor, several techniques have been employed to oppose the wound contraction. One option is to leave an indwelling Foley catheter for six weeks after urethrotomy, hoping the urethra will mold around the catheter as it heals. Studies have shown that the failure rates with this technique are equal to those leaving a catheter for 3–7 days. Another option used to oppose the wound contraction forces is home self-catheterization. The catheter is left in place for 3–7 days and once removed the patient is started on a urethral catheterization program. This usually requires more catheterizations in the first 3–6 months but then tapering thereafter. It is our experience that once the patient stops the self-catheterization the stricture recurs, but this technique can effectively manage motivated patients. However, as already discussed, protocols using catheters or balloon obturation can successfully manage patients.

Other techniques used to decrease recurrent stricture formation at the time of DVIU include the injection of steroids or mitomycin C (MMC) at the time of DVIU. MMC has been proposed because of its ability to mitigate scar formation via inhibition of fibroblast proliferation. MMC is injected 0.4 mg/ml in 0.2–0.4 ml for a total of 5–10 ml. This was initially described by Vanni et al. for bladder neck contractures but has been also used recently in urethral strictures with promising results, although longer follow-up is needed [15]. There have been significant complications associated with the use of MMC in bladder neck contractions and therefore its use in urethral strictures need to be monitored closely. Injection of steroids into the stricture may prevent scar formation by enhancing endogenous collagenase and reducing recurrent stricture formation. Mazdak et al., in a randomized control trial using DVIU and 40 mg triamcinolone versus DVIU alone, showed a decrease in recurrence from 50% in the control group to 21% in the treatment group [16]. Standardization of the use of MMC and steroids has not been done so comparisons at this time are difficult.

It has been shown that the length of follow-up as well as length and location of the stricture are of utmost importance in determining success. Boccon-Gibod and Le Portz had a 56% cure rate at 6 months, 43% at 12 months, but only 25% at 2 years [17]. Albers et al. confirmed the lower success rates over time with 95% at 6 months cured, but with longer follow-up at 38 months the success rates dropped to 55% [11]. With a repeat urethrotomy the success rates appear to decrease. One study showed a success rate of 75% with the initial treatment but only 45% success for a secondary treatment. Length of stricture also has a significant effect on recurrence. Steenkamp et al. showed success rates for strictures greater than 4 cm to be less than 20% compared to a success rate of 40% for strictures less than 2 cm at 12 months [6]. Finally a number of studies have shown higher success rates with strictures in the bulbar urethra compared to the penile urethra.

Dilations and/or urethrotomies may be used as part of a palliative strategy almost anywhere in the urethra. With some persistence on the part of a motivated patient and a favorable stricture etiology, some strictures may only need periodic maintenance. Conditions such as lichen sclerosis that have a high propensity for recurrence are often treated in this fashion as few if any "curative" options have been discovered. If either of these methods, however, are being used with a notion of curative intent, the characteristics of the process must be carefully evaluated. The highest reported success rate is in short (<1.5 cm) mucosal strictures of the proximal bulbous urethra as mentioned above. Attempts to manage more distal anterior urethral strictures or stenoses of the posterior urethra will likely have no durable result. In addition, if a single attempt at dilation or urethrotomy fails, subsequent attempts should also be expected to fail. Particularly dismal are the results after dilation or incision of a vesicourethral distraction defect or posterior urethral distraction defect. Incision of a bladder neck stenosis after transurethral resection or radical prostatectomy may be the only exception to the rule of posterior urethral stenoses; these do respond nicely to endoscopic management.

## Lasers

The ideal laser for use in the treatment of urethral strictures is one that totally vaporizes the scar, exhibits negligible peripheral tissue destruction, is not absorbed by water, and is easily propagated along the fiber. As with previously described treatment modalities, care should be taken to minimize injury to adjacent tissues as this may worsen the disease process. There are several types of lasers used for the treatment of urethral stricture disease, including carbon dioxide, argon, potassium titanyl phosphate (KTP), Nd:YAG, holmium:YAG, and excimer lasers. Although carbon dioxide laser appears to be ideally suited, it must be used with a gas cystoscope, which carried the potential risk of carbon dioxide embolus.

For both the argon and Nd:YAG lasers the mode of action is thermal necrosis, which has significant potential for peripheral tissue injury rather than vaporization. The Nd:YAG laser is also used with a bare fiber in contact mode, which carries a risk of forward scatter. Used in the contact mode the YAG energy is transferred to a sapphire tip which will obliterate the scar by vaporization of the tissue. There are no data showing improved results when comparing obliteration to DVIU.

A KTP laser is essentially a Nd:YAG laser that has passed through a KTP crystal, resulting in a reduced depth of penetration. The internal urethrotomy accomplished with the KTP laser is done by passing the fiber over the scar tissue. The holmium:YAG laser has properties similar to the KTP laser and provides both direct cutting and vaporization with minimal scatter. Numerous studies have shown safety with the use of holmium:YAG laser in the treatment of urethral strictures, but success rates appear to be comparable to those for DVIU.

The excimer laser is a vaporizing laser with little forward scatter or peripheral tissue necrosis. Little experience with this laser has been reported but its characteristics warrant further investigation.

The results of laser urethrotomy are mixed but with the advent of new lasers future data may show improved results. A laser with perfect characteristics for treating urethral stricture disease does not seem to exist at this time. Currently, no data exist to show superiority of laser urethrotomy over other techniques. Its indication for usage is similar to that of dilation or cold knife urethrotomy, as previously discussed. Short bulbous strictures, prostatic urethral stenoses, and bladder neck stenoses are the most likely to respond to laser urethrotomy. Little to no durable results should be expected from utilizing laser urethrotomy in more distal anterior urethral strictures, vesicourethral distraction defects, or posterior urethral distraction defects.

### Urethral stents

As discussed previously, when wounds heal, the healing process may turn into contraction. Urethral stents (removable or permanent) are another modality used in opposing the forces of wound contraction after internal urethrotomy or dilation, allowing re-epithelization prior to recurrent stricture formation.

The UroLume® stent (American Medical Systems, Minnetonka, MN, USA) is a permanent, biocompatible, nonmagnetic superalloy woven into a tubular mesh which is self-expanding to 42 Fr. After being deployed it is incorporated into the wall of the urethra and the corpus spongiosum. The UroLume stent is for patients with short bulbar strictures less than 3 cm in length and at least 1 cm from the external sphincter. Available data show that the stent is best employed for short strictures associated with minimal spongiofibrosis. Initial results with the UroLume stent were encouraging, with retreatment rates decreasing from 75.3% to 14.3% after insertion in 105 patients who were followed for 1 year [18]. With longer follow-up, the findings of the North American Study Group show of the 179 patients originally enrolled, 24 patients completed 11 year follow-up. The overall success rate for all patients enrolled at 11 years was less than 30% [19]. This was confirmed in a study with 10-year follow-up from the Netherlands which reported that only 2 of the 15 patients implanted were satisfied [20]. Complications rates with this stent were high and included recurrent stricture, migration of the stent, dysuria, hyperplastic tissue growth, migration of the stent, recurrent urinary tract infections, dysuria, calculus formation and hematuria. The UroLume was removed from the market and is currently not available for implant.

The concept of a temporary rather than permanent stent is appealing. The idea is to leave the stent in place long enough to act as a mold until the wound stabilizes, preventing scar contraction during the healing process. The Memokath urethral stent (PNN Medical, Kvistgaard, Denmark) is made of nitinol and is currently available in Europe, but not in the United States (it is currently under investigation). The Memokath is a thermo-expandable stent, Once it has been placed in position, prewarmed saline is flushed through the stent and urethra, expanding the stent and the bell-shaped ends, which secures the stent in place. The main body of the stent is 24 Fr, with the bells expanding to 44 Fr. The tight spiral structure of the stent prevents urothelial ingrowth.

A large multicenter study evaluated Memokath stents compared to no stent after urethral dilation or urethrotomy in patients with recurrent stricture [21]. The authors concluded that after internal urethrotomy or dilation the stent significantly prolonged time to retreatment compared to the control group. In another study 22 consecutive patients with a recurrent bulbar stricture, mean length 2.4 (1–4.5) cm, underwent DVIU or dilation and subsequent placement of a Memokath stent [22]. All patients underwent stent removal three months after and were then followed clinically with a cystoscopy at 12 months. In this study 17/22 (78%) of the patients remained stricture-free with a median follow-up at 23 months. Those that recurred usually did early and this was thought by the authors to be secondary to spongiofibrosis. Another stent under investigation is the Allium™ bulbar urethral stent (BUS), which is a fully covered, self-expandable, large-caliber metal stent designed for treatment of bulbar urethral strictures. Early studies look promising but more data are needed [23].

## Conclusion

Initial evaluation of a patient with a urethral stricture/stenosis should include a thorough history and physical exam. Length of duration of symptoms, history of trauma, infection, or surgery should be noted. The genitalia should be inspected for scars, inflammatory changes, stigmata of previous treatment, and the entire course of the corpus spongiosum should be palpated and assessed for fibrosis. Thorough radiographic and endoscopic evaluation should also be performed. After the length, location, depth, density, and proposed etiology of the process is known, the patient should be counseled as to palliative versus curative intent of any intervention. In cases of acute urinary retention, thought should be given to placement of a suprapubic cystostomy catheter in lieu of dilation in selected patients.

Only in very carefully selected processes should endoscopic attempts at management be considered to have a reasonable chance at cure. Although both dilation and DVIU have similar rates of success, these rates are only favorable in short, superficial, noninflammatory, proximal bulbous strictures. Any other attempts should be considered palliative. Multiple attempts should not be made in patients who are considered candidates for an open reconstructive procedure. Certain types of strictures, such as those of the meatus and fossa navicularis, may respond well to interval dilation. Other processes, such as posterior urethral or vesicourethral distraction injuries typically do not. That being said, endoscopic management may be very reasonable for a variety of patients and is appropriate as long as the goals are clearly stated and understood.

Currently, there is no laser or urethral stent available that has been shown to drastically revolutionize endoscopic management of urethral stricture/stenosis with or without injection of MMC or steroids. Further study is needed to identify and replicate the characteristics of these tools so that they provide ideal minimally invasive management of this often difficult disease process. For many patients who desire a curative procedure, open surgical reconstruction remains the gold standard at this time.

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# 159

# Endoscopic Management of Bladder Neck Contracture Following Radical Prostatectomy

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## Introduction

Bladder neck contracture (BNC) is a well-recognized phenomenon following radical prostatectomy. Also referred to as a vesicourethral anastomotic stricture, this is a different entity from strictures following nonextirpative prostate surgery (e.g. transurethral resection) [1]. Both the definition and the reported incidence of BNC vary within the literature, but recent reports suggest that such fibrosis is becoming less common in the era of robot-assisted radical prostatectomy (RARP). Most providers recognize problematic stenosis as that which precludes passage of a 16 Fr flexible cystoscope. Previously reported rates were as high as 30%, but this has decreased to less than 5% across most modern series [2–5]. Fortunately, many clinically diagnosed cases can be managed effectively with endoscopic intervention. However, recalcitrant contractures may require chronic dilations or patient self-calibration, aggressive open reconstruction, or formal urinary diversion. Some patients may even adopt chronic indwelling catheters to avoid repetitive procedures and the need for pad use or anti-incontinence surgery.

## Etiology

Fibrosis stems from a pathological accumulation of extracellular matrix as part of a wound-healing response. Ideally, healing of the vesicourethral anastomosis would involve optimal blood flow and the absence of excess inflammation. Numerous technical and patient-related factors have been implicated as risk factors for the development of BNC. Urinary extravasation, operative time and blood loss, radiotherapy, surgeon experience, prior outlet procedures, tobacco usage, age, and body mass index (BMI) have all been suggested [6]. Comorbidities such as hypertension, diabetes, and heart disease also seem to increase risk of BNC [7]. Although duration of postoperative catheterization does not appear to be associated with BNC development, early urinary retention after radical prostatectomy increases the risk by nearly fivefold [8]. It seems possible that some cases of obliteration may be due to intrinsic fibrosis (e.g. related to ischemia), whereas others may be from extrinsic fibrosis (e.g. external compression spurred by urinary extravasation).

In 2013, Mucciardi et al. reported on an association between preoperative detrusor underactivity and formation of subsequent BNC [9]. Based on their design, 100 men underwent urodynamic testing prior to radical prostatectomy, with underactivity seen in 60%. This was determined via bladder contractility index ($5Q_{\max} + P_{\det}Q_{\max}$), power at maximum flow, and maximum velocity of detrusor contraction. Following radical prostatectomy, 12 men developed BNC, all of whom had detrusor underactivity, with significant correlation to the severity of dysfunction. The functional state of the bladder may be a surrogate for the overall integrity of the tissue, which may reflect the potential for optimal wound healing.

The ideal surgical technique to prevent BNC is not firmly established. Traditional surgical principles in mucosal anastomoses involve eversion of mucosa with direct apposition, and a well-vascularized and watertight approximation. Failure to properly appose mucosa has been shown to increase the rate of contracture [10]. However, this dogma was brought into question based on reports of improved outcomes with minimally invasive surgery which, unlike open radical prostatectomy, commonly involves a running anastomosis.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Multiple groups have since incorporated a running suture without mucosal eversion during open radical prostatectomy, and have reported an absence of subsequent BNC [11, 12],

As with any anastomosis, visualization is critical. The superior optics afforded by robotic surgery may partially explain the falling rate of BNC, as open radical prostatectomy has become much less common. A multi-institutional study noted a BNC rate of 4.7% following open radical prostatectomy, versus a 0% rate after RARP [5]. Based on multivariate analysis, the only predictive factor was increased length of time before drain removal. This was felt to be a surrogate marker for urinary extravasation. Other authors have suggested that extravasation does not increase the rate of BNC as long as the urethral catheter is maintained until resolution [10]. Laparoscopic and RARP may allow for BNC development via an alternative mechanism. In 20% of BNC after a series of RARP, a foreign body had migrated into the anastomosis [3]. Multiple reports describe this phenomenon as related to Hem-o-lok clips [13–16] (Figure 159.1).

The issue of bladder neck caliber has been debated over time. Previously, it had been thought that sparing of the bladder neck would lead to preservation of continence based on the internal sphincter. However, doing so actually seems to predispose patients to development of BNC based on a small prospective trial [17]. Multiple series have shown that a nonsparing approach with tailoring of the bladder neck to approximately 24 Fr results in lowering the incidence of BNC [18, 19]. Adoption of a nonsparing approach may also alleviate concerns about unnecessarily increasing the risk for a positive surgical margin. However, the potential benefit from increased surgeon experience over time cannot be dismissed. Thus, when surgeons attempt to attribute improvement in outcomes to changes in technique over time, this is confounded by the fact that their experience increases with each additional case.

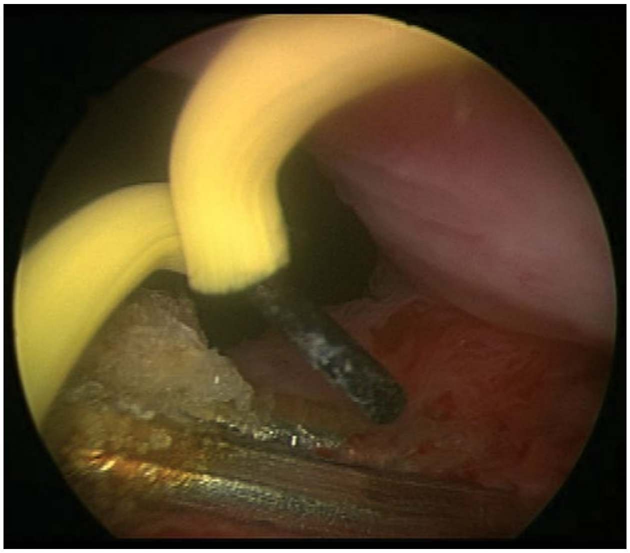

**Figure 159.1** Metal clip at bladder neck.

The impact from radiotherapy seems to vary based on whether it comes before or after surgery. Radiation is felt to result in obliterative endarteritis that predisposes to fibrosis and even tissue necrosis. When administered after radical prostatectomy, the rate of BNC is relatively low (2.6%), without a significant difference between adjuvant versus salvage cases [20]. Salvage radical prostatectomy after radiotherapy, however, results in a higher rate of BNC when compared to open radical prostatectomy in the absence of radiation [21]. BNCs in this setting were also found to be much more difficult to manage [22].

## Evaluation

Patients may be diagnosed with BNC based on obstructive symptoms, urinary retention, or incidentally, based on difficulty with placement of a urethral catheter. Thus, the incidence is likely underestimated. Once patients have been identified, a thorough history should identify all details related to prior surgery, radiation therapy, transurethral instrumentation, and status of urinary continence. It is possible that some patients may owe some of their urinary control to “pathologic continence” consequent to a fibrotic outlet and must be informed that intervention may result in worsening of incontinence [23]. With regard to modifiable risk factors that could impact success of intervention, it is conceivable that tobacco cessation may offer benefit. On multivariate analysis, smoking has been found to be a risk factor for failure of endoscopic management of BNC [24].

Cystoscopy offers formal evaluation of the degree of stenosis. The examining urologist can also acquire a visual impression of the area of the external sphincter and the remainder of the urethra is inspected for any other areas of stricture. It is important to determine, if possible, if the area of obstruction is actually a sphincteric stricture rather than a BNC. Although many cases may be successfully managed at the time of initial cystoscopy with concomitant dilation, others may be recalcitrant and additional data gathering becomes important. If the bladder can be inspected prior to management of a recurrent BNC, one should examine for worrisome changes, such as trabeculation and/or inability to tolerate a reasonable volume of infused irrigation. The location of the ureteral orifices relative to the bladder neck should be noted. Formal urodynamic studies may be useful in some cases, especially if the patient has received radiotherapy. A negative urine culture should be verified prior to procedural intervention.

## Management

### Transurethral dilation

Most BNC will be identified within six months of surgery and can be successfully managed with an initial dilation. This is commonly performed in the office with urethral sounds or filiforms and followers. Blind dilation is ill-advised and may result in false passage and even fistula. Placement of a guidewire via a cystoscope can facilitate the use of a dilating balloon. This applies radial force for controlled dilation and avoids the shearing forces and multiple passes of rigid dilators. Balloons chosen for this purpose may vary between 3 and 6 cm in length, and may increase the lumen to as large as 30 Fr. Controlled inflation under cystoscopic guidance is typically performed up to 14–18 atm for several minutes before deflation and repeat inspection of the bladder neck. Others have described using contrast in the balloon and performing this maneuver via fluoroscopic guidance until the compressive deformity is no longer evident [25]. Success rates with balloon dilation range from 59% to 100% [7, 25–27].

### Transurethral incision

Although commonly employed after failure of an initial office dilation, transurethral incision of bladder neck contracture (TUIBNC) may also be used as a first-line intervention. The typical technique involves 2–4 radial incisions into the fibrosis until the appearance of vascularized tissue or, in some instances, perivesical fat (Figure 159.2). The goal is to enlarge the bladder neck to approximately 24–30 Fr, or to a level where stenosis would be clinically insignificant, and to disrupt the scar in multiple places. Cold knife, electrocautery (Collings knife), or laser can be used to incise the contracture. Once incision has traversed the depth of the fibrosis, bleeding may result and having a modality that also allows hemostasis seems advantageous. Incisions should be directed laterally and the 6 o'clock position should be avoided to prevent inadvertent entry into the rectum. An indwelling urethral Foley catheter (typically 20 Fr or larger) is typically left at the conclusion of the procedure and for 3–7 days.

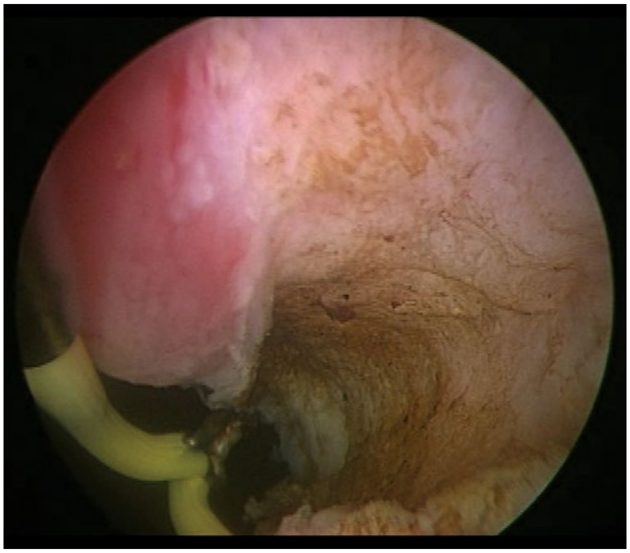

Figure 159.2 Deep lateral incision to perivesical fat.

Review of a 15-year experience with cold-knife TUIBNC for recalcitrant BNC noted a success rate of 73% with either one or two total interventions [22]. Ramirez et al. reported use of a dilating balloon to 24 Fr followed by Collings knife incisions into the fat at 3 and 9 o'clock [28]. Of their 50 patients, 72% achieved success with one procedure, and an additional 14% remained patent with two procedures at a mean follow-up of nearly 13 months.

The holmium laser has also been used in multiple series, and affords the ability to both incise and ablate tissue; it has a defined depth of penetration (0.4 mm). In a comparison between this modality and balloon dilation, TUIBNC, and UroLume stent placement, holmium laser was felt to be most successful in management of BNC, with a success rate of 60% following a single procedure [24]. In a series of 10 patients, Largerveld et al. used a 365 μm fiber at settings of 1 J and 10 Hz (up to 20 Hz if necessary), to incise at 6 o'clock and vaporize from 3 to 9 o'clock [29]. At a mean follow-up of 18 months, there were no recurrences, complications, or worsening of incontinence. Hayashi et al. also found unanimous success in three patients with recurrent BNC using similar technique with follow-up at 11 months [30].

### Intralesional injections

Based on the fibrosis inherent to BNC, multiple attempts have been made to incorporate intralesional injection of agents with potential to augment the wound-healing response after TUIBNC. These have included steroids and antifibrotic agents, most notably mitomycin C (MMC). Following holmium laser incision, Eltahawy et al. injected triamcinolone (40 mg/ml) in 24 patients with recurrent BNC [31]. The majority (83%) had success with one procedure at 24 months, with the remainder only requiring one additional treatment.

In 2011, Vanni et al. reported on outcomes of TUIBNC with concomitant intralesional injection of MMC in 18 patients [32]. Despite having recalcitrant BNC, 72% of patients achieved patency with a single procedures, and another 22% found success with an additional 1–3 procedures. Similarly, Koslov noted patency in all patients treated with this regimen with only 11% of patients requiring a second procedure [33]. In contrast, a combined study of TUIBNC with MMC across eight institutions reported a success rate of only 58% at nine months [34]. In addition, they noted two cases of osteitis pubis and two instances of partial bladder necrosis following subsequent urinary diversion, which led to chronic pain in one patient and rectourethral fistula in the other. At least one group has tried to assert the strength of simple TUIBNC in the absence of intralesional MMC [28]. However, nearly a quarter of the patients in that retrospective single-surgeon study had no prior treatment and many cases were clinically insignificant as they were found incidentally after referral for incontinence. Even with a more favorable population, the outcomes were inferior to those of Vanni et al., and when aggressive TUIBNC was repeated, half the patients failed again. Thus, it seems that further investigation of intralesional adjunctive therapy is worthwhile.

## Intraluminal stenting

Previously, the UroLume Wallstent was used to stent the bladder neck after TUIBNC with initial reports of reasonable success. Unfortunately, there was a high rate of adverse events, including encrustation, tissue ingrowth, infections, hematuria, and pain [35]. Many recipients also developed severe stress urinary incontinence following placement of the device. In 2014, American Medical Systems ceased production of the UroLume, with no alternatives available in the United States. Trials of removable stents (e.g. Memokath SW 28, Allium RPS) in other countries have generated enthusiasm, but future studies are required.

## Endourethroplasty

Although it was originally described for urethral strictures, endoscopic incision and grafting has also been applied to management of BNC [36]. Following TUIBNC, a cystostomy catheter is placed. After 3–5 days, a meshed preputial graft is tubularized around a 22 Fr urethral catheter, which is placed across the bladder neck. The graft is anchored to both the catheter and the perineum with dissolvable suture. Chiou et al. reported success with this approach in two patients at 11 months follow-up [36]. In a similar approach that involved antegrade passage of a fenestrated forearm graft on an endobronchial catheter, Kuyumcuoglu et al. achieved success in 6/11 (54.5%) patients based on cystoscopy at 12 months [37]. Although this is an intriguing concept, given that simple TUIBNC affords similar success the data do not seem robust enough to support this form of management.

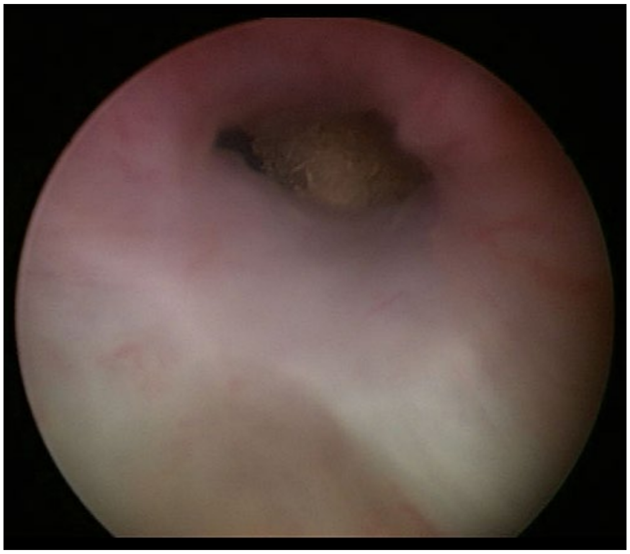

**Figure 159.3** Bladder neck contracture with calculus.

## Surgical reconstruction and urinary diversion

Some patients may not find durable patency despite multiple attempts at endoscopic management. Repeat trips to the operating room can be both frustrating and costly for patients. In addition, failure to definitively correct the BNC may preclude anti-incontinence surgery (e.g. artificial urinary sphincter) for otherwise eligible patients. Although some patients may be offered regimens of self-dilation, data suggest this affords a poor quality of life [38]. Findings on open reconstruction are limited to small series, and this approach has been discouraged by some because of the potential for complications [39]. However, a recently reported single-surgeon series of open reconstruction achieved 92% patency in 12 patients at a median follow-up of 75.5 months [1]. Only 25% of patients were continent postoperatively. In some instances, the degree of tissue devastation and the clinical picture (i.e. small/contracted bladder, dystrophic calcifications of the bladder neck, desire to avoid multiple future procedures to achieve continence, etc.) may prompt consideration of urinary diversion (Figure 159.3).

See accompanying Video 159.1.

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# 160

# Single-incision Slings

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## Introduction

Stress urinary incontinence (SUI) is the complaint of involuntary leakage of urine with effort, exertion, sneezing, or coughing as defined by the Standardization Sub-Committee of the International Continence Society [1]. SUI affects approximately 25% of women in the United States between the ages of 30 and 60. Surgical therapy has remained the mainstay treatment, although several alternative treatments are available. Anti-incontinence surgical procedures initially emerged in the form of pubovaginal slings, Burch colposuspensions, and bladder neck suspensions, which are still viable treatment options. However, over the last decade, minimally invasive synthetic sling procedures have evolved into the most commonly performed surgical treatment for SUI [2–4].

The era of minimally invasive sling procedures began when Petros and Ulmsten introduced the "integral theory" of female urinary incontinence in 1990 [5]. The theory suggests that a weak pubourethral ligament causes inactivation of the muscle forces which contribute to urethral and bladder neck closure in the regulation of continence. Their subsequent exploration of this topic demonstrated that a damaged or lax ligament is unable to be tightened effectively with sutures, but could be supported at the mid urethra with an artificial neoligament. Thus, Petros and Ulmsten developed the first tension-free polypropylene mesh sling to support the mid urethra. The sling successfully provided continence by reinforcing the pubourethral ligaments with a midurethral tape anchored retropubically [5, 6]. The benefits of this new methodology resulted in acceptable cure rates with decreased morbidity compared with previous pubovaginal slings and Burch colposuspension procedures [6].

Since Petros and Ulmsten's groundbreaking work, synthetic midurethral slings, from retropubic to transobturator, and now single-incision slings (SIS) have steadily evolved. Development of slings has focused on decreasing the unexpected morbidity associated with minimally invasive sling procedures, while striving to retain the 82–95% cure rates seen at 1 year with the "gold standard" Burch procedure [2].

## Midurethral slings

### Retropubic polypropylene tape sling

Petros and Ulmsten developed tension-free vaginal tape (TVT), the first minimally invasive retropubic polypropylene tape (RPT) sling procedure performed under local anesthesia for SUI. The TVT procedure begins with the injection of local anesthetic abdominally and vaginally along bilateral trocar paths. Through a 1.5 cm vaginal incision, bilateral periurethral dissection is performed to the inferior aspect of the pubic symphysis. Trocar needles with attached prolene mesh tape, covered by a plastic sheath, are inserted into the vaginal incision and then passed through the urogenital diaphragm, into the retropubic space just deep to the pubic bone and then out through the suprapubic area. Cystoscopy is routinely performed post procedure to rule out bladder perforations. After the tape is placed at the mid urethra and adjusted with a cough test to ensure continence, the plastic sheath is removed and incisions are closed [5, 6].

Initial 3-year data demonstrated that Petros and Ulmsten's new RPT sling resulted in 86% cure rates and 11% improvement rates [6]. Long-term results observed

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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by Nilsson et al. over an 11.5-year period reported subjective cure rates of 77% and improvement rates of 20% [7]. Randomized controlled trial evidence suggests that TVT has a similar cure rate to colposuspension [8, 9]. Since 1998, several RPT slings have been marketed as either transvaginal or suprapubic needle insertion techniques.

Although the reported efficacy of RPT slings was promising, the blind passage of trocar needles into the retropubic space created a new set of potential complications. A review by Atherton et al. showed that RPT procedures were associated with a 0.2–1% postoperative urinary retention rate, a 3–4% risk of bladder, urethral, or intestinal perforation, and a 1–2.5% risk of major vessel and nerve injury and hematoma in the retropubic space [10]. The incidence of these complications, although infrequent, led surgeons to further explore modifications and improvements in minimally invasive urinary incontinence surgical procedures.

## Transobturator polypropylene tape sling

In an attempt to avoid rare, but unwanted, complications associated with the retropubic trocar needle passage, Delorme developed the "outside-in" transobturator approach to polypropylene sling placement in 2002. By avoiding the retropubic space with trocar passage, the transobturator approach avoids vascular, bowel, and bladder injury while maintaining proper midurethral support [11]. Transobturator tape (TOT) slings involve insertion of trocars around the ishiopubic ramus through the obturator membrane and out through a 1.5 cm midline vaginal incision. After loading the tape onto the trocar, the sling is positioned for midurethral support. In 2004, De Leval reported on a modification of the TOT procedure whereby the trocar was passed "inside-out" from the vaginal incision to the groin incision [12]. Other than the trocar passage technique, this "inside-out" TOT sling is similar to the "outside-in" TOT procedure where the polypropylene tape is positioned at the mid urethra and extends to the obturator space and groin incisions.

Initial TOT sling cure or improvement rates have been shown to be 90% effective, which was comparable to the RPT sling [13–15]. Several other studies have supported the transobturator method and demonstrated TOT slings to be as efficacious as RPT slings [16–22]. Compared to RPT slings, the TOT procedure demonstrates minimal risk of bladder perforation and bowel injury; however, reports of subjective groin pain, possibly related to obturator nerve compression or muscle irritation, have been associated with TOT slings [20]. *De novo* urgency rates also appear to be less after a TOT sling compared to a RPT sling. Botros et al. found decreased *de novo* urgency rate with TOT: 8% for TOT versus 33% for transvaginal RPT and 17% for suprapubic RPT [23].

## Single-incision sling

Soon after the introduction of the TOT slings, engineers began designing the next generation of midurethral slings; the single-incision sling (SIS). Their goal was to mimic the safety and efficacy of traditional RPT and TOT slings, yet lower the complication rate and achieve a better patient experience. The idea was to create a sling that reduced morbidity by avoiding the passage of trocars through the retropubic or transobturator space (and thus limiting injury to major organs), reduced operative time, limited external incisions, minimized anesthesia and postoperative pain, and afforded the possible option of office-based placement.

There have been seven different SISs introduced to the market since 2006. All of the devices are placed via a single vaginal incision and are made of type 1 uncoated polypropylene mesh; however, each SIS device is unique, and they are not interchangeable products. The SISs differ in sling length, trajectory pathway, delivery device, fixation method, and fixation location (Table 160.1). Because of these significant differences, categorizing all SISs as a group is inappropriate and each SIS should be evaluated on its own merits.

The European Association of Urology 2014 guidelines on the treatment of SUI critically analyzed the data on SIS [24]. Level 1b evidence suggests that SISs are just as efficacious as RPT or TOT at 18 months, but that TVT-Secur is less effective than conventional midurethral slings at medium-term follow-up. Although blood loss and postoperative pain are lower for SIS compared to RPT and TOT, other adverse outcomes cannot be fully assessed (Table 160.2). In addition, not all SIS devices have been subjected to randomized controlled trial evaluation and it may be unsafe to assume that they are collectively technically similar devices. Although results to date are promising, further long-term efficacy data on SIS are needed. In addition, appropriate patient selection needs further study, as most SIS studies have been reserved for women without prior anti-incontinence surgery or intrinsic sphincter deficiency.

Contraindications to SIS include: coagulopathy, pregnancy or planned pregnancy, renal insufficiency, immune compromise, and urinary tract infection or obstruction.

On January 4, 2012, the US Food and Drug Administration (FDA) ordered SIS manufacturers to complete postmarket surveillance studies of their products (522 Orders). The FDA's orders came after considering reports of adverse events from manufacturers, physicians, and patients; the September 2011 meeting of the Obstetrics-Gynecology Devices Panel meeting at the FDA; and a critical evaluation of the literature. Manufacturers were not only required to submit study plans to the FDA that address safety and efficacy

**Table 160.1** Single-incision slings.

| | **AJUST™** | **MiniArc™** | **Needleless®** | **Ophira™** | **Solyx™ SIS System** | **TVT-Secur™** | **Altis** |
|---|---|---|---|---|---|---|---|
| Manufacturer | Bard (Covington, GA) | American Medical Systems (Minnetonka, MN) | Neomedic International (Terrasa, Spain) | Promedon (Córdoba, Argentina) | Boston Scientific (Natick, MA) | Ethicon (Somerville, NJ) | Coloplast (Peterborough, UK) |
| Year introduced | 2009 | 2007 | 2007 | 2012 | 2008 | 2006 | 2012 |
| Trajectory | Transobturator | Transobturator | Transobturator | Transobturator | Transobturator | Transobturator or retropubic | Transobturator |
| Fixation point | Obturator membrane | Obturator internus muscle | Obturator internus muscle fascia | Obturator internus muscle | Obturator internus muscle | Obturator internus muscle ("hammock") or urogenital diaphragm ("U") | Obturator membrane |
| Fixation tips | Permanent self-fixating polypropylene anchors | Permanent self-fixating tips | Pocket positioning. No anchor tips | Multipoint fishbone-like polypropylene tips | Permanent polypropylene carriers | Absorbable 2 cm fixating tips coated with PDS™ and Vicryl™ | One static and one dynamic polypropylene anchor |
| Tensioning method | Bidirectional independent adjustment | Optional redocking feature | Bilateral and bidirectional | Only by advancement, prior to device release | Only by advancement, prior to device release | Only by advancement, prior to device release | Bidirectional intraoperative adjustment |
| Intraoperative tightening | Yes (and loosening) | Yes (optional redocking feature) | No | No | No | No | Yes |
| Mesh size (cm) | 1.2 × 5 | 1.1 × 8.5 | 1.4 × 12 | 0.9 × 10.2 | 9 | 1.1 × 8 | 1.1 × 7.75 |
| Needle | One needle driver and flexible stylet | One needle and driver | None | One needle and driver | One needle and driver | Two needles and driver | Two introducers |
| Needle diameter (mm) | 5 | 2.3 | – | 2.2 | 3.81 | 8 | – |
| Needle disengagement | One step | One step | – | One step | One step | Two step | – |
| Midline mark | Yes | Yes | Yes | Yes | No | No | No |
| Pull-out force (lb) | 6.56 | 5.5 | 1.9 | – | 4.64 | 1.9 | 6.7–8.2 |
| Available on the market | Yes | No. Discontinued in 2016 | Yes | Yes | Yes | No. Discontinued in 2012 | Yes |

**Table 160.2** European Association of Urology 2014 guidelines on single-incision slings.

| Guideline | Level of evidence/ grade of recommendation |
|---|---|
| Self-fixing single-incision slings are as effective as conventional midurethral slings in improving SUI in women at up to 18 months | 1b |
| Operation times for insertion of single-incision midurethral slings are shorter than for standard retropubic slings | 1b |
| Blood loss and immediate postoperative pain are lower for insertion of single-incision slings compared with conventional midurethral slings | 1b |
| TVT-Secur is less effective than conventional midurethral slings at medium-term follow-up | 1b |
| There is no evidence that other adverse outcomes from surgery are more or less likely with single-incision slings than with conventional midurethral slings | 1b |

Adapted from Lucas et al. [24].

concerns of SIS for SUI, but also to conduct premarket studies comparing SIS to traditional midurethral slings. On June 4, 2012 the first SIS (TVT-Secur™, Ethicon Women's Health & Urology, Somerville, NJ, USA) was voluntarily removed from the market due to concerns over commercial viability in light of changing market dynamics and not over safety or efficacy. Subsequently two other SIS devices (MiniArc™, American Medical Systems Inc., Minnetonka, MN, USA and Ajust™, CR Bard Inc., Murray Hill, NJ, USA) have also been voluntarily withdrawn from the market. The four remaining SIS manufacturers are complying with the FDA 522 Orders and beginning their comparative studies on SIS efficacy and safety.

Over the years, data have emerged regarding the safety and efficacy of each SIS. All of the SIS devices have demonstrated minimal invasiveness with less surgical dissection, shorter procedure time, and less attendant morbidity; however, the long-term results regarding efficacy are now starting to emerge [25–27].

## TVT-Secur system

In 2006, the SIS generation began with the introduction of the Tension-Free Vaginal Tape-Secur™ (Ethicon Women's Health & Urology, Somerville, NJ, USA). TVT-Secur measures 8.0 × 1.1 cm and utilizes the same proprietary macroporous polypropylene fiber used in Ethicon's RPT and TOT slings (Figure 160.1). Besides the shorter length, TVT-Secur's other unique properties include: laser-cut mesh, absorbable fixation tips, and multiple placement approaches. Unlike the tanged mesh edges, laser-cut mesh edges offer the benefits of consistent width and minimal stretch to facilitate proper placement. The innovative 2 cm absorbable fixation tips made of polyglactin 910 (Vicryl) and poly-*p*-dioxanone (PDS) theoretically provided immediate mechanical fixation which, over roughly three months, was replaced by tissue ingrowth. TVT-Secur fixation demonstrated strength over time with initial animal mean pull-out force of 864 g (vs. 771 g for the original TVT) that increased to 6509 g at 12 weeks [28]. The versatile design of the TVT-Secur allowed placement in either the "U" retropubic trajectory position or the "hammock" transobturator trajectory position [25–27] (Figure 160.2). The "U" configuration mimics the RPT placement with the fixation tips placed into the connective tissue of the urogenital diaphragm against the periostium on the pubic bone. The hammock position imitates the TOT trajectory and the absorbable fixation tips anchor into the muscle complex of obturator internus muscle against the posterior edge of the inferior ischiopubic ramus [29]. As the procedure evolved, it became evident that the fixation tips must remain in contact with the respective bony structures in order to maintain stable long-term fixation. Stabilizing the fixation tips to mobile muscular structures alone was found to provide less than satisfactory results [3].

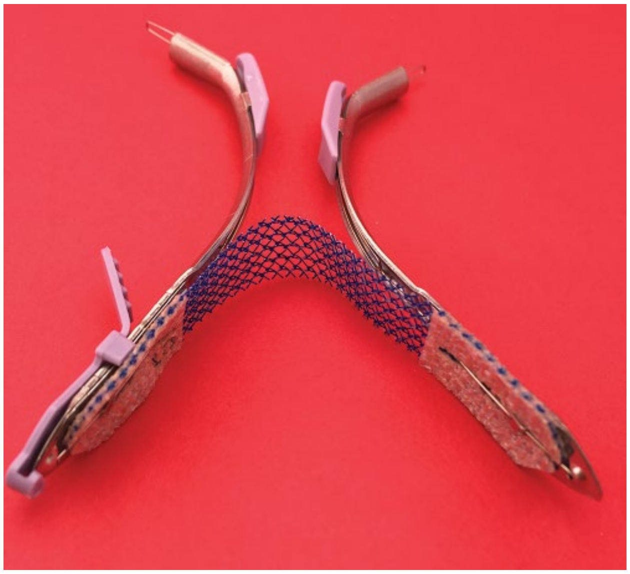

**Figure 160.1** TVT-Secur has laser-cut mesh edges with 2 cm absorbable fixation tips. This mesh measures 8.0 × 1.1 cm.

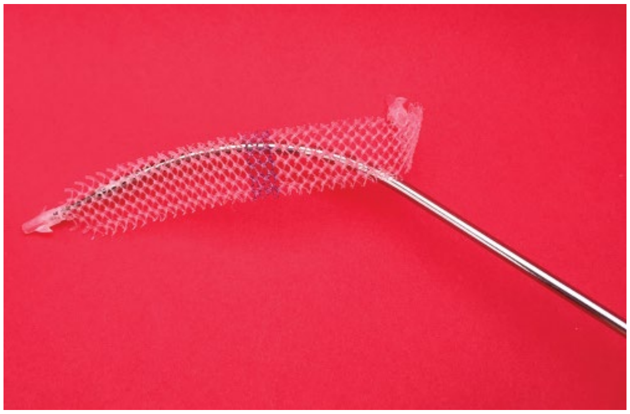

**Figure 160.2** The MiniArc is composed of a macroporous polypropylene mesh measuring 1.1 × 8.5 cm and is fused to self-fixating tips. The 2.3 mm needle and slip-fit mesh-to-needle connection allows easy engagement and disengagement of mesh to needle.

## Procedure

After local infiltration, a 1.5 cm midurethral incision is made in the anterior vaginal wall [29]. The vaginal and paraurethral incision should be made slightly larger than with conventional slings in order to accommodate the TVT-Secur device. To avoid dragging paravaginal tissue during insertion, the paraurethral dissection must maintain its width.

### TVT-Secur "U"

Similar to RPT placement, the dissection is performed to the inferior edge of the pubic bone. The urogenital diaphragm should not be penetrated by the scissors, as this will reduce the holding ability of the fixation tips. Before placing the TVT-Secur, a urethral catheter with guide should be placed to minimize injury to the lower urinary tract by the TVT-Secur inserter. The TVT-Secur is placed flat to and in contact with the back of the pubic bone, while being pushed into the dense connective tissue of the urogenital diaphragm and aimed toward the ipsilateral shoulder. Close contact with the pubic bone assures correct placement. The procedure is repeated on the contralateral side.

### TVT-Secur "hammock"

Similar to TOT placement, the dissection is performed laterally to the lower edge of the ischiopubic ramus. The obturator internus muscle should not be penetrated by the scissors, as this may reduce the holding ability of the fixation tips. The TVT-Secur is placed flat to and in contact with the lower edge of the ischiopubic ramus, while being pushed into the obturator internus muscle. The inserter blade must always stay in contact with the bony surface to achieve long-term fixation. The procedure is repeated on the contralateral side. Proper mesh tension can be achieved with bilateral incremental advancement of the device. Optimal results may not be achieved if the placement is complicated by rotating movements, tearing of the obturator muscle, or placing the device away from the bony pelvis.

### Tensioning

Proper device tensioning is essential to successful placement of the TVT-Secur in the "U" or "hammock" position. Unlike traditional midurethral slings that are pulled into place, the tension of the TVT-Secur SIS will not increase postoperatively. Tensioning options include dynamic cough/Crede stress test or visual assessment, making sure that the sling is flush with the urethra, causing a pillowing effect (filling of the tape pores with suburethral tissue) [29]. Adjustments in tensioning can only be done with the inserters in place and, once the release wires are pulled, it is not possible to reconnect for further adjustments. Cystoscopy may be performed at the physician's discretion and the vaginal incision is closed according to usual method.

## Efficacy

Several of the initial reports of TVT-Secur demonstrated unfavorable outcomes with poor success rates ranging from 67% to 83%, much lower than with the existing traditional RPT and TOT slings [30–32]. Many authors also noted a significant learning curve in the adoption of the TVT-Secur. Improper sling tensioning and lack of immediate mechanical fixation by not placing the fixation tip against the pubic bone or ischiopubic ramus resulted in device dislocation and recurring SUI [30–32]. As experience has evolved, data emerged demonstrating a decline in efficacy of the TVT-Secur in the years following insertion. Several meta-analysis reports demonstrated the TVT-Secur displayed lower efficacy in 1–3 years compared to standard midurethral slings [33–35]. A recent Cochrane review (31 trials, involving 3290 women) comparing SIS operations concluded that the TVT-Secur is inferior to standard midurethral slings for the treatment of SUI. It has been recognized that there was a problem with the fixation method of the TVT-Secur device and other subsequent SIS designs have been modified to eliminate this problem. In March of 2013, Ethicon Inc. decided to voluntarily withdraw the TVT-Secur from the market due to commercial reasons [36].

# MiniArc

One year after the introduction of TVT-Secur, the MiniArc™ (American Medical Systems Inc., Minnetonka, MN, USA) was released in the United States and Europe

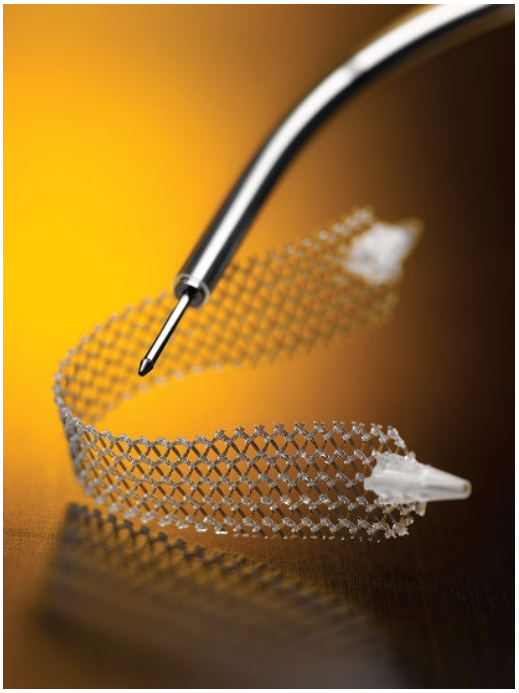

**Figure 160.3** Solyx single-incision sling system. The 9.0 cm polypropylene sling consists of a mesh assembly with carriers fixed to the ends. The delivery device has a handle, needle tip, and midline marker. *Source:* Boston Scientific Corporation, Natick, MA, USA. Reproduced with permission of Boston Scientific Corporation.

as the second SIS on the market. The MiniArc consists of an 8.5 cm × 1.1 cm polypropylene sling with integrated self-fixating tips that anchor into the obturator internus muscle through a single vaginal incision (Figure 160.3). MiniArc's simplified design and approach capitalized on some of the early design criticisms of the TVT-Secur device. Differential design features include the narrow inserter, self-fixation tips, tanged mesh edges, redocking feature, and insertion into the obturator internus muscle. The MiniArc mesh utilizes the same type 1 knitted polypropylene mesh used in American Medical System's RPT and TOT procedures.

The slip-fit mesh-to-needle connection allows easy engagement and disengagement of mesh to needle. Compared to the TVT-Secur, this smooth disengagement feature dramatically lessens the risk of inadvertently moving or loosening the mesh while removing the inserter device. By redocking the needle to the mesh after removal of the inserter, MiniArc's design allows further intraoperative tensioning during placement if desired. With the small 2.3 mm needle diameter, the push-in force required to deliver the MiniArc (2.56 lb) was less than that for the TVT-Secur (4.52 lb) (data on file, American Medical Systems). The polypropylene permanent self-fixation tips were designed to provide short-term holding force that prevents migration during initial tissue ingrowth. Compared to a pelvic floor event at a force of 1.3 lb, cadaver bench testing showed that 5.5 lb of pull-out force is required to remove the MiniArc [37, 38].

Initial skepticism regarding the MiniArc SIS was the initial and long-term fixation strength of the obturator internus muscle and learning the proper tensioning techniques for success.

## Procedure

Similar to other SIS procedures, a 1.5 cm vaginal incision is made at the level of the mid urethra. Bilateral periurethral tissue dissection is performed at a 45° angle toward the vaginal sulcus and the ischiopubic ramus. The sling/needle assembly is guided along the posterior surface of the ischiopubic ramus in a transobturator trajectory toward the obturator internus muscle. Once the integrated sling tip is fixed into the obturator internus muscle, the needle is removed and the procedure repeated on the contralateral side. Upon sling placement, further tensioning of the sling is performed by advancing the needle carrier/sling. The mesh should lie flat against the urethra without any mesh distortion or space between the urethra and sling. Dynamic stress testing (cough stress test and/or the Valsalva test) or visual inspection aids in proper sling tensioning. Cystoscopy may be performed at the physician's discretion and the vaginal incision is closed [39, 40].

## Efficacy

Several promising results have been reported with the MiniArc SIS. Early clinical reports indicate a shortened procedure time (<10 minutes), minimal blood loss, quick learning curve, and ability to perform the procedure under local anesthesia [39–42]. Although the number of long-term studies is limited, those to date support the safety of this minimally invasive procedure with efficacy rates that are similar to those for RPT and TOT.

The first prospective multicenter international trial was published by Kennelly et al., with 157 of the 188 women enrolled available for follow-up at 1 year. Based upon procedural data, the MiniArc was minimally invasive with a quick procedure time (mean 11.0 minutes), minimal estimated blood loss (mean 41.7 ml), short length of hospital stay (mean 9.5 hours), and minimal discomfort post procedure (mean pain score 1.3). At 1-year follow-up, 90.6% of patients had a negative cough stress test and 84.5% had a 1-hour pad weight test of less than 1 g. No complications such as injury to bowel, bladder, urethra, blood vessels, abscess or leg neuropathy occurred in this study. Adverse effects are uncommon and likely due to sling

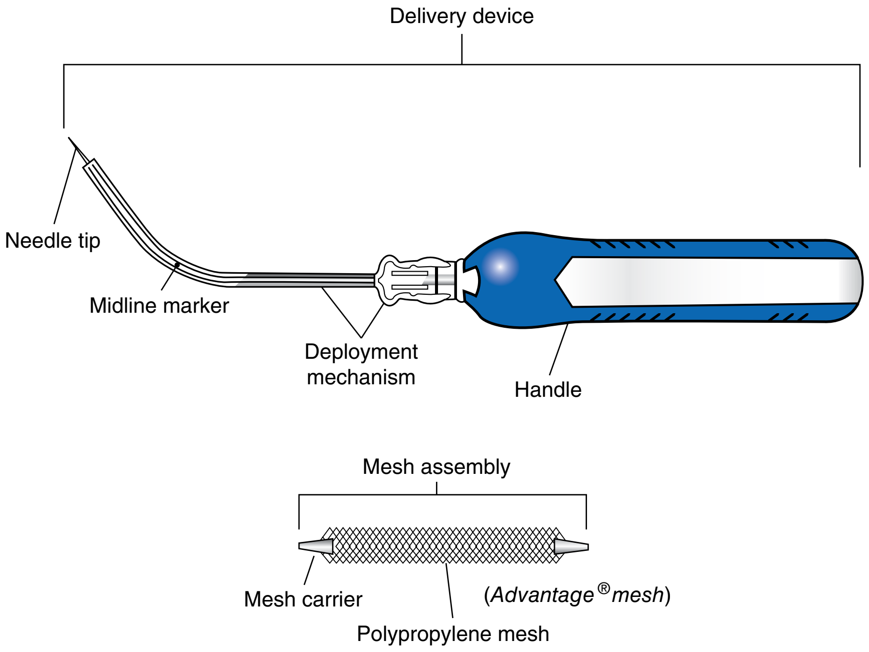

**Figure 160.4** Solyx single-incision sling system. The 4 cm central portion of the mesh is heat sealed and detanged to resist deformation and potentially reduce irritation to the anterior urethral wall. *Source:* Boston Scientific Corporation, Natick, MA, USA. Reproduced with permission of Boston Scientific Corporation.

placement outside the transobturator space or medial groin muscles [27]. However, Gauruder-Burmester and Popken reported that 36.8% of patients developed *de novo* urge incontinence [43]. The placement of self-fixating tips in a tension-free manner is a challenge and depends on factors such as tissue properties, insertion techniques, and tape position/retraction.

Longer term studies have demonstrated the MiniArc's efficacy. Kennelly et al. demonstrated in a 2-year clinical follow-up study that objective improvement/cure rates using the cough stress test and pad weight test were 84.5% and 80.1%, respectively. The subjective efficacy rate in this study was 92.9% [44]. Overall, the MiniArc data regarding efficacy, safety, and patient tolerability is very encouraging. Preliminary reports from the multicenter, prospective 522 postmarket surveillance study comparing 86 patients treated with MiniArc and 86 patients treated with Monarc™ TOT sling as controls were equivalent; however, the final 3-year data have not yet been released. In fact, as of April 2016, the MiniArc is no longer commercially available as the manufacturer ceased market distribution of the device amidst product liability concerns on transvaginal mesh products and because they failed to find a buyer.

## Solyx

The Solyx™ SIS system (Boston Scientific Corporation, Natick, MA, USA) was introduced in North America in 2009. It consists of a delivery device and a 9 cm mesh assembly with nonabsorbable polypropylene carriers on each end (Figure 160.4). These carrier barbs serve to anchor the sling into the obturator internus muscle while permanent tissue ingrowth occurs over time. The mesh assembly is composed of the same polypropylene mesh used in Boston Scientific's RPT and TOT procedures. The 4 cm central portion of the mesh is heat sealed and detanged to resist deformation and potentially reduce irritation to the anterior urethral wall. The delivery device has a snap-fit on the delivery tip, which is designed to prevent premature carrier slip-off during insertion. In addition, this delivery/carrier attachment allows micro-adjustability to loosen and tighten the sling prior to releasing the carrier. The tanged lateral mesh portion may allow for minimal loosening and once the carrier is deposited in the obturator internus muscle, it cannot be reconnected onto the delivery device for additional adjustment [25].

### Procedure

After local infiltration, a 1.5 cm vaginal incision is made at the level of the mid urethra. Bilateral dissection is performed at a 45° angle toward the inferior pubic ramus, creating a pathway for delivery device placement. The mesh assembly is placed onto the delivery device until it is flush with the end and an audible "click" is heard. The delivery device is inserted and advanced toward the obturator foramen just lateral to the inferior pubic ramus and until the midline mark on the mesh is at the mid urethra. The mesh carrier is released into the surrounding obturator internus muscle tissue by holding the deployment mechanism with one hand and pulling the delivery device handle with the other. The delivery device is removed from the incision and the second mesh assembly is placed on the delivery device and contralateral side placement is repeated. Tensioning options include a cough stress test and visual assessment to ensure the sling is positioned against the urethra (allowing a small enough space to place a small instrument or checking that the periurethral tissue "pillows" through the pores in the mesh). With the delivery device still attached to the mesh assembly, modest advances and retreats can be made to tighten or loosen the sling as needed to achieve the desired tension. However, it is important to note that once a carrier is deposited into the tissue, it is not possible to reconnect it for further adjustments [25]. Cystoscopy may be performed at the physician's discretion and the vaginal incision is closed according to the usual method (see Video 160.1).

## Efficacy

There is a paucity of peer-reviewed data on Solyx. In a retrospective review, Serels et al. reported their three-center preliminary results for the Solyx SIS system in patients with urethral hypermobility (Q-tip >30°); 59% of patients had concomitant repairs [25]. At a mean follow-up of 6.5 months (range 5–8 months), 95% (60 of 63) were dry both by subjective patient assessment (patient states they are completely dry) and objective physician assessment (negative standardized cough stress test). Only 2 of 63 patients had transient urinary retention and there were no adverse events of bladder, bowel, vessel or nerve perforations, and no erosions, extrusions, muscle or groin pain. Castellier et al. performed a review on 43 prospective and comparative studies looking at patients who underwent SIS placement. According to their research, the efficacy for Solyx SIS was as high as 95% [45]. These short-term, prospective analyses provide encouraging data that will need to be confirmed in larger, prospective studies with longer follow-up. Currently the multicenter, prospective 522 postmarket surveillance study comparing 140 patients treated with Solyx SIS and 140 patients treated with Obtryx II™ TOT sling as controls is currently on going and no data have been released.

## Needleless

The Needleless® System (Neomedic International, Terrasa, Spain) quietly emerged from Europe in 2007. It consists of a 12 cm × 1.4 cm macroporous monofilament polypropylene mesh with a blue midline suture (Figure 160.5). Unique to this device is the lack of inserter needle or anchor system. The patented lateral pocket positioning system provides the initial holding strength in the obturator internus muscle. With only 16% less surface area for tissue ingrowth than a traditional TOT sling, the Needleless sling hopes to offer the same clinical benefits as a TOT sling through a single vaginal incision [46]. In addition, no sharp introducer needles are required to implant the sling, which enhances patient comfort and is fundamentally attractive for local anesthesia.

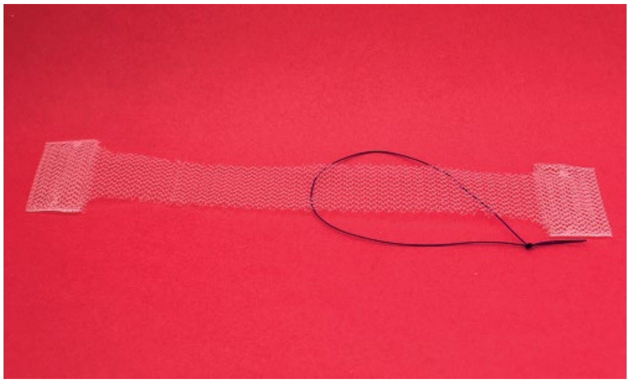

**Figure 160.5** The Needleless sling has a patented lateral pocket positioning system. The midline blue suture can be removed intraoperatively or left in place for a postoperative adjustment.

## Procedure

After local infiltration, a 2 cm incision is made at the mid urethra on the anterior vaginal wall. A horizontal submucosal tunnel is dissected to the edge of the ischiopubic ramus. The Needleless sling is prepared by introducing a surgical forceps (i.e. tonsil) in one of the terminal pockets of the sling. The forceps are inserted into the pocket of the sling, and the pocket is folded between the jaws of the forceps. The folded pockets are introduced through the dissected spaces directed at approximately 30° from the midline. The Needleless mesh pockets should be guided to the 10 o'clock and 2 o'clock positions, respectively, relative to the urethra. The surgical forceps and mesh sling are pushed into the obturator internus muscle to the point that the central sling traction thread is within 1 cm from the urethral midline. Release of the sling is accomplished by opening the forceps, extending the sling pocket positioning/anchoring system, and then carefully closing and removing the forceps. The process is then repeated on the contralateral side. The sling is placed flush with the urethra while countertraction is used on the central thread to aid in centering the sling. Intraoperative adjustments of the sling can be made by reinserting the forceps into the pockets on either side and advancing the sling further into the muscle. Cystoscopy may be performed at the physician's discretion and the vaginal incision is closed according to the usual method. The traction thread should be cut off, although it may be left in place for a maximum of 48 hours, and can be used to loosen the mesh in the case of postoperative urinary retention [46] (see Video 160.2).

### Efficacy

Several promising results have been reported with the Needleless sling since 2007. Navazo et al. reported their preliminary experience with their first 120 patients undergoing the Needleless procedure [46]. All patients had urodynamically confirmed SUI and 83% (100 of 120) had concomitant repairs. The mean procedure time was 10 minutes (range 5–15 minutes). Based upon a negative cough test, 100 patients (84%) were objectively cured, 10 (8%) improved their incontinence, and 10 (8%) were considered failures. This series did not report any cases of inguinal pain, hemorrhage, hematoma, vascular, or visceral damage; however, there was one sling extrusion managed successfully with estrogen cream.

Amat et al. compared the Needleless system with transobturator TVT-O™ sling (Ethicon Women's Health & Urology, Somerville, NJ, USA). A total of 158 women were studied and followed up 1 year after the procedure. This noninferiority test demonstrated that 87.5% of study participants who received the Needleless SIS (63 patients) and 90% of the TVT-O group (54 patients) presented with negative stress test after the study. The satisfaction rate and complication rate were similar across the two groups [47]. Another study published by Martinez Franco and Amat Tardiu compares Needleless SIS and TVT-O over a 3-year period. This was a single center, noninferior, randomized study that looked at 257 patients who received either the TVT-O or the Needleless SIS. One hundred and eleven women in the Needleless group (84.7%) and 54 women in the TVT-O group (88.9%) had negative stress tests. The complication rates were similar between the two groups, but the TVT-O group had statistically more significant postoperative pain [48].

The manufacturer used data from the study by Martinez Franco and Amat Tardiu to fulfill the 522 postmarket surveillance order. This was a prospective study that compared the safety and effectiveness outcomes of 143 patients treated with Needleless SIS and 114 patients treated with TVT-O [48]. At 3 years, the Needleless sling success rates were noninferior to the TVT-O sling, with 86% (112/130) of the Needleless SIS patients having a negative cough stress test as compared to 87.9% (95/108) of the TVT-O group. The most common adverse events reported were *de novo* urge incontinence (ranged from 8.3% to 11.7% in the Needleless sling group through 36 months and from 13.0% to 15.8% in the TVT-O group) and recurrent incontinence (ranged from 13.6% to 15.6% in the Needleless sling group through 36 months and from 5.9% to 12.0% in the TVT-O group) for both groups. There were no reports of mesh erosion in the bladder, other pains, *de novo* dyspareunia, infection, other urinary problems and neuromuscular problems in either group through 36 months [48].

Initial reports of the Needleless procedure are encouraging. Further multicenter studies with longer follow-up need to be published to confirm the long-term effectiveness of this technique.

## Ajust

The Ajust™ Adjustable Single-Incision Sling System (CR Bard Inc., Murray Hill, NJ, USA) was introduced in Europe in 2008 and North America in 2009. It was designed to offer all the benefits of a TOT sling procedure through just one vaginal incision. The Ajust sling system includes: a fully adjustable sling with self-fixating polypropylene anchors; an introducer designed to place the sling in the obturator membrane; and a flexible stylet used to lock the sling after adjustment (Figure 160.6). Unlike other SISs, the Ajust sling is placed through the obturator membrane, mimicking a traditional TOT sling placement. This new sling utilizes the obturator membrane fixation through a single-incision approach versus the three-incision pull-through approach of traditional TOT slings.

For most SIS devices, adjustment is dependent upon manipulating the introducer/needle mechanism and postinsertion adjustment is not feasible. The Ajust polypropylene mesh sling features two anchors, one fixed and one adjustable, and is constructed with a suburethral section, as well as a tubular adjustment mesh that slides in either direction through the anchor. These mesh design features allow bidirectional independent adjustment (tightening and loosening) of the sling mesh relative to the anchors without visual obstruction from the introducer in the surgical field. After optimal sling tension setting, the flexible stylet is utilized to lock the sling into place.

### Procedure

After local infiltration, a 1.5 cm incision is made at the midurethral level on the anterior vaginal wall, and a horizontal tunnel is created up to the edge of the ishiopubic ramus. The device is then inserted horizontally toward

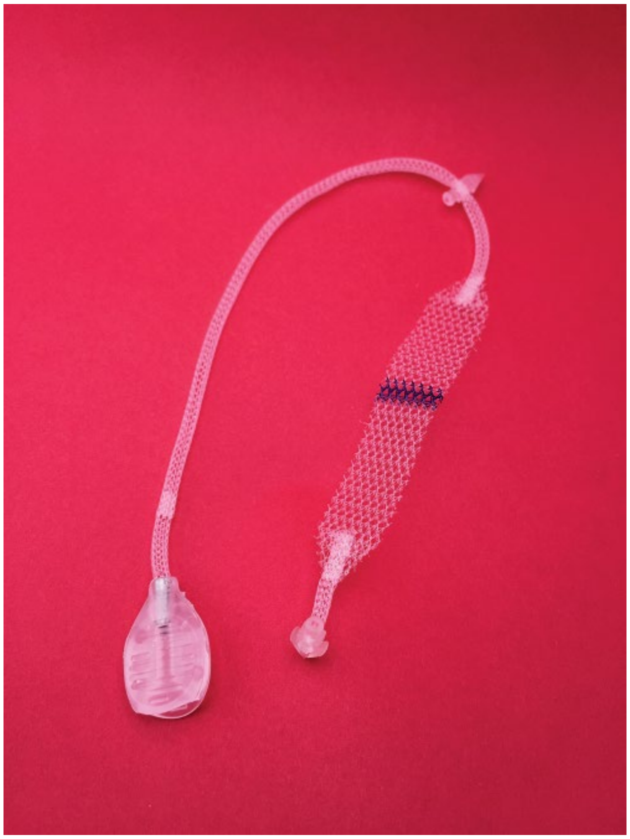

**Figure 160.6** Ajust adjustable single-incision sling. The Ajust polypropylene mesh sling features two anchors, one fixed and one adjustable. Postinsertion adjustments can be made by loosening or tightening the mesh relative to the fixed anchors.

the cephalad margin of the ischiopubic ramus, and pushed straight into the obturator internus muscle. Once the fixed anchor passes the ischiopubic ramus, the surgeon must pause from the original push while pivoting the introducer handle past the midline, and then resume a second straight push maneuver to place the anchor completely through the obturator muscle and membrane. The midline indicator must be deviated past the midline toward the fixed anchor side to confirm proper depth of placement. The fixed anchor is then released and traction is applied to the suburethral portion of the sling to confirm proper anchor engagement. The adjustable anchor is then loaded into the introducer and the steps are repeated on the opposite side. Once the adjustable anchor is correctly placed, the adjustment tab and tubular mesh is then pulled until the surgeon achieves the desired "set-point" of the suburethral sling. Once optimal setting has been achieved, the flexible stylet is used to advance the sling lock into the adjustable anchor, locking it in place.

The system is designed to permit post-anchor insertion bidirectional tension adjustability (loosening and tightening) after the sling implantation without further insertion of the introducer. Cystoscopy may be performed at the physician's discretion and the vaginal incision is closed according to the usual method.

## Efficacy

Several peer-reviewed studies of Ajust SIS demonstrate favorable outcomes with high success rates, short operative times, minimal morbidity, and the ability to perform the procedure under local anesthesia [49–51]. Since then, more peer-reviewed studies have emerged. Natale et al. looked at 95 females in a 2-year prospective, multicenter, randomized control trial. Of the 95 study participants, 92 had completed the 2-year follow-up. Objectively, the cure rate was 83.7% and subjectively, 81.5%. No intraoperative complications were noted. However, postoperatively, 9 patients presented with *de novo* urgency. Other adverse postoperative events also included leg pain, mesh extrusion, and recurrent urinary tract infection. Patients in this study demonstrated a statistically significant improvement in their quality of life (based on the King's Health Questionnaire) [49]. Martan et al. presents a multicenter, prospective randomized study with a 2-year follow-up for 66 study participants (of whom only 63 completed the study). The authors divided the cohort into two groups: the Ajust ($n = 33$) and the MiniArc ($n = 33$). The study found that approximately 83.9% of the Ajust group were cured or improved, based on a Likert scale. Objective cure rates, as evidenced by a negative cough test, was 93.5% in the Ajust group [50]. Xin et al. also studied the Ajust single-incision mini sling versus the more traditional TVT-O. In their reports, the subjective and objective cure rates between the two midurethral slings did not have any statistically significant differences (94.4% vs. 90.7%, $P = 0.171$; 97.2% vs. 90.7%, $P = 0.195$). Postoperatively, the Ajust group had much less pain. Also, the intraoperative blood loss, operative times, and recovery were significantly shorter [51].

Overall, the various reports of the Ajust sling have demonstrated its short-term effectiveness in treating genuine SUI, with limited and mild complications or adverse events. Unfortunately, as of May 2016, the Ajust SIS is no longer commercially available in the United States as the manufacturer ceased market distribution of the device amidst product liability concerns on transvaginal mesh products.

## Ophira

The Ophira™ Mini Sling System (Promedon, Cordoba, Argentina) was introduced in South America in 2008 and received FDA approval in 2012. It consists of a retractable insertion guide and a 0.9 × 10.2 cm mesh assembly made of type 1 polypropylene mesh with thermos-sealed edges and a multipoint fishbone-like polypropylene anchor tip at each end. The anchor tips serve to anchor the sling into the obturator internus muscles on the same plane as the tendinous arc. The Ophira SIS system has blue loosening sutures at the base of the fixation arms which gives the provider the ability to correct tensioning during sling placement.

### Procedure

After local infiltration, a 1.5 cm horizontal incision is made at the midurethral level on the anterior vaginal wall. Bilateral dissection is performed in the direction of the ascending pubic ramus bilaterally. Next, dissection is performed in the direction of the ascending pubic ramus bilaterally. The fixation arm of the sling is fixed to the retractable insertion guide. The guide is inserted in the vaginal incision along the posterior surface of the ishiopubic ramus in a transobturator trajectory and advanced toward the obturator membrane until the central mark on the sling disappears under the ipsilateral side of the incision. The center mark ensures the depth of the sling is correct and the sling is centered. Once the sling is centered, the sliding button mechanism on the insertion guide is activated to release the mini sling. The procedure is repeated on the contralateral side. However, the depth of insertion of the second fixation arm on the contralateral side will be the determining factor of final tension. Dynamic stress testing (cough stress test/Valsalva test) or placement of an instrument (i.e. tonsil) between the urethra and sling to act as a spacer may be performed to obtain correct tension. If excessive tension is noted, the loosening suture on the sling may be pulled to loosen the sling. Once the optimal tension is achieved, the blue loosening suture is removed. Cystoscopy may be performed at the physician's discretion and the vaginal incision is closed according to the usual method.

### Efficacy

Despite being developed in 2008, there are only a few peer-reviewed studies available for the Ophira sling. Smith et al. compared outcomes at 12 months between the Ophira SIS and a TOT sling. This prospective observational study looked at 30 patients who received the Ophira sling and 31 patients who received the Obtryx™ TOT sling. At 12 months, approximately 93.3% (29 patients) with the Ophira slings reported significant improvement in symptoms and 90% (27 patients) had a negative cough stress test. These numbers are very similar to the TOT group in that 29 of those patients (93.5%) reported improved symptoms and 29 patients (93.5%) had a negative cough stress test [52].

From February 2008 until February 2011, Palma et al. conducted a multicenter international clinical trial that followed 178 patients who received the Ophira sling for SUI. A total of 77.5% (138/178) patients completed the 1-year study follow-up. Only 3.9% of patients continued to have a positive stress test. The authors suggest that the successful treatment of SUI in this population was due to the multiple point fixation arms that provide stability over time. In addition, no major complications were noted in this study. Minor complications included: mesh exposure (3 patients), urinary retention (3 patients), urinary tract infection (8 patients), and *de novo* urge incontinence (7 patients) [53].

Regarding the 522 postmarket surveillance study, the manufacturer changed the indications for use and therefore the 522 Order is no longer applied to this device [54]. The initial reports of Ophira efficacy and safety are encouraging.; however, more studies with long-term follow-up are needed to fully evaluate the Ophira sling to prove sustained durability and efficacy.

## Altis

The Altis® SIS (Coloplast Corp., Minneapolis, MN, USA) was introduced in the United Kingdom and received FDA approval in 2012. Similar to the Ajust, this sling was designed to offer all of the benefits of a TOT sling through one vaginal incision. Mimicking a traditional TOT sling placement, the Altis sling is placed through the obturator membrane with the aid of helical introducers and allows postinsertion adjustability. The Altis polypropylene mesh sling features two anchors, one fixed and one adjustable, connected to a 1.1 × 7.75 cm central portion of heat-sealed mesh by polypropylene monofilament suture (Figure 160.7). The dynamic anchor is designed for bidirectional adjustment intraoperatively via the size one polypropylene monofilament suture sonic welded to the sling.

### Procedure

After local infiltration, a 1.5 cm incision is made at the midurethral level on the anterior vaginal wall, and a horizontal tunnel is created up to the edge of the

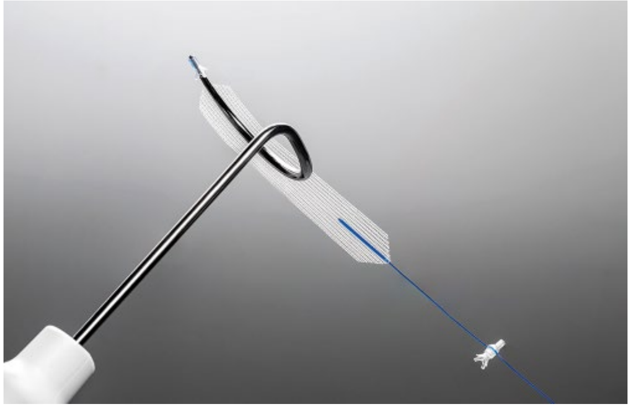

**Figure 160.7** Altis single-incision mini sling. The anchor is placed on the introducer delivery tip. *Source:* Coloplast Corporation, Minneapolis, MN, USA. Reproduced with permission of Coloplast Corporation.

ishiopubic ramus. The static nontensioning anchor of the sling assembly is placed on the appropriate introducer. The introducer/sling assembly is placed into the midline vaginal incision using an inside-out technique. Once the introducer/anchor tip is passed posterior to the ishiopubic ramus, the introducer/anchor tip is turned approximately a quarter turn, which advances the anchor through the obturator membrane. The dynamic anchor is placed on the opposite introducer delivery tip and the same technique of delivery is performed to place the dynamic anchor into the opposite obturator internus muscle. Tensioning of the sling is performed by pulling the monofilament suture loop across the patient's midline until desired support is achieved. If necessary, a blunt instrument may be used to gently pull down the sling to loosen it. Once desired support is achieved, the tensioning suture is cut as close as possible to the pelvic side-wall. Cystoscopy may be performed at the physician's discretion and the vaginal incision is closed according to the usual method (see Video 160.3).

### Efficacy

The Altis SIS was the first SIS to undergo an investigational device exemption (IDE) clinical study collecting safety and effectiveness data required to support their premarket notification 510(k) approval application. A 12-month IDE clinical study was conducted at 17 sites with 113 female subjects with confirmed SUI [55]. At the end of 12 months, 90.1% of patients had a 50% reduction in pad weight and 90.1% had a negative cough stress test. With regard to quality of life, 89.3% and 90.3% of patients had at least a 50% improvement in Urogenital Distress Inventory (UDI-6) and Incontinence Impact Questionnaire (IIQ-7) scores, respectively. In total, 89.3% of patients reported improvement of very much or much better on the Patient Global Impression of Improvement (PGI-I) at 12 months. Three serious adverse events were reported: a pelvic hematoma which drained spontaneously and two of four mesh extrusions which occurred in the study. The IDE study concluded that the Altis SIS system met all endpoints of the study and performed comparably with legally marketed predicted devices. At 12 months, subjective measures reported a cure rate of 84.0% and an objective cure rate of 90.2%. Adverse events included one case of vaginal extrusion, and three cases of vaginal exposure of the adjustment thread which were managed conservatively [56].

Currently the prospective, 522 postmarket, multicenter, cohort assessment comparing Altis SIS ($n = 178$) and transobturator and/or retropubic slings ($n = 178$) in the treatment of SUI at up to 40 US and international sites is ongoing and no data have been released. Longer term outcome studies are not currently unavailable. These longer term studies are needed to fully evaluate the Altis sling. However, initial reports on the safety and efficacy of Altis are encouraging and show it to be competitive with other comparable products that are legally marketed.

## Conclusions

SUI is debilitating and treatable with surgical interventions. Excellent success rates have been reported with both the RPT and TOT slings; however, both approaches require blind passage of trocars that risks visceral and vascular damage. Since 2006, SIS devices have been used in an attempt to decrease the morbidity associated with the minimally invasive approach. However, these procedures must be approached with caution and providers must understand that minimally invasive slings are not simpler, but require much attention and detailed dissection. Due to the significant differences in technical design between SIS devices, it would be misleading to make general statements about them as a class of operations. It is anticipated that decreased complications, high continence rates, and ease of application under local anesthesia may eventually allow SIS placement to become an office procedure. The encouraging initial results from SISs must be demonstrated over the long term, and comparative trials to the current gold standard RPT and TOT slings continue to be needed to solidify SIS device placement as a first-line treatment option for women with SUI.

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# Bioinjectables for Stress Urinary Incontinence

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## Introduction

Recent advances in our understanding of the underlying pathophysiologic mechanisms responsible for stress urinary incontinence (SUI) in women have led to the development of innovative new surgical methods for its treatment. A number of different surgical options are present for patients with SUI, including retropubic suspensions, sling and tape procedures, artificial urinary sphincters, and periurethral bulking agents. Concerns over the morbidity associated with open surgical treatment and the safety of the use of surgical mesh implants has driven investigators to investigate the role of periurethral bulking agents as a minimally invasive alternative treatment. The lower morbidity of the endoscopic approach and ability to be performed in an outpatient setting under local anesthesia are appealing for patients with significant medical comorbidities and is part of the current trend towards less invasive surgical treatments. A recent study of case volumes at the time of certifying examinations for urologists demonstrated that the use of endoscopic injections has remained a stable element of the urologist armamentarium, comprising 15% of all female incontinence procedures [1]. While male SUI is a common problem following surgical treatment such as radical prostatectomy, bulking agents have demonstrated limited efficacy and have fallen out of favor in the treatment of male SUI [2, 3]. As such, this chapter will focus on bioinjectables in the treatment of female SUI. Although the long-term efficacy and durability of these treatments has been questioned, for the appropriately selected patient, bioinjectables can play an important role in the treatment of SUI.

## History

Bulking agents have a long medical history in fields outside of urology. They have been used for gastroesophageal reflux, scars, and wrinkles, as well as for patients with glottic insufficiency [4, 5]. The first use of urethral bulking agents (UBAs) in the treatment of SUI occurred in 1938 when Murless used sodium morrhuate or cod liver oil as a sclerosing agent in the anterior vaginal wall of 20 patients, attempting to create an fibrotic inflammatory response [6]. Others used similar agents, but until 1973 this approach was seldom used due to high complication rates. Berg [7] and Politano et al. [8] popularized the use of polytetrafluoroethylene (Teflon) during the 1970s. Reports of significant complications including particle migration to the lungs limited the utilization of Teflon in periurethral injections [9]. Urethral bulking only became widely popular following the US Food and Drug Administration (FDA) approval of bovine glutaraldehyde crosslinked collagen, marketed as Contigen (Allergan, Dublin, Ireland) in 1993. While Contigen was withdrawn from the market by its manufacturer in 2011, several different bulking agents remain available for use [10].

## Mechanism of action

The mechanism of action of injectable agents results from augmentation of the urethral wall and subsequent increase in urethral resistance. The resulting improvement in urinary incontinence is not associated with a corresponding increase in voiding dysfunction. This is because the “seal” that is formed by restoring mucosal

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coaptation does not occlude the urethra. The urethra maintains the ability to funnel and open, with no change in detrusor pressure to initiate a flow. Interestingly, most agents are placed short of the bladder neck, within the smooth muscle layer in the zone of the continence mechanism. Klarskov and Lose measured pressure and cross-sectional area in the urethra of women with SUI and mixed incontinence before and after urethral injection therapy, using a pressure profile reflectometer [11]. This novel technique detected a significantly greater increase in squeezing opening pressures in patients who had subjectively noted an effect. They suggested that injection therapy functions as a central filler volume that increases the length of muscle fibers and thereby the power of the urethral sphincter. The external sphincter consists of muscle fibers, collagen, vessels, and nerves, with a central component compressing the lumen [12]. An increased central filler volume will augment the sarcomere length of muscle fibers, strengthening muscle power up to a sarcomere length of 2.2 μm [13, 14].

## Economic considerations

Rising healthcare costs and an aging population requiring greater medical care has led to an interest in clinicians evaluating the economic considerations associated with surgical interventions. Given the variety of different surgical treatments available for SUI and its prevalence within the general population, a rigorous understanding of the economic aspects of treatment represents an area which could yield significant economic benefit. Each year, the estimated direct cost associated with the treatment of SUI is in excess of US$12 billion [15]. A recent cost utility analysis of midurethral sling (MUS) compared to UBAs over a 1-year timeframe demonstrated that MUS cost US$436 465 more than UBAs per 100 women treated with an estimate that MUS was cost effective at a cost of US$5132 or less and cost saving (less expensive than UBAs with improved outcomes) at a cost of US$2035 or less [16]. Although MUS demonstrated a greater reported rates of dryness at 12 months (65% vs. 38.7%) within this model, the increased initial costs with MUS as well as a higher rate of significant complications (sling excision, repeat sling, erosion) led the authors to conclude that over a short-term follow-up that UBAs may be a cost-effective treatment for 47.6% of patient while MUS is only cost effective in less than 1% of patients [16]. Although this study relied on a theoretical model based on previously reported outcomes, patients would benefit from a prospectively designed trial of UBAs versus MUS which includes economic analysis as a key design outcome. This is particularly important given a recent study that demonstrated significant variation in reporting surgical outcomes with less than 40% of studies utilizing validated questionnaires in reporting surgical outcomes for SUI [17]. Greater utilization of validated questionnaires for surgical outcomes are a critical component for accurately assessing the economic impacts of SUI and the available surgical treatments.

## Patient selection

The index patient for bulking should have demonstrated stress incontinence and evidence of intrinsic sphincter deficiency (ISD). While there exists some argument over a fixed versus a mobile urethra, most would agree that a relatively fixed urethra (nonradiated) may respond well to bulking. The patient with hypermobility may have some improvement, but usually the shearing force of a cough is too great to maintain dryness if mobility exists. The traditional inclusion criteria for bulking agents are patients with poor urethral sphincter function with isolated ISD (defined as urodynamically confirmed abdominal leak point pressures $<100\,\mathrm{cmH_2O}$), limited urethral mobility, and an absence of detrusor instability [18]. Presently, the European Association of Urology (EAU) guidelines on SUI recommend the consideration of periurethral injection treatments in women with stress incontinence or mixed urinary incontinence, stress predominant symptomatology [19]. This indication is based on the fact that support is a key factor to consider in urethral bulking. Specifically, if there is poor vaginal support and significant mobility of the bladder neck/urethral complex, other options usually have been thought to deliver better results. However, as UBAs were more widely adopted, some clinicians have investigated their role in patients with urethral hypermobility. Herschorn et al. in Toronto demonstrated that the patient with hypermobility could derive benefit from UBA treatment [20, 21]. In fact, no significant difference in outcomes was seen in patients with or without hypermobility in their studies. Interestingly, patients with hypermobility required less collagen for a successful outcome. Similarly, Monga et al. reported on 60 women with genuine stress incontinence and urethral excursion ("mobility") of up to 25 mm [22]. Objective cure rates (according to urodynamic assessment) were 61% at three months and 48% at 24 months. Subjective success rates were 86% and 68% at three months and 24 months, respectively. A logical conclusion derived from these studies is that ISD can exist in the presence of hypermobility and that this alone should not be a criterion for exclusion from bulking therapy. There is, of course, a gray area, where the patient and physician agree to use these agents fully anticipating a partial improvement in an otherwise poor surgical candidate. A key element to remember from the current EAU guidelines is an "A" recommendation not to offer periurethral bulking agents for women who desire a permanent cure for SUI [19]. Finally, in addition to physical examination, urodynamic studies need to be performed to document a low leak point pressure, as well as to rule out other sources of incontinence. Video urodynamics may be helpful for directing visualizing the bladder neck and proximal urethra, but is not necessary to confirm low urethral resistance.

Ultimately, good patient selection with a careful preoperative assessment as well as management of preoperative patient expectations about the duration and degree of efficacy with UBAs are critical for obtaining the best possible patient outcomes and satisfaction with this intervention.

## Techniques

There have been numerous approaches to placement of UBAs, including intraurethral or transurethral, periurethral, and even transvaginal [23–25]. The two most common routes are transurethral or periurethral, with the former being the most commonly utilized approach. Yet, two transurethral techniques evolved for a short time: the obvious visual approach and a "blind" technique. The nonendoscopic approach was designed ostensibly to eliminate operator variability. First described by Henalla et al., a device was developed to control the placement of the injected material in predetermined areas [26]. This technique is rarely used today in the United States, likely due to the additional cost of the implantation system and the familiarity and ease of injection by urologists with the transurethral and periurethral techniques.

Both transurethral and periurethral techniques utilize visualization with an injection system scope or a female cystourethroscope to aid in guiding the injection of the bulking agent. After the bladder is drained, the scope is placed mid urethra. Most techniques describe needle placement at 4 and 8 o'clock with a submucosal injection. The trial with Macroplastique™ added an injection at the 6 o'clock position. The goal of the injection is to achieve either horizontal or concentric coaptation of the bladder neck and proximal urethra. The bulking agent should be injected relatively slowly to allow for tissue accommodation and to prevent extrusion of injected bulking agent. For the transurethral injection, a transurethral needle is placed through the scope, whereas the periurethral technique uses a spinal needle placed alongside the urethra through the vaginal wall.

Faerber et al. reviewed the outcomes and differences between the transurethral and periurethral routes of injection [23]. There were no statistically significant differences in outcome, although current guidelines state that there is a higher risk of postoperative urinary retention with percutaneous access as required for the periurethral approach [19]. In a prospective study by Schulz et al., the authors concluded that both periurethral and transurethral methods were comparable [24]. However, the amount of material utilized was much greater in the periurethral group, which would, of course, drive the expense of the procedure upward.

Many patients require additional treatments and various waiting periods are required for each unique agent. Postoperatively, a small amount of bleeding or bulking agent leakage can be noted for 1–2 days. Retention can occur and should be treated with 24-hour catheterization with a small 8–10 Fr Foley or clean intermittent catheter technique to avoid molding the newly injected material. Urinary retention is usually self-limiting. If prolonged retention is apparent, then a suprapubic tube should be considered to avoid crossing the urethra which has been treated. Moreover, it is not uncommon to have temporary irritative urinary symptoms. Stothers et al. reported a 12.6% incidence of *de novo* urge incontinence in a large prospective trial [27].

## Materials

The ideal injectable agent should primarily be safe (i.e. biocompatible, nonimmunologic, and hypoallergenic). It should retain its bulking characteristics for a prolonged interval and not biodegrade or migrate, but it should also be easily explanted or degraded if necessary. In addition, it should be easy to prepare and implant. In the United States, there are presently three available injectable bulking agents approved by the FDA. These are calcium hydroxylapatite particles in a gel carrier (Coaptite™), carbon-coated zirconium beads (Durasphere™), and polydimethylsiloxane (Macroplastique™). Internationally, polyacrylamide hydrogel (Bulkamid™) is another bulking agent that is widely used. For many years, the most commonly utilized and studied bulking agent was glutaraldehyde crosslinked bovine collagen (Contigen™), however this agent was voluntarily withdrawn from the market by its manufacturer in 2011. Given the prevalence of collagen, many head-to-head trials with other currently available bulking agents were performed as comparison trials to collagen. However, presently there is no evidence that any available bulking agent provides superior outcomes [19].

### Calcium hydroxylapatite (Coaptite)

Calcium hydroxylapatite (Coaptite) is a synthetic injectable implant composed of smooth calcium hydroxylapatite bioceramic microspheres that have a diameter range of 75–125 μm, suspended in an aqueous gel carrier. A normal constituent of bone, it is also nonimmunogenic, and was previously used in dental and orthopedic surgery. A 12-month prospective, randomized, comparative, multicenter, single-blind, parallel, clinical trial of calcium hydroxylapatite and collagen for soft tissue augmentation of the urethral sphincter in the treatment of SUI enrolled 296 women. Essentially comparable results, 63% and 57% improvement, respectively, were reported [28]. Approved by the FDA in November of 2005, it is used for the treatment of ISD. Some serious side-effects have occurred with Coaptite that were reported in the Mayer et al. study: one erosion through the vaginal wall and one injection which dissected into the bladder, causing a tissue bridge to form [28]. In addition, urethral prolapse has been reported in a delayed fashion months after injection [29].

### Carbon-coated zirconium beads (Durasphere)

Carbon-coated zirconium beads (Durasphere) is a sterile, nonpyrogenic injectable bulking material composed of pyrolytic carbon-coated graphite beads suspended in a 97% water, 3% beta-glucan carrier gel. It is inert and nonimmunogenic, and therefore does not require skin testing, unlike collagen which requires a skin test within 30 days of injection to assess for hypersensitivity. In a head-to-head trial, Durasphere and collagen were randomized to similar patients. The Durasphere group showed an improvement of 1 or more Stamey grades in 80% of patients compared to 69% in the collagen group. Although this analysis demonstrated a trend favoring Durasphere over collagen, there was not a statistically significant difference improvement [30]. One theoretical concern with Durasphere was phagocytosis and migration of bead particles as it is known that macrophages can phagocytize particles of less than 80 µm, which could result in transportation throughout the body. To address this concern, the carrying gel was re-engineered as Durasphere EXP, with an optimized bead size of 90–212 µm. Although Durasphere beads should not migrate because of their size, it is possible that the zirconium beads found in lymphatics and other ectopic locations may result from high-pressure injection. Durasphere is safe and has no risk of allergy. Results have been comparable to those with collagen, but the immediate complications with it are slightly higher, as reflected in the rate of urinary retention, but this rarely persists or requires surgical intervention [31].

## Polydimethylsiloxane (Macroplastique)

Silicone (Microimplants, Macroplastique, and Bioplastique) is a soft, flexible irregular material made of vulcanized polydimethylsiloxane macroparticles or simple silicone rubber. The silicone particles are inert, biocompatible, nonbiodegradeable, and nontetratogenic. The mean particle size is 100–300 µm, limiting the chances of migration via phagocytosis. The material, however, must be injected with a special injection system because of its high viscosity. The material was approved by the FDA for treatment in SUI. Reported cure and improvements rates are 60% and 80%, respectively [32, 33]. Complications are similar to those with other agents and include transient hematuria, retention, and urinary tract infection. Henly and others have expressed concern about small particle migration; however, this is not a common outcome [34]. In a multicenter randomized trial between Macroplastique and collagen, 61.5% of the former agent improved by 1 or more Stamey grades, in contrast to 48% of the collagen group. A total of 36.9% of patients in the Macroplastique group were dry compared with 24.8% of the collagen patients [30]. A recent review and meta-analysis demonstrated improvement rates of 75% for short-term (<six months) results, which were reasonably durable over long-term follow-up, with 64% of patients reporting improvement for long-term (>18 months) results [35].

### Polyacrylamide hydrogel (Bulkamid™)

Bulkamid UBA is a crosslinked synthetic polymer of polyacrylamide hydrogel that is available internationally but has not yet been approved by the FDA in the United States. A unique aspect of this agent is a homogeneous composition of the agent as it does not contain any particles. In the original clinical trial on the use of this agent by Lose et al., eight patients (38%) were subjectively dry and a further nine (43%) improved [36]. Objectively, urine leakage/24 hours decreased by 93% and the number of incontinence episodes decreased by 87% [36]. Quality-of-life measures improved significantly in all domains other than general health perception. There were no significant changes in urodynamic variables. The most commonly reported treatment-related adverse events were urinary tract infection and urinary retention [36]. The 2-year follow-up data from this trial reported stable response outcomes to their 1-year data. At 2 years of follow-up, although there was a relatively low cure rate of 17%, a majority (64%) reported either cure or improvement in symptoms for a relatively robust sample of 135 patients [37]. The results of the North American trial were recently published that compared Bulkamid to collagen with a 2:1 allocation. In this study, 50% of the 229 women treated with Bulkamid reported zero stress incontinence episodes at 1 year and 77.1% of women reported cure or improvement [38]. These results were noninferior to those for patients randomized to collagen treatment.

### Other agents

There have been attempts to use other materials, including dermal collagen implants, autologous fat, and even autologous chondrocytes [39]. A systematic review of randomized trials for noninvasive anti-incontinence procedures included seven randomized controlled trials (RCTs) on a total of 882 women implanted with different injectable bulking agents [40]. The overall level of evidence was classified as low. Rates of continence and improvement were similar among the different agents in most of the RCTs. Curative effects were shown after intraurethral collagen injection in women with SUI (51.5% were dry during a 24-hour pad test) [41]. Transurethral injection of a porcine dermal implant resulted in a negative pad test results (i.e. cure) in 60% of women with urodynamically proven SUI [42]. Transurethral injection of the bulking agent dextran copolymer resulted in objective cure in 15% of women with stress or mixed incontinence (minor and controlled urge component) in whom previous conservative treatments had failed [24]. Only one RCT reported statistically significant relative benefit. This benefit was seen in 63 women with SUI at 12-month follow-up. A literature review by Chapple et al. concluded that quality-of life improvement after urethral injections appears to be significant and is comparable to that obtained with surgery, despite the observation of superior objective surgical efficacy [43].

## Future agents

Although the currently available UBAs are chemical polymers, the future of these treatments may be found in the field of tissue engineering, particularly with stem cells. Autologous stem cells are an especially appealing treatment option as they have no risk of immunological reaction because they are derived from the patient. The role of stem cells in promoting antiapoptotic, antiscarring, and neovascular effects and ability to replenish cells in case of injury could be an ideal treatment for SUI and ISD [44]. However, this field has not been without controversy. One study by Strasser et al. [45] that initially garnered significant attention and promise looked at using injections of autologous myoblasts and fibroblasts for urinary incontinence. Although the results were promising, closer scrutiny of the technology and numerous inconsistencies in the documentation, records and a lack of ethics approval for this trial resulted in suspicion over the veracity of these results and a subsequent withdrawal of the paper by the *Lancet* [46].

Since this study, several other investigators have performed trials utilizing tissue engineering to create hybrid bulking agents with significant promise. Shi et al. [47] published their results of a tissue-engineered bulking agent created with adipose-derived stem cells and silk fibroin microspheres, which demonstrated improvement in urethral function in a rat ISD model with both neo-tissue and nerve regeneration noted after treatment with this novel bulking agent. Similarly, Watanabe et al. [48] were able to demonstrate increased urethral resistance and increased leak point pressures following injection of autologous derived adipose stem cells in a rat model. In addition to adipose-derived stem cells, investigators have looked at muscle [49], urine [50], and bone marrow [51] as potential sources for stem cells to improve urethral function.

Although these therapies have not yet been translated to clinical practice, these results are an exciting frontier in regenerative medicine that may lead to a safe and effective minimally invasive approach to treating SUI.

## Conclusions

The role of UBAs has evolved over the last two decades in parallel to the developing technology of slings. As a result, they are more frequently used in patients with multiple medical comorbidities whose increased surgical risks prevent them from having open surgery. Moreover, once considered a primary treatment, today these agents are best used as an adjunct to a failed sling or other anti-incontinence surgery. They can improve the quality of life for a subset of patients. The search for a better injectable agent continues as the fields of biomaterials and regenerative medicine now look to better understand SUI.

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## 162

# Midurethral Slings for the Treatment of Female Stress Urinary Incontinence

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## Introduction

Stress urinary incontinence (SUI) is a condition that affects the psychosocial welfare, interpersonal relationships, quality of life, productivity, and general health of afflicted women. Its prevalence has been reported to be from 14% to 46% in women older than 18 years of age [1–3]. The prevalence of SUI in women peaks at middle age and then declines slightly in favor of mixed urinary incontinence (MUI) and urge urinary incontinence (UUI) thereafter [1, 2, 4, 5]. Despite this significant prevalence, due to the invasive nature and associated prolonged recovery of surgical options offered in the past, many women did not undergo treatment.

Since Ulmsten and Petros described the tension-free vaginal tape (TVT, Ethicon, Somerville, NJ, USA) procedure in 1995, "An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence" midurethral synthetic slings (MUSS) have grown in acceptance and popularity to gain a leading position in stress urinary incontinence surgery [6]. They have become a new gold standard for the surgical treatment of female SUI, not only because of their simplicity for both the surgeon and the patient, but also because of excellent surgical outcomes and low morbidity. There are numerous studies, both randomized controlled trials and well-designed prospective studies, which provide a large amount of level 1 and 2 evidence that supports the concept of a sling placed at the level of the midurethra. In addition, there is growing evidence regarding how different approaches for placing a MUSS (retropubic and transobturator) can be applied to specific patient groups. This evidence base will be reviewed to help resolve clinical dilemmas concerning the selection of candidates for MUSS.

In this chapter we also describe the anatomic basis and techniques of MUSS, examine their indications and outcomes in select patient populations, describe "less invasive" techniques, and discuss the management of complications that can occur after MUSS placement.

## Determining which patients are candidates for MUSS

Patients who could or should have MUSS placed are those with uncomplicated SUI or mixed incontinence with urethral hypermobility. The MUSS is the most widely studied procedure with SUI and has very low morbidity and complication rates. The American Urogynecologic Society (AUGS)/Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) Position Statement on Mesh Midurethral Slings gives "full support" to their use, calling attention to the fact that mesh midurethral slings (MUS) have been extensively studied with positive short- and long-term outcomes demonstrating "superior safety and efficacy" [7]. There are three unique complications of mesh that may require reoperation: extrusion, pain, and erosion.

Patients for whom placement of MUSS is questionable are those with a fixed urethra. Slings have been found less effective in women without urethral hypermobility [8]. This is discussed further in the section on intrinsic sphincter deficiency.

Patients who should not have MUSS placed include women with prior mesh erosion or two failed prior MUSS, women undergoing simultaneous urethral reconstruction, women with neurogenic SUI and the goal of clean intermittent catheterization (CIC), and finally patients with a preference to avoid synthetic mesh.

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

Two good alternatives exist for these patients, the pubovaginal sling (PVS), in which a strip of mesh or fascial tissue is placed under the urethra to provide support and compression, and Burch colposuspension, in which an abdominal approach is taken to attach the paravaginal fascia to Cooper's to suspend and stabilize the urethra.

## MUSS: anatomy and surgical technique

### Mechanism of action

The theoretical basis for the original TVT procedure was the "integral theory of female urinary continence" based on a series of anatomic studies of the female urethral closure mechanism performed by Petros and Ulmsten in the 1990s [9]. An important alternate theory advanced by DeLancey in 1994 is his description of the "hammock theory" [10]. Both of these theories strive to explain how urethral pressure can be maintained above vesical pressure during increased intra-abdominal pressure. In the integral theory this is explained by opposing forces; the pelvic floor muscles act through their vaginal attachments to stretch the vaginal hammock against the pubourethral ligaments, shutting the urethra off from behind. Weakness in the pubourethral ligaments would lead to similar forces opening the urethra. The more practical "hammock theory" proposes that both urethral support and constriction are important. In this model the support is provided by the layers outside the urethra on which it rests: the anterior vaginal wall, the endopelvic fascia between the arcus tendineus facia pelvic on each side, and pelvic floor muscles. With increased intra-abodominal pressure the urethral remains shut against this backboard, as long as it is intact. When the backboard is not intact, urethral hypermobility and/or SUI may result. It has been shown by ultrasound studies that placement of a sling at the midurethral level causes a dynamic kinking of the urethra with stress and thus can cure stress incontinence without affecting position or urethral mobility [11].

### Anatomic approaches

**Retropubic MUSS (see Video 162.1)**

The original TVT procedure placed polypropylene sling at the level of the midurethra via a "bottom to top" approach (Figure 162.1). This involved the passage of a trocar from a midurethral vaginal incision through the endopelvic fascia and the retropubic space to a suprapubic exit point. The "top to bottom" technique was developed in 2001 [12] with the introduction of the Suprapubic Arc system SPARC (SPARC, American Medical Systems, Inc., Minnetonka, MN, USA) sling. This technique involved passage of the trocar from a suprapubic incision (lateral to the midline) to a subepithelial vaginal dissection. Subsequently, there have been a number of different modifications of the bottom to top and top to bottom approaches using minor modifications of sling material and surgical instrumentation.

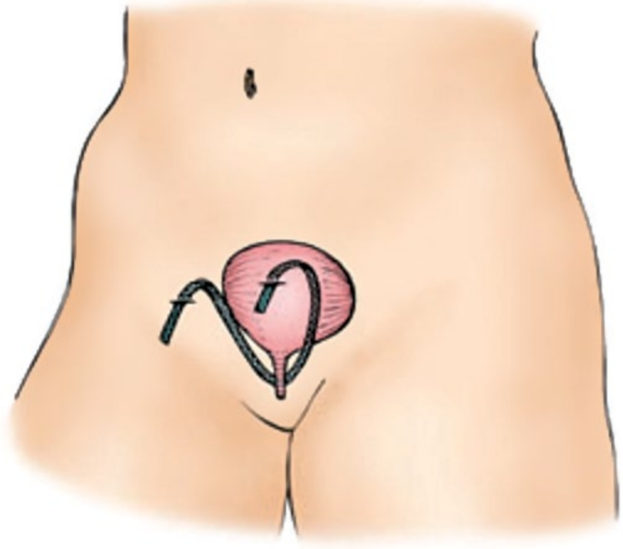

Figure 162.1 Tension-free vaginal tape *in situ*. *Source:* Bullock TL. Advances in female stress urinary incontinence: mid-urethral slings. *BJU Int* 1999;98(s1):32–40. Reproduced with permission of John Wiley & Sons Inc.

**Transobturator MUSS**

The transobturator approach was introduced by Delorme in 2001 [13] to avoid trocar passage in the retropubic space/pelvis addressing concerns over bladder, bowel and major vessel injury, and voiding dysfunction following TVT (Figure 162.2). In this approach vaginal dissection is performed as per the retropubic approach. The original transobturator tape (TOT) operation was described as an "outside-in" technique with the tape being passed from the thigh into the vaginal incision (Uratape, Porges-Mentor, Le Plessis, Robinson, France). In 2003, DeLeval further modified the technique as an "inside-out," approach with a vaginal incision in through the obturator foramen and out the inner thigh as the TVT-Obturator (TVT-O, Ethicon, Somerville, NJ, USA) [14]. Both transobturator approaches involve trocar passage between the vaginal incision, through the obturator membrane and obturator internus muscle to a groin incision below the adductor muscle insertion.

### Types of mesh

A number of different synthetic materials have been used as slings over the past decades. Both monofilament

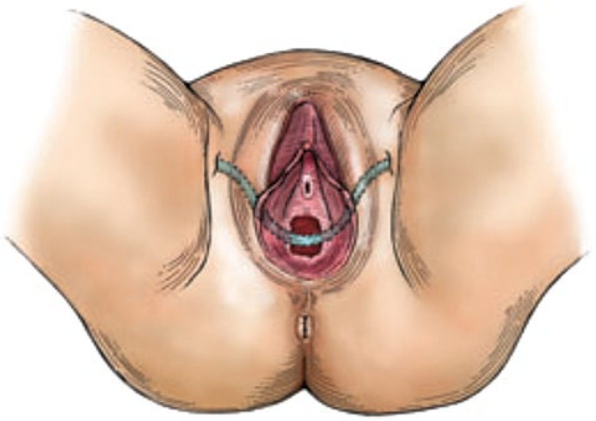

**Figure 162.2** Transobturator tape *in situ*. *Source:* Bullock TL. Advances in female stress urinary incontinence: mid-urethral slings. *BJU Int* 1999;98(s1):32–40. Reproduced with permission of John Wiley & Sons Inc.

and multifilament materials have been tried. The ideal sling material should be inert, nonallergic, and relatively resistant to inflammation and infection. Synthetic meshes are divided into four groups: type 1 – macroporous, monofilament; type 2 – microporous; type 3 – macroporous, multifilament; and type 4 – submicronic, coated biomaterials with pore sizes of <1 μm. Since the introduction of the MUSS, it has become clear that slings made from type 1 mesh are superior to other slings, predominately because they are relatively resistant to infection and inflammation. Slack et al. [15] showed in an *in vivo* study that type 1 mesh had an early and sustained filling with fibrous connective tissue and capillaries showing that macroporous meshes promote tissue host in growth with resultant integration allowing anchoring of the mesh within the tissue. The inflammatory response provoked decreases markedly with time, thus reducing the risk of infection. Both type 2 and 3 meshes had a much more marked inflammatory response without as much fibrous ingrowth. Obtape in particular had barely any fibrous tissue or capillary ingrowth. These findings are in concordance with several other studies that support type 1 mesh as having optimal qualities for use in suburethral slings [15]. The largest trial comparing monofilament and multifilament slings was published by Meschia et al. of 190 patients randomized to TVT or intravaginal slingplasty (IVS). At 24 months follow-up only vaginal erosion was significantly more common after IVS than TVT [16]. In 2005, Domingo et al. reported a 13.8% extrusion rate for the ObTape [17]. Based on the above animal and clinical studies, all commercially available MUS are now made from type 1, noncoated mesh (Table 162.1). Of note, in 2008 the US Food and Drug Association (FDA) released a warning on the safety of vaginal mesh for prolapse repair and SUI that raised significant concern among patients concerning the use of mesh. This was amended in July 2008 when the FDA released an Update on the Safety and Effectiveness of Vaginal Placement for Pelvic Organ Prolapse that applies specifically to pelvic organ prolapse repair [18]. In 2013 the FDA released another statement that multi-incision, midurethral polypropylene slings are safe and effective [19].

## Surgical technique

### Retropubic MUSS

The down-to-up and up-to-down techniques are described. Ulmsten's original technique described the use of intravenous sedation to allow for an intraoperative cough test and adjustment of sling tension [6]. This is not always employed now, so that general, regional, or sedation may be used.

**Table 162.1** Some commonly used commercially available type 1 mesh slings.

| Name | Type | Manufacturer |
|---|---|---|
| Tension-free vaginal tape (TVT) | Retropubic "Bottom to top" | Ethicon Inc., Somerville, NJ, USA |
| Advantage | Retropubic "Bottom to top" | Boston Scientific Inc, Maple Grove, MN, USA |
| Lynx | Retropubic "Top to bottom" | Boston Scientific |
| Prefyx PPS | Prepubic "Bottom to top" | Boston Scientific |
| ObTryx | Transobturator "Outside-In" | Boston Scientific |
| Aris | Transobturator "Outside-In" | Coloplast A/S, Copenhagen, Denmark |
| TVT-Obturator (TVT-O) | Transobturator "Inside-Out" | Ethicon |
| Ajust | Single Incision | Bard Medical Division, Covington, GA, USA |
| Solyx | Single Incision | Boston Scientific |

Adapted from [20].

The crucial steps of the down-to-up procedure (modified from Ulmsten's report [21]) are as follows:

1) The bladder is emptied at the outset of surgery. This allows passage of trocars around an empty bladder, reducing the chance of bladder perforation.
2) Local anaesthetic can be injected in the path of trocar placement and just below the vaginal epithelium to facilitate dissection in the correct anatomical plane beneath the epithelium but above the periurethral fascia.
3) A 1.5 cm midline longitudinal vaginal incision is made, beginning approximately 0.5 cm proximal to external urethral meatus but not extending to the bladder neck to avoid bladder neck obstruction with the sling.
4) The subepithelial plane is dissected laterally from the midline vaginal incision to the endopelvic fascia, minimizing disruption of structures through which the sling will pass. A space large enough to insert an index finger to palpate the endopelvic fascia is made.
5) A stainless-steel catheter guide is placed within the Foley catheter allowing identification of the urethra and bladder neck during trocar passage. This may also help to position the bladder neck for trocar passage.
6) The trocar with attached sling is placed within the previously dissected subepithelial plane. The endopelvic fascia is perforated and the trocar is guided into and through the retropubic space. Close contact with the back of the pubic bone (and avoidance of lateral deviation) is ensured so as to avoid vascular or visceral injury.
7) A small suprapubic incision is made bilaterally just above the pubic bone, about 2 cm lateral to the symphysis pubis, and the trocars exit here.
8) Cystoscopy is preformed with a full bladder to make certain that there is no bladder or urethral injury. If there is an injury the trocar is removed and repositioned.
9) The trocar and attached tape are pulled up and the sling is placed at the level of the midurethra without tension (a Hagar dilator, clamp or pair of scissors can be used beneath the sling to prevent overtightening).
10) In the awake patient, a cough test may be performed to help adjust tension.
11) The casing of the tape is removed.
12) The vaginal wall is closed.
13) The excess tape is excised at the level of the skin incisions on both sides and these are closed.

In most cases a catheter is not necessary postoperatively.

The up-to-down technique is very similar except that the trocars are placed from the suprapubic incision downwards [12]. The vaginal incision is performed as described above. After bilateral paraurethral dissection of the vaginal wall, two small horizontal suprapubic incisions are made, no more than 2 cm lateral to the midline, for needle entry. The needle is grasped with one hand on the handle and the other hand on the curved portion of the needle, near the abdominal incision, to control the direction of the needle tip. Then the needle is passed through one of the suprapubic incisions, down the posterior side of the pubic bone toward the vaginal incision. The needle tip should remain in contact with the posterior pubic bone until it is passed through the endopelvic fascia. Using the index finger of the other hand, the surgeon locates the tip of the needle, then guides it through the vaginal incision. With the first needle in place, the surgeon inserts the second needle on the contralateral side, in the same way [12]. Cystoscopy is performed to check for a bladder or urethral injury. The sling is attached to the end of each trocar and pulled up through the suprapubic incision. The sling is tensioned.

### Transobturator MUSS

As with retropubic MUSS a number of similar devices have been introduced, both outside-in [13] and inside-out [14]. Anatomical studies have shown that in this method the synthetic sling is entirely outside the pelvis (and also retropubic space), within the foremost extension of the ischiorectal fossa [22, 23]. For outside-in placement, the vaginal dissection is performed as per the original TVT operation. A puncture incision is made 15 mm lateral to the ischiopubic ramus on a horizontal line level with the clitoris. The trocar is held in the same hand as the side on which the operator is working. It is held vertically with the handle downwards; it is then introduced through the skin incision and crosses the obturator membrane. As the membrane is crossed, a specific resistance is felt and the handle is rotated to allow palpation of the tip on the finger within the vaginal fornix [24].

The inside-out technique differs in that a small introducer is placed beneath the vaginal epithelium and perforates the obturator membrane. The trocar is then introduced into its grooved surface and rotated 90° toward the thigh, exiting a skin incision made at the level of the clitoris and below the adductor longus tendon. For both techniques it is important that the trocar (and tape) exit/enter the obturator foramen at its superior-medial border, away from the obturator vessels. TOTs tend to tighten when the casing is removed, therefore extra care needs to be taken to avoid this. Although the risk of bladder and urethral perforation are lower for transobturator versus retropubic sling placement, it is not zero. Therefore we recommend performing cystoscopy after all transobturator sling placements to ensure that the bladder and urethra have not been injured.

## Results of midurethral slings

Comparisons of outcomes in incontinence surgery are hampered by variations in definition of success. Definitions of cure may be subjective, where the patient reports absence of stress incontinence, preferably by a validated questionnaire or instrument, or objective, where the absence of incontinence is proven by a negative cough or pad test. In addition, various levels of subjective and objective improvement may constitute success depending upon the study protocols. Long- and intermediate-term data are now available from a number of MUSS trials that provide level 2 evidence for durability of treatment. Long-term data has been published for the original TVT procedure from Nilsson et al. [25]. Their most recent publication provides level 2 evidence with mean follow-up of 16.75 years of 58/90 (78.4%) of patients in their original series. Objective cure, defined in this group as negative cough test, was found in 91.3% of women. Only one woman from the cohort had a further stress incontinence procedure. Subjectively, 87.2% considered themselves cured or significantly better than before surgery based on the Patient Global Impression of Improvement (PGI-I). Long-term data are now also available for the transobturator technique. Liapis et al. recently reported follow-up at 4 years for TVT-O with a cure rate of 82.4% in 74 patients and Waltregny and colleagues reported follow-up at 3 years for the original TOT series described by DeLeval, with a cure rate of 88.4% [26, 27].

Perhaps the best way to describe the results of MUSS is to look at the level 1 and 2 evidence of various randomized controlled and comparator trials. These trials compare MUSS to other surgical procedures. Most of these studies contain “index” patients, which are patients with SUI only and evidence of urethral hypermobility. Here we discuss the use of slings in patients other than these patients and present the evidence regarding their success in these groups. There have been several high-quality reviews of the literature on synthetic slings. A recent Cochrane review by Ford et al. found 81 randomized trials including synthetic slings [28]. These included comparisons between retropubic top-down versus bottom-up approach, transobturator outside-in versus inside-out, and retropubic versus transobturator route. An earlier Cochrane review by Rehman et al. included comparisons between synthetic slings and traditional sling operations or colposuspension [29]. Prior to this Novara et al. had reviewed the complication rates in a meta-analysis published in 2010 [30].

### Comparison trials of MUSS to other surgical procedures for SUI

Initial level 1 evidence for TVT comes from the Ward and Hilton trial, a multicenter randomized controlled trial of TVT versus Burch colposuspension. In the original publication, the authors showed TVT and colposuspension have equivalent efficacy (based on very strict criteria with losses to follow-up considered failures) with 51% cure for TVT versus 63% for Burch [31]. The authors also reported 5-year follow-up data on 117 patients [32]. For the primary efficacy variable of a negative 1-hour stress pad test, there was no difference in success (81% vs. 90%). Furthermore, secondary variables of cure of stress leakage (63% vs. 70%), and satisfied or very satisfied (91% vs. 90%) showed no difference. Hospital stay was significantly shorter for the sling group. There was no difference in the chance of reoperation. However, patients who had colposuspension were more likely to require prolapse surgery (7.5% vs. 1.8%). The authors did note that identifying true durability of cure was somewhat hampered by loss to follow-up across both groups as only 119 of the original 377 patients had full 5-year subjective and objective data sets. A subanalysis of the trial by Manca et al. showed that TVT was more cost-effective than Burch colposuspension, with greater gains in quality-of-life (QOL) years gained [33].

The Cochrane review found 12 randomized trials comparing MUSS to traditional slings [28]. MUSS had a shorter operating time (42 versus 102 minutes) and shorter hospital stays (RR 0.49). Different QOL measures were used in each study, but all showed similar outcomes for traditional versus synthetic slings. For open colposuspension versus traditional slings seven randomized trials were included. Objective cure rates at 12 months ($N = 729$) were 79% for synthetic slings versus 82% for colposuspension. For laparoscopic colposuspension versus slings, the combined results of six trials showed no significant difference in patient-reported outcomes within 12 months; 80% for slings versus 74% for colposuspension. By clinician assessment there was a significant difference in favor of synthetic slings (89% vs. 78%).

### Comparator trials for retropubic MUSS

The Cochrane review found three trials reported on patient-reported cure (defined as absence of leakage on stress) showing a significant difference in favor of bottom to top versus top to bottom at 12 months (87.34% versus 79.58%) [28]. The combined analysis of objective cure rate in five trials (by pad test or stress test) also favored bottom to top by a smaller margin (94.2% vs. 89.1%).

### Comparator trials for transobturator MUSS

There are eight randomized studies that directly compare “outside-in” to “inside-out” transobturator slings [34–41].

These demonstrate equivalent cure rates over the short and medium term; objective cure rates range from 83% to 98% for outside-in and 87% to 90% for inside-out. By subjective measures, most often the PGI-I, inside-out ranged from 76.7% to 100% and outside-in from 77.3% to 97.9%. Similarly in Latthe et al.'s meta-analysis of transobturator slings, indirect comparison of TVT-O and TOT showed equivalent cure rates [42].

### Comparison of retropubic and transobturator approaches

One meta-analysis compared retropubic with transobturator slings with medium-term and long-term results. Tommaselli et al. found 49 eligible studies, both randomized and cohort, with a minimum of 36 months follow-up [43]. In total, 1200 patients were in randomized and 5206 were in cohort studies. When the cohort studies were considered, there was an 83.2% success rate for the retropubic and an 83.5% for the transobturator approach. The pooled estimates for objective cure were similar for retropubic and transobturator with odds ratio (OR) 1.15, 95% confidence interval (CI) 0.75–1.76. The pooled odds ratio for subjective cure in three randomized studies reporting this was 1.76 (95% CI 1.08–2.86) in favor of the retropubic approach. The authors attribute the higher subjective cure rate with retropubic approach to one study that defined success as the absence of reoperation for recurrent SUI on request by the patient [44]. When the cohort studies were included there was 72.7% subjective cure in the retropubic versus 82.1% in the transobturator. The authors caution that differences in long-term subjective cure rate may be confounded by recall bias, including new onset of urgency incontinence unrelated to the original procedure.

In the recent Cochrane review, Ford et al. reviewed 55 trials that compared retropubic and transobturator approaches of MUSS placement [28]. Subjective cure was reported in 36 trials with a total of 5514 participants, and showed no statistically significant difference between routes. In 40 trials with 6145 participants, women were slightly less likely to be objectively cured when using the transobturator route (85.7%) compared with the retropubic route (87.2%); although there was no significant difference, the relative risk for objective cure rate was 0.98 at 12 months. Similarly Latthe et al. found a total of 14 trials comparing either TVT-O or TOT to TVT, showing no difference in subjective cure rate [45]. Sung et al. [46] in a review of 6 randomized controlled trials and 11 cohort studies in 2591 women showed no difference in subjective failure between the two routes; 5.7% for transobturator versus 7.8% for retropubic in randomized controlled trials and 15.4% for transobturator versus 12.8% for retropubic in cohort studies. They did, however, note a lower risk of complications and *de novo* irritative voiding symptoms for the transobturator group. They concluded that it would take a randomized controlled trial of 30 000 women to demonstrate superiority of one approach over the other.

An important study recently characterized long-term outcomes after retropubic and transobturator slings [47]. In this study, women who had been randomized in the TOMUS trial to retropubic or transobturator slings were evaluated at 5 years for treatment success, defined as no retreatment or self-reported stress incontinence symptoms. In total, 404 women (68% of the original cohort) participated. The authors found that there was a 7.9% greater success rate in the retropubic sling compared to the transobturator (51.3% vs. 43.4%, 95% CI 1.4, 17.2). Patients with a retropubic sling also reported greater urinary urgency ($P = 0.001$), more negative impact on QOL ($P = 0.02$) and worse sexual function ($P = 0.001$), however. The authors noted that while both arms reported worsened urinary symptoms and QOL with time, there was no statistically significant difference in satisfaction with high satisfaction for both retropubic (79%) and transobturator slings (85%) at 5 years.

Based on these studies it appears that for the index patient the retropubic MUSS offer slightly higher efficacy over time with perhaps a slight advantage to the transobturator approach with respect to intraoperative and long-term complications.

## Results of MUSS in special populations

### Mixed incontinence

With any SUI operation in the patient with mixed symptoms, there are always concerns about lower cure rates for the stress component and persistent urgency and urgency incontinence for the overactive bladder component. With respect to cure of SUI, studies on MUSS have shown varied results. A systematic review of seven prospective studies found that patients with MUI had an overall subjective cure rate of 56.4% [48]. The overall cure for SUI varied from 85% to 97%, while urgency and UUI were present in 15–75% at up to 5 years follow-up. The authors also performed a meta-analysis on six randomized trials that included women with MUI and found no difference in subjective cure whether retropubic or transobturator MUS was used, regardless of the presence of detrusor overactivity on urodynamics. Nilsson's update of his original series in 2001 included 59 (of 161) patients with MUI, but no detrusor overactivity. At a mean follow-up of 16.7 months, the cure rate for MUI patients (81.4%) was not statistically different from those with pure stress incontinence (88%) [49]. In contrast, a recent retrospective cohort study of 534 women who underwent primary MUSS surgery for SUI reported that those with MUI, defined by at least "moderately" bothersome stress and urgency incontinence, were less likely to have successful improvement in SUI than women with SUI only (64% vs. 84.5%) [50]. These results were calculated from the Urogenital Distress Inventory (UDI-6) subscale that all women completed before and after surgery. Of note, women with MUI had greater improvements in the UDI-6 than those with SUI only, indicating substantial improvement in their urinary symptoms and QOL.

To further stratify patients with MUI, a study of 1113 patients compared those who presented with predominant stress, equal stress and urgency, and predominant urgency incontinence [51]. Preoperative urodynamic parameters, including detrusor overactivity, were not reported in this study. Overall outcomes in these MUI populations were good; 87.3% and 82.7% were stress test dry at 7 and 38 months of follow-up. These authors had strict standards for cure; for subjective cure this was both being very satisfied and having stress and urgency indices of 2 or less on standardized questionnaires, while objective cure had to include negative stress test, pad test <10 g. There was no difference in rates of "stress test dry" at 7 and 38 months between groups, though there was a trend to lower cure rates for urgency-predominant incontinence at 38 months (75.3% compared to 84.7% for stress-predominant incontinence). There were, however, statistically significant differences between objective, subjective cure, pad test dry, and patient satisfaction for stress-predominant versus urgency-predominant patients at 7 and 38 months, with urgency-predominant incontinent patients worse in all parameters. These authors also found that compared with preoperative status, rates of urgency incontinence deteriorated between 7 and 38 months. Holmgren et al. [51] also showed deterioration over time in 2–8 years follow-up. Women with pure stress incontinence maintained a cure rate of 82% to 8 years, whereas women with MUI had a lower cure rate at 60% to 4 years, with a further decline to 30% at 4–8 years after surgery.

Overall, these results suggest that women with mixed incontinence can do well with sling surgery with respect to SUI, but they should be carefully counseled that urge symptoms can persist, with significant impact on patient satisfaction. We believe that women should not be excluded for MUSS surgery based on the presence of urgency incontinence or symptoms.

## Obesity

There is one prospective randomized study that has examined obesity as an independent variable across different surgical procedures to treat SUI, though this was a secondary analysis [52]. The authors found no difference in cure for obese women between TVT and TOT, though this analysis was limited by sample size. They did find a significant difference between nonobese women compared to obese women for both objective (85.6% vs. 67.8%) and subjective (85.8% vs. 70.7%) cure rates. Stav et al. performed a multivariate analysis on 1225 women following MUS that revealed that body mass index (BMI) >25 kg/m$^2$ was a significant predictor (OR 2.9) for MUS failure (along with mixed incontinence (OR 2.4), previous incontinence surgery (OR 2.2), intrinsic sphincter deficiency (ISD) (OR 1.9), and diabetes mellitus (OR 1.8)) [53]. Seven published studies have shown no decrease in cure after TVT, whereas five studies showed a difference [52]. Another retrospective study by Killingsworth et al. reviewed outcomes of TVT at 1 year by PGI-I, UDI-6, and Incontinence Impact Questionnaire (IIQ-7), finding no differences in satisfaction, improvement in QOL, and complications between three groups of normal (BMI <25 kg/m$^2$) overweight (BMI 25–30 kg/m$^2$) and obese (BMI >30 kg/m$^2$) women [54]. A single study by Hellberg et al., where 970 women post-TVT were telephone surveyed at mean follow-up 5.6 years, showed significant differences in cure from 81.2% in BMI <25 kg/m$^2$ to 52.1% cure in BMI >35 kg/m$^2$ [55]. However, this study did not control for preoperative symptom severity and did not use a standardized questionnaire. A more recent study, specifically for transobturator slings in obese (BMI 30–34 kg/m$^2$) and severely obese (BMI ≥35 kg/m$^2$) women reported that at follow-up of at least 12 months, there was no significant difference in failure of TOT, but on subgroup analysis severely obese patients were more likely to have postoperative UUI [56].

## Elderly

The effect of age on outcomes of MUSS is relatively undefined. There are a number of confounding variables such as a higher rate of detrusor overactivity and ISD in the elderly. Also the definition of elderly varies between studies. At best we can say that there is conflicting evidence regarding age and its impact on MUSS outcomes. Liapis et al. showed a cure rate of 76.4% in 55 patients with a mean age of 75.4 years [57]. Pugsley et al. showed a cure rate of 77% for women over 70 years compared to 92% for those younger than 70 years who underwent TVT or colposuspension; however, there was considerable disparity in number with only 22 in the older group versus 100 younger than 70 [58]. Sevestre et al. demonstrated a cure rate of 67% in 76 patients with a mean age of 76 years [59]. Hellberg et al. also analyzed their results in TVT for the "very old" versus other patients, finding a reduced cure rate of 56% for those above 75 compared to 80% for those below 75 years [55]. Conversely, in the retrospective study mentioned above by Stav et al., age was not found to be a risk factor for MUSS failure [53]. Gordon et al. demonstrated similar cure rates between younger (mean age 57.8, $n = 208$) and older (mean 74.9, $n = 123$) patients undergoing TVT at 12 months by absence of persistent stress incontinence at 6% and 7%, respectively. A significant difference between these groups was the frequency of concomitant prolapse repair, at 81% for older women and 67% for younger women [60]. Two other studies also showed equivalence in TVT [61, 62]. Malek et al. showed no difference in SUI failure rates between older (mean age 75.4, $n = 160$) and younger (mean age 56.2, $n = 536$) women [63]. Interestingly, they found the younger patients reported a greater impression of improvement compared to older women (67.7% vs. 56.6%). Campeau et al. compared immediate to six-month delayed placement of TVT in 69 women aged >70 years. At six months, the sling group had improved QOL and patient satisfaction compared to the delayed group [64].

Perioperative morbidity and complications are also a consideration in older patients, with several authors showing higher rates in elderly patients. The study by Gordon et al. [60] showed the risk of *de novo* urge was 18% at 1 year in older versus 4% in younger patients. Also in the elderly group there were 2 cases of pulmonary embolism, 2 cases of cardiac arrhythmia, 1 case of severe pneumonia, and 1 case of deep vein thrombosis versus the younger group, where none of these occurred except one cardiac arrhythmia. Pugsley et al. showed that there were higher rates of patients requiring intermittent self-catheterization, urinary tract infection (UTI), and division of tape (OR 29) [58]. Campeau et al. [64] showed significant perioperative complications: bladder perforation (22.6%), urinary retention (12.9%), urinary tract infection (3.2%), and *de novo* urgency (3.2%). At present there are no studies that report on transobturator slings specifically in an elderly population.

## Recurrent stress incontinence

There are several studies that specifically address surgery for recurrent stress incontinence after failed transobturator or retropubic or mini-slings. On meta-analysis of 14 studies of MUS placement after failed anti-incontinence surgery, Pradhan et al. determined that the repeat retropubic approach was significantly more successful than repeat transobturator approach (79.8% vs. 54%) [65]. They found overall reported cure rates based on objective measurements, such as cough stress test or pad test, for repeat MUSS placement to be 73.3%. Liapis et al. [66] published a series of 31 such patients. They found the overall cure rate when placing a TVT in patients with recurrent SUI was 74%. However, it was best (>80%) in those who had urethral hypermobility and no ISD. Success was reduced but satisfactory (63%) with low urethral mobility (<30°) and no ISD, and was low (40%) with both ISD and a fixed urethra (40%). Meschia et al. included 25/301 patients with previous anti-incontinence procedures in their series using TVT, in which they demonstrated a lower cure rate of 72% for recurrent versus 89% for primary treatment [67]. A review by Stav et al. [68] comparing outcomes of repeat and primary MUS slings in over 1000 patients found 65% subjective success in repeat slings compared to 86% in patients undergoing primary sling placement ($P < 0.001$). They also showed that a repeat retropubic was more successful than a repeat transobturator sling (71% vs. 48%). Both of these results may in part be due to the higher rate of ISD in repeat candidates (31% vs. 13%). Also of note, the rates of *de novo* urgency (30% vs. 14%) and *de novo* urgency incontinence (22% vs. 5%) were higher in the repeat group. The EAU Guidelines on Surgical Treatment of Urinary Incontinence recommends that before a repeat sling procedure is performed, the patient should be warned that the outcome is likely to be inferior to first-line treatment, with chance of both an increased risk of harm and reduced degree of benefit [69].

## Concomitant prolapse surgery/hysterectomy

Groutz et al. published their series of 100 clinically continent women with occult SUI with prolapse reduction [70]. At mean follow-up of 27 months, results were comparable with "index" patients. Only two patients had symptomatic SUI at 1 year. In addition, perioperative morbidity was low, with only two patients requiring catheterization of more than 7 days and *de novo* urgency in 8%, which is comparable with sling-only series. Liang et al. reported a series of patients undergoing hysterectomy and prolapse repair who underwent pessary reduction of the prolapse during preoperative urodynamic testing [71]. Patients with a positive pessary test (occult SUI) were randomized to TVT or no TVT. The rate of postoperative subjective SUI was significantly lower in those who had a TVT placed (10% vs. 65%). No patients with a negative pessary test (none of whom had a sling) had postoperative SUI. A previous prospective trial with 3-year follow-up by Meltomaa et al. found that concomitant vaginal surgery did not affect the outcome of TVT, but there was an increased rate of complications such as infection, bladder perforation, and transient retention after TVT [72]. Ballert et al. [73] used urodynamics to decide which patients should have a MUSS placed with prolapse repair. Patients who had urodynamic proved SUI and occult SUI (with the prolapse reduced, SUI demonstrated during urodynamic studies) had a MUSS placed. The OPUS Trial was designed to address the issue of prophylactic sling placement at the time of prolapse repair in women without SUI [74]. In this trial 337 women were randomized to TVT or sham incisions and the authors found that the rate of *de novo* SUI was significantly higher in the women who did not receive the TVT (27.3% vs. 43% at 12 months). Although the benefit was higher for women with occult SUI, a benefit was seen even in women who had a negative preoperative prolapse reduction stress test. Based on the currently available literature, it would appear that MUSS is a good choice to treat concomitant SUI and prolapse, and is effective in reducing the risk of postoperative SUI in women with occult SUI.

### Intrinsic sphincter deficiency

ISD represents the portion of SUI that is not due to a support defect or urethral mobility. ISD is difficult to quantify and even more difficult to diagnose in patients who also have urethral mobility. Most of the literature has used a definition of an abdominal leak point pressure (ALPP) of $<60\,\text{cmH}_2\text{O}$ or a maximum urethral closure pressure (MUCP) of $<20\,\text{cmH}_2\text{O}$. While we would agree that these lower resistance urethras are probably more difficult to treat, it is difficult to say that the lower resistance is due to true ISD rather than a support defect (except in the fixed urethra). Nevertheless the literature has made that distinction and for the purpose of this review we will accept that as "ISD," but prefer to use the term "low ALPP." More recently, ISD and urethral hypermobility have been viewed as a spectrum of disease with overlap. Thus recent research examines the contributions of ISD and urethral hypermobility to outcomes.

Patients with low ALPP are more likely to develop recurrent SUI after MUS than those without low ALPP [68]. Retropubic MUSS have been shown to be effective in treating this group of patients. Rezapour et al. [75] reported on their long-term results in patients with low ALPP, defined as MUCP $<20\,\text{cmH}_2\text{O}$, at 2 years, with cure rates of 74%, 12.5% improved, and 12% no change. These results compare favorably with their and other author's results for all comers with SUI. There are eight studies reporting data specifically for women with low ALPP which favor retropubic over transobturator MUSS and one RCT [76] showing equivalence in patients with low ALPP [77]. Fritel et al. [8] showed that TVT was most effective in treating the hypermobile urethra but had acceptable success rates for the relatively fixed urethra. Success rates at nine months were 97% with Q-tip test >60°, 86% for Q-tip test 30–60°, and 70% for Q-tip test <30°. There was no difference in success based on MUCP greater or less than $20\,\text{cmH}_2\text{O}$. A small study ($n = 65$) by Haliloglu et al. [78] of urethral hypermobility (Q-tip test >30°) and low ALPP (ALPP $<60\,\text{cmH}_2\text{O}$) with TOT found that cure rates at 24 months (defined as a negative cough test) were: urethral hypermobility, no low ALPP 96.4% ($n = 31$); urethral hypermobility and low ALPP 87.5% ($n = 18$); and no urethral hypermobility and ALPP 66.7% ($n = 16$). They concluded that a lack of urethral hypermobility may be a risk factor for TOT failure and suggested that even in the presence of low leak point pressures suggestive of low ALPP, the coexistence of urethral hypermobility still indicates likely good outcomes with transobturator MUSS.

The literature suggests that patients with low ALPP may do better with retropubic MUSS but the evidence is not strong enough to support a high-level recommendation. Since urodynamic studies are no longer recommended for uncomplicated SUI, and thus ALPP will not be determined in these patients, one might lean toward a retropubic MUS in cases of a more fixed urethra.

## Single-incision slings

Although the retropubic and transobturator MUSS are considered minimally invasive procedures, efforts have been made to make the procedures even less invasive. The single-incision slings or "mini-slings" were designed to be placed via a small vaginal incision (like the traditional MUSS) but without any exit incisions. They sit like a hammock (mimicking the transobturator slings) or like a U (mimicking retropubic slings).

A number of single-incision slings were brought to the market through the FDA's 501 k process. There was promise that single-incision slings would yield easier implantation with lower complications and quicker recovery, but this has not been borne out in early trials. In 2012 following a series of lawsuits concerning the mesh slings, some prolapse repair kits and single-incision slings have been removed from the market. Currently, several single-incision slings are still available, but they do not have long-term outcomes [79–81].

A recent Cochrane review analyzed 31 peer-reviewed studies including 3290 women that compared single-incision slings to traditional MUSS [80]. Of note, many of these trials studied the TVT-Secur, which is no longer available. They found higher rates of incontinence after surgery with single-incision slings compared to both retropubic (RR 2.08) and transobturator (RR 2.55) slings. When compared to retropubic slings, the reported duration of surgery for single-incision slings was slightly shorter, but risk of *de novo* urgency was higher (RR 2.39). The analysis also found higher rates of adverse events such as lower urinary tract injury, postoperative voiding difficulties, mesh erosion, *de novo* urgency, or worsening of preexisting urgency with the single-incision slings. This difference disappeared when the TVT-Secur was removed from analysis, but groin pain rate was significantly lower with the single-incision sling (RR 0.30). The authors report that when studies including the TVT-Secur were removed from analysis there was insufficient evidence to show a difference between single-incision slings and transobturator slings or to compare the other single-incision slings to each other.

More high-quality trials are needed to determine whether the single-incision sling is equivalent to the retropubic and transobturator. Available data are short- and medium-term only, with mixed results. Further research is also required to determine whether there are differences between the many available single-incision slings still available.

## Complications of MUSS and their management

Here we outline the incidence of complications and briefly discuss management for intraoperative complications (bladder, urethral, bowel, and vascular injury), immediate postoperative complications (voiding dysfunction and obstruction, groin pain, infection), and chronic problems (obstruction requiring surgical intervention, *de novo* urgency, sling erosion/extrusion).

### Intraoperative complications

#### Bladder perforation

Bladder perforation occurs at approximately 3.4% during TVT [30]. Transobturator slings were conceived to reduce the risk of bladder (and vessel) injury by avoiding the retropubic space. Three reviews have confirmed this. The recent Cochrane review found 40 trials reporting on bladder perforation and pooled data to show that TOT had significantly lower rates of bladder injury than retropubic slings (0.6% vs. 4.5%) [82]. Novara et al. [30] showed that in analysis of nonrandomized data, TOT was statistically less likely to cause perforation than retropubic slings and Latthe et al. showed in their meta-analysis of trials comparing TVT-O and TOT versus TVT the ORs of bladder injury were 0.11 and 0.15, respectively [42].

Bladder perforations recognized intraoperatively can be managed by removal of the tape and replacement of the tape. Cystoscopic confirmation that the final position is indeed outside the bladder is crucial.

Urethral injury is a rare occurrence with both retropubic and transobturator MUSS. Like bladder injuries, they are treated by removing the tape. In cases of a large injury, consideration should be given to aborting the procedure and allowing urethral healing for three months before inserting a new sling.

#### Vascular and bowel injuries

An important paper was published by Deng et al. in 2007 regarding the reporting of major complications after MUS surgery [83]. They reviewed the literature and compared this to reporting through the FDA Manufacturer and User facility Device Experience (MAUDE) database queries for self-reported complications for the same time period. Their review of the world literature 2001–2005 found the rate of major complications to be 0.8% with no reported deaths. In the MAUDE database from the United States 928 total complications were reported in that time period, including 161 major complications with 10 resulting in death. Notable differences were noted, with 36 serious vascular injuries and 38 bowel injuries in the MAUDE database but only 2 vascular and 3 bowel injuries in the literature 2001–2005.

Vascular injury occurs very rarely but this is a devastating complication for a QOL procedure. The MAUDE database was discussed and published by Deng et al. in 2007. National registries provide the best indicators of worldwide incidence and are summarized in a case report and literature review by Sivanesan et al. for 2006 [84]. The incidences of vascular injury reported include: 0 (of 1455) in the Finnish registry, 0.8% (from 5578) reintervention or conversion rate in the Austrian registry, 0.03% (of 2280) in the French registry, and 0.1% of 809 in the Netherlands registry [85, 86].

Management depends on the patient's hemodynamic status. In those who are stable angiographic embolization avoids further operative morbidity, while those who are unstable may require laparotomy and control of bleeding.

Bowel injury is also a very rare complication in the literature, estimated at less than 1%. Two were reported in 12 280 cases in the French registry for TVT [86]. Ten cases were reported after TVT in the FDA MAUDE database in Daneghasri's review of complications in 2008 [87]. Six deaths had resulted from bowel injury. No cases of bowel injury have been reported after TOT.

### Postoperative complications

#### Voiding dysfunction and obstruction

Voiding dysfunction is reported at varying levels after sling surgery. A population-based cohort study of 188 454 women who had a MUSS calculated the postoperative risk of urinary retention to be 0.9% at 1 year, with a cumulative 9-year risk of 2.5% [88]. The recent Cochrane review found that transobturator slings had a lower incidence of voiding dysfunction than retropubic (RR 0.53, moderate quality evidence) [82]. The TOMUS trial reported equivalent outcomes with retropubic compared to TOT at 12 months, but by 2-year follow-up the incidence of voiding dysfunction was significantly higher, with retropubic sling at 3% compared to 0% with transobturator placement [89].

Symptoms of *de novo* urge may be secondary to urethral obstruction and while not an absolute indicators in themselves of voiding dysfunction, refractory symptoms with timing associated with intervention or association with voiding symptoms should alert the clinician to the possibility of obstruction. It is especially important to document the relationship of symptom onset to surgery. If patients report symptoms of voiding dysfunction, a free flow rate should be measured. The necessity of urodynamics in this setting is controversial. We would not consider them always necessary in the setting of classic obstructive voiding symptoms, retention, or high postvoid residual (PVR) (with normal preoperative PVR) [90]. However, video-urodynamics would be useful in patients with storage symptoms to determine whether obstruction is present at the level of the sling.

Conservative management includes observation for irritative/storage symptoms and clean intermittent selfcatheterization for high PVR and retention.

With respect to timing of sling loosening or cutting, we favor an approach of early tape loosening for severe obstructive symptoms and retention. Several small series now suggest that early intervention should be favored as delayed intervention may lead to irreversible bladder symptoms. Leng et al. published a series of 21 patients who underwent sling lysis. When they stratified patients by their postoperative symptoms or absence of symptoms, there was a statistically significant difference in mean time to sling lysis: 9 months in the no symptom versus 31 months in the persistent symptom group [91]. South et al. showed a similar trend, although their series had relatively small numbers of synthetic slings [92]. Nguyen published a series of 10 women who underwent tape loosening (under anesthesia) at 3–10 days with all spontaneously voiding after this and no recurrence of obstruction or SUI at 1-year follow-up [93]. Price et al. published their series of 33 women who had early sling loosening (mean 7.7 days) under general anesthesia. This was successful in 29 women, with 4 requiring tape division at 4–8 months. All patients had resolution of voiding symptoms with 1 of the 4 tape division patients having the only recurrence of stress incontinence [94]. In contrast, a recent retrospective review of 63 patients who underwent sling revision did not find a significant difference in outcomes in women who underwent early (revision compared to late with 13% of the early group and 11% of the late group experiencing persistent voiding dysfunction) [95]. However, this study defined early as <1 year, which included patients with significantly longer time to removal than the other studies mentioned.

We consider intervention for patients who have retention or near retention at 1–2 weeks. For early intervention, sling loosening in the office or operating room can be considered. We perform this procedure in a similar fashion under local anesthesia in the office and have found this to be well tolerated. After injection of local anesthesia, the incision is opened by removing the prior closure suture. The sling is hooked with a clamp and the clamp is spread. If this fails to loosen the sling, it can be cut. Animal studies have shown fibroblast infiltration of the tape at one week, which supports Price et al.'s observation that tapes cannot be loosened after 2 weeks [94]. At this point, it is easiest to cut the tape in the operating room setting.

### Groin pain

Groin pain may occur after transobturator sling but has not been noted after retropubic slings. In the systematic review by Latthe et al. this occurred in 12% in the transobturator group compared to 0.9% in the TVT group (OR 8.28). Similarly, the Cochrane review found 6.4% incidence of groin pain in the TOT group versus 1.3% in the retropubic group (RR 6) [82]. The differential diagnosis of persistent groin pain after TOT includes adductor muscle strain, osteitis pubis, obturator/groin abscess, structural adhesions, and inflammation, edema or nerve entrapment of the anterior branch of the obturator nerve. There is a limited amount of literature regarding treatment of pain.

Workup should include examination and lab tests to exclude hematoma and infection. Magnetic resonance imaging can visualize edema, hemorrhage, and the obturator nerve itself; however, it cannot see the polpropylene tape nor smaller branches of the nerve. Described methods include pain medications, steroids, and excision of part or all of the sling. Hazewinkels et al. advised against delaying sling removal, as further scar tissue deposition can hamper removal and nerve damage may become irreversible [96]. Reynolds et al. described eight cases of intractable groin pain treated with complete removal of MUS arms via an extended obturator foramen dissection in conjunction with orthopedic surgery [97].

### Infection

UTI is the most common complication following MUSS placement and should be treated with appropriate antibiotics [87].

Seven cases of abscess (associated with vaginal erosion) following TOT were reported in the Austrian registry.

The authors concluded that these seemed more common after TOT than retropubic tapes, although four of the abscesses were associated with the Obtape, which is a 50 μm pore tape that has been removed from the market [98]. Infections are rare with the current type 1 macroporous meshes. Treatment requires complete excision of the infected tape.

## Chronic complications

### Obstruction requiring surgical intervention

Patients may present early, with retention as described above, or late with obstructive voiding symptoms: feeling of incomplete emptying, straining or hesitancy, needing to lean forward or stand, partial or complete urinary retention, or symptoms suggesting overflow incontinence. Obstruction requiring surgical intervention occurs in about 2% [82]. This is significantly lower than the rates of obstruction with pubovaginal sling, which was observed to be 6.2% in the SISTEr trial [99].

A few small series have been published reporting techniques and outcomes for sling loosening/lysis. Klutke et al. [100] described 17 patients (2.8% of a 600 patient series) who presented with obstructive symptoms following TVT. The time to sling loosening or cutting ranged from 6 to 228 days. Two techniques were used in this study: the "Washington University" technique used a right-angle clamp to identify the sling which was then transected or the "Minneapolis" technique, in which the sling was identified and loosened with Metzenbaum scissors with downward traction without sling transection. All 17 patients in this series had immediate postoperative relief of symptoms with ability to void. One patient had recurrence of stress incontinence.

Rardin et al. [101] described 23 patients (1.9% of 1175) who underwent TVT who had persistent voiding dysfunction. The mean interval between TVT placement and release was 17.3 weeks. In this study all tapes were transected or segmentally excised. Presenting symptoms were impaired bladder emptying in 20, 3 had severe irritative symptoms, and 7 had both. Seven patients had urethral dilation after TVT placement without resolution of symptoms. Resolution of voiding symptoms differed by symptom. Impaired emptying resolved in all cases. However, complete resolution of irritative symptoms occurred in only 30% of cases at the study endpoint after six weeks. Stress incontinence recurred partially in 26% and completely in 13% of patients.

Patients with storage/irritative symptoms should also be warned that in a study of 44 patients undergoing sling takedown or urethrolysis, two-thirds of patients with preoperative storage/irritative symptoms still had them postoperatively. Only 14 patients with suburethral synthetic slings (all TVT) were included in this study, so the numbers may not be sufficient to draw conclusions from this study alone [102].

For persistent voiding dysfunction after a MUSS has been formally cut, a formal transvaginal urethrolysis is the next step. It can be done through a midline vaginal incision. Fortunately this is rarely required.

### Lower urinary tract symptoms

*De novo* urgency can occur following sling surgery with rates ranging from 3% to 25.9%. The Cochrane review showed no significant difference in rates of storage symptoms between retropubic and transobturator slings with either short or medium term follow up [82]. It found the average short-term rate of *de novo* urgency for both groups was 8.35%. A recent review by Abraham et al. identified modifiable causes of postoperative urgency, including UTI (7.4–14.7%), bladder outlet obstruction (1.9–19.7%), perforation of the urinary tract (0.5–5%), and idiopathic 0–28% [103].

Risk of postoperative urgency or UUI was found on retrospective review of nearly 1000 patients to be higher for women with intrinsic sphincter deficiency, prior surgery for SUI or prolapse, and preexisting detrusor overactivity [104]. Holmgren et al. reported on a series at a mean follow-up of 5.6 years and discussed several important findings, such as patients with urgency will experience lower quality of life even if their stress incontinence is cured and urgency incontinence may not be reported in sling failure figures. In addition, urgency symptoms may not be transient and in fact the proportion of the group with urgency remained consistent over time [105]. The study compared women with and without *de novo* urgency and showed there were large and significant differences in QOL scores; the women with *de novo* urgency had an IIQ-7 of 28.1, as compared to 5.6 for those in the comparison group ($P = 0.0001$), and for the UDI-6 the corresponding figures were 49.6 and 13.6, respectively ($P = 0.0001$). They noted that "persistent incontinence" may not be reported as failure in many series if that incontinence was urgency incontinence (i.e. success is sometimes defined by absence of leakage on stress testing or patient-reported stress incontinence). As these authors note, urge and urgency incontinence may, in fact, be more bothersome to women in everyday life than stress incontinence. In their series, 51/67 patients with *de novo* urgency had actual incontinence episodes. Although most authors report that *de novo* urgency will be transient, these authors showed that 14.5% of women experienced this symptom with similar frequency across duration since TVT surgery (from 2 to 8 years).

Urgency caused by bladder outlet obstruction or urinary tract perforation should be treated as described above, while idiopathic postoperative urgency may be treated as idiopathic overactive bladder. A prospective study found onabotulinum toxin A to be equivalent for treatment of *de novo* urgency following MUS ($n = 49$) and idiopathic overactive bladder ($n = 53$) [106]. The exception to this is solifenacin, which was found in a recent study of 230 women to have lower efficacy for patients with *de novo* urgency following TOT compared to patients with idiopathic urgency [107]. Further work remains to be done to identify the optimum treatment of urgency following MUS placement.

#### Vaginal erosion/extrusion

Vaginal erosion/extrusion is reported at 2.09%. The Cochrane review found no significant difference of vaginal erosion in the TOT or TVT group [82]. In contrast, Latthe et al. found the transobturator path had a higher risk of vaginal injury (OR 3.58) [42]. Similar to bladder mesh erosion, some vaginal erosions may represent unrecognized vaginal perforation (especially at the vaginal fornices) intraoperatively. Symptoms of vaginal extrusion include malodorous vaginal discharge, postcoital spotting, dyspareunia (patient and partner), vaginal bleeding, and UTI.

Management of extrusion optimally involves surgical removal of that portion of the tape. Some authors have described a trial of conservative therapy with estrogen cream.

#### Sexual function

There are several studies that show equivalent results for sexual function after TOT and retropubic slings. They also demonstrate that while there are significant numbers who improve (29–32%) there are also some who deteriorate following anti-incontinence surgery (12.5–17.3%), with no difference demonstrated by Senthilhes et al. in their recent comparison between transobturator and retropubic synthetic slings [108].

#### Bladder and urethral erosion

Fortunately, erosion of MUSS into the bladder or urethra is a rare occurrence. When it is recognized, the first question that must be asked is whether it is a true erosion or a missed injury. In 14 randomized trials reviewed by Novara et al., only three trials reported on this, with rates from 0 to 1.8% for transobturator and 0–1.9% for retropubic slings. In assessment of four randomized trials with bladder or urethral tape erosion, no significant difference was seen between retropubic and transobturator sling placement (RR 0.34) with range from 0 to 2.9% [82].

Many authors believe that erosions into the bladder are actually slings inadvertently placed through or in the wall of the bladder at the time of surgery. McLennan and Melick demonstrated a learning curve with respect to bladder perforation [109]. Residents' cases were placed in groups of five; the rate of injury in the first five series was 40.9%, 30.7% in the second series of five, and 25.9% in the third series of five. The differences were statistically significant. Overall, there was a significant rate of missed perforation on cystoscopy with 35 of the 95 injuries missed by residents (37%). This emphasizes the need for thorough cystoscopic examination at the time of surgery to avoid missed perforations, which present as "bladder erosions." Such injuries may present with UTIs, bleeding, or bladder stones. Treatment requires removal of the sling from the bladder. Endoscopic techniques have been described with endoscopic scissors and lasers; laparoscopic techniques via the bladder and open excision are also used.

The mechanism by which urethral erosion occurs is probably due to dissection into the incorrect anatomical planes around the urethra if dissection is too close to the urethra or in the periurethral fascia or if the sling is placed under tension. Data from the Austrian registry reported urethra/bladder erosion at 0.5%.

A series of 14 urethral injuries following sling surgery was published by Morton and Hilton [110]. These patients had undergone TVT, TVT-O, SPARC, and TOT types of slings. Their pathologies included 6 perforation/erosion, 4 diverticulae, and 4 urethrovaginal fistulas. Most of the patients had had abnormal symptoms following sling insertion, including urinary retention, persistent incontinence or obstructed voiding. Each of these patients required reconstructive surgery, with 7/14 having significant persistence of overactive bladder symptoms, 1 having voiding difficult, and 1 persistent groin pain. These authors also performed a literature search for further cases, finding four further reports of urethral diverticulum and 15 of urogenital fistula. The authors used case series reports of urethral perforation to calculate rates of urethral perforation of 0.88% for retropubic slings and 1.09% for transobturator slings. Although the authors acknowledge that it is difficult to determine the true denominator, they conclude that the incidence of urethral injury appears no lower for transobturator than for the retropubic route. Thus they emphasize the importance of operative cystoscopy in all types of slings.

Urethral erosion requires removal of the eroded portion of sling and primary closure or urethral reconstruction with vaginal/Martius flaps.

## Conclusions

MUS have revolutionized female incontinence surgery. From their inception they offered comparable efficacy to existing operations with improved ease of performance for the surgeon and improved postoperative morbidity for the patient.

These results have proven durable in the long term. Further innovation of the technique includes the emergence of transobturator and mini-slings. Although complications of these slings are relatively rare, surgeons who perform these operations should be mindful of their symptoms so that management is expedient.

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# 163

# Maxi/Pubovaginal Sling

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## Introduction

Urinary incontinence is a common symptom affecting almost a third of adult women [1]. It can occur due to hypermobility or intrinsic sphincter deficiency of the urethra (stress urinary incontinence (SUI)) and/or bladder dysfunction. Whatever its etiology, urinary incontinence is associated with poor quality of life and most incontinent women develop symptoms such as anxiety, depression, and social isolation over time [2, 3]. The American Urological Association (AUA) guidelines for SUI list several surgical options, of which the most common are pubovaginal and midurethral sling [4]. In 2010, approximately 560 000 women with SUI underwent surgical repair with mesh products; however, the use of various synthetic biomaterials from a variety of manufacturers gave rise to a wide range of mesh-related complications [5]. For these reasons, despite the advantages of minimally invasive procedures for SUI, use of pubovaginal fascial slings has increased over the last few years [5]. This chapter addresses the following subjects regarding pubovaginal fascial slings: indications, surgical technique, postoperative complications, and surgical outcomes.

### Historical landmarks

In 1907, Von Giordano described the use of gracilis muscle wrapped around the urethra for the treatment of women with SUI [6]. Three years later, instead of gracilis muscle Goebell used the pyramidalis muscle to improve the urethral support [7]. Autologous fascial sling was first reported by Price in 1933 when he used a suburethral strip of fascia lata for the treatment of women with recurrent SUI [8]. In 1942, Aldridge used a rectus fascia segment placed inferiorly through the rectus abdominis muscle to provide urethral support [9]. Thirty years later, in 1978 McGuire and Lytton reintroduced the concept of fascial slings for women with SUI. They used an autologous rectus fascia segment to suspend the bladder neck and promote urinary continence [10]. In 1991 Blaivas and Jacobs described midurethral slings and outlined the importance of mid urethra in urinary continence control [11, 12]. Midurethral synthetic slings were first described in 1996, with the tension-free vaginal tape (TVT) [13]. Since then, the development of different types of nonabsorbable biocompatible materials, minimal invasiveness, and availability of easy-kits has resulted in an exponential increase in the number of mesh surgical procedures performed by both urologists and gynecologists [14, 15].

### Hammock theory

The hammock theory was described by DeLancey in 1995 [16]. According to his theory the urinary continence relies on urethra and bladder neck compression by a hammock-like musculofascial layer. When this layer is deficient, funneling of the bladder neck during increased intra-abdominal pressure can result in urinary incontinence. Thus, the placement of pubovaginal slings around the mid urethra aims to provide an additional support for the continence mechanism.

## Diagnosis

By definition, SUI is an involuntary leakage of urine with effort or exertion, such as physical exercise, sneezing, or coughing. SUI is a clinical diagnosis based on a patient's history and physical examination [4].

*Smith's Textbook of Endourology*, Fourth Edition. Edited by Arthur D. Smith, Glenn M. Preminger, Louis R. Kavoussi, and Gopal H. Badlani.
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Companion website: www.wiley.com/go/smith/textbookofendourology

When urinary incontinence is not demonstrated on physical exam, additional tools such as a three-day bladder diary and pad test can be helpful. The three-day bladder diary assesses associated symptoms, such as urinary frequency and nocturia, and measures the functional bladder capacity, whereas the pad test can objectively demonstrate urinary leakage [17, 18].

Urogenital prolapse and postvoid residual volume (PVR) should be well documented prior to any therapeutic intervention. Women with prolapse can unmask occult SUI after prolapse reduction, and patients with high PVR are at risk of postoperative urinary voiding difficulty [19].

The role of urodynamic study (UDS) is still controversial in the literature. Overall, UDS is recommended by the AUA guidelines for women with mixed incontinence, significant anterior pelvic organ prolapse and SUI, recurrent SUI, patients with neurological diseases, diabetes mellitus, and those with high PVR [4, 20].

## Indications

Pubovaginal fascial slings are indicated for patients with SUI due to intrinsic sphincter deficiency and/or urethral hypermobility. They are also recommended for the following conditions [21, 22]:

- patients with prior midurethral synthetic sling who had any mesh-related complication;
- patients with urethral diverticulum and SUI;
- patients with SUI and prior pelvic irradiation;
- patients with urogenital fistula;
- patients with urethral stenosis who need urethral reconstruction.

## Preoperative preparation

Estrogen cream can be prescribed for 4–6 weeks preoperatively in postmenopausal women with vaginal epithelial atrophy if there are no contraindications. If the patient uses a pessary, it should be discontinued two weeks prior to surgery. Patients using only “baby” aspirin do not need to stop the medication prior to procedure. In the presence of urinary tract infection, coagulopathy, or other significant medical comorbidity, surgery should be postponed. All patients should be counseled about the risk of retention and recurrence. Laxative diet and fluid intake is advisable to avoid postoperative complications. Regarding antibiotic prophylaxis, first- or second-generation cephalosporin is given intravenously at least 1 hour prior to the procedure and continued for the next 24 hours [23].

## Choice of tissue/biomaterial

### Autologous fascial tissue

Autologous fascial tissue can be harvested from patient’s rectus fascia or fascia lata for sling procedures, so there is no risk of rejection. Nevertheless, the quality and strength of the tissue will depend on the patient’s age and previous surgical manipulation [24, 25]. Overall, autologous fascial slings have better long-term outcomes than Burch procedure and are comparable to synthetic slings but are associated with postoperative morbidity and convalescence [26].

**Rectus fascia**

Rectus fascia is the most common autologous tissue used in pubovaginal fascial slings. Tissue is obtained through a low transverse abdominal incision. Then dissection is carried out down to the level of the anterior rectus fascia. Following the dissection, a 1 cm × 12–16 cm fascial segment at least 5 cm above the pubic symphysis is marked with a marker pen. Two sutures are placed at either end of the fascia, perpendicular to the fascial fibers. The fascial strip is mobilized and removed carefully. Then the fascial defect is closed in a running fashion with delayed absorbable or nonabsorbable sutures.

**Fascia lata**

The main advantages of fascia lata are the lower risk of abdominal wall hernias, greater tensile strength than rectal fascia, and no previous surgical tissue manipulation. The disdvantages are that for tissue harvesting the patient needs to be repositioned, the procedure carries a risk of pain/disability, and most urologists are not familiar with the surgical field [27, 28]. The fascia lata can be harvested using different surgical approaches. We have used the technique described by Govier et al. [27]. The patient is placed in the full lateral position with the entire thigh, from the iliac crest to the tibial plateau, being prepped and draped into the surgical field. A vertical line is drawn from the greater trochanter of the femur to the lateral condyle of the knee. A 3 cm perpendicular incision is made at the midpoint of this line. Two additional perpendicular incisions of 3 cm in length are made, flanking the first incision 9 cm superior and inferior. Then the fascia lata is cleared off from the overlying subcutaneous fat. At the three skin incision sites, incisions parallel to the direction of the fascial fibers are made 2.5 cm apart. At the distal and proximal ends of the fascia, two stay sutures are placed perpendicular to the fibers of the fascia and the fascial incisions are connected to a free segment of fascia lata approximately 24 cm in length and 2.5 cm in width. After a careful hemostasis, the fascia lata is not approximated, and the

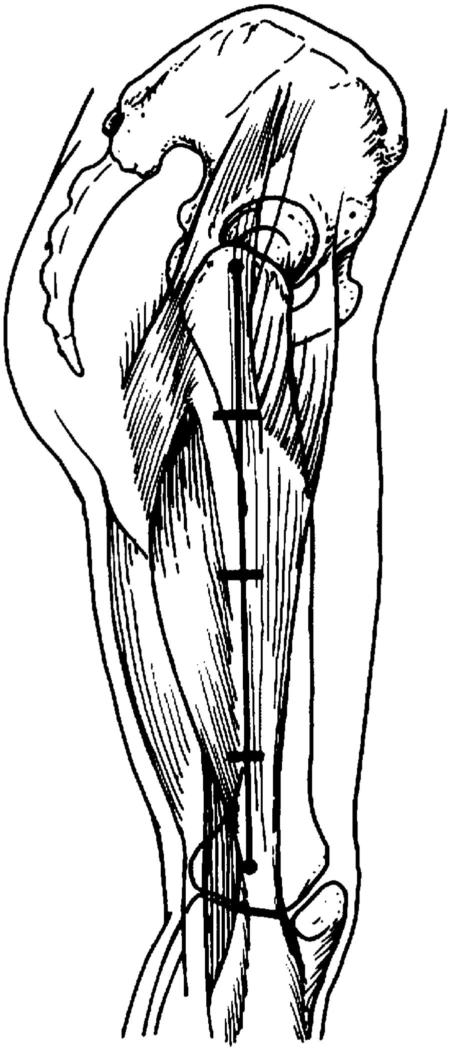

**Figure 163.1** Fascia lata – skin incisions. *Source:* Govier FE, Gibbons RP, Correa RJ et al. Pubovaginal slings using fasica lata for the treatment of intrinsic sphincter deficiency. *J Urol* 1997;157:117–121. Reproduced with permission of Elsevier.

skin is closed with a stapler. The leg is then wrapped with an elastic dressing, which is removed 8 hours postoperatively. Early ambulation is required for all patients (Figure 163.1).

### Synthetic slings

In the last decade there has been widespread use of synthetic slings. The main advantages when compared to autologous fascial slings are: (i) lower operating time; (ii) minimal invasiveness; (iii) no risk of disease transmission; and (iv) strength maintenance over time [29–31]. Monofilament polypropylene mesh with large pore size (>75 µm) is the "gold standard" synthetic biomaterial for slings. The monofilament polypropylene decreases bacterial adherence and reduces the risk of infection and foreign-body response, and the large pore size promotes mesh flexibility, facilitates host tissue integration, and allows immune cells to scavenge bacteria [31–33]. The incorporation of mesh into the sling surgical setting has decreased patient's morbidity. However, and not less important, vaginal mesh placement is associated with unique potential risks such as vaginal mesh exposure, infection, dyspareunia, and chronic pelvic pain. All of these postoperative complications should be addressed with the patient prior to the procedure [34–36].

#### Synthetic mesh substitutes

Several types of allogenic and xenogenic materials have been used as fascial sling substitutes aiming to provide readily available biomaterial without additional morbidity associated with fascia harvesting [37].

Xenografts for pubovaginal sling include material derived from porcine dermis (Pelvicol, C.R. Bard Inc., Murray Hill, NJ, USA), porcine small bowel (SIS™, C.R. Bard Inc.), and, more recently, bladder extracellular matrix. These are available as off-the-shelf biomaterials and are not used routinely for pubovaginal sling procedures. Some xenograft-related issues are the higher product costs, biomechanical variability, risk of rejection, and disease transmission [38, 39].

Like xenografts, allografts have the advantage of not requiring fascial harvesting and have similarly decreased operative times, less postoperative pain, and shorter convalescence. They are also available as an off-the-shelf material that can be used as needed. Allograft materials have lower erosion rates compared to synthetic meshes, but these advantages must be weighed against the higher cost and the risk of disease transmission [40].

## Operative techniques

After anesthetic induction, the patient is positioned in the dorsal lithotomy. The abdomen, pubis, and perineal area are shaved using clippers and then prepped with chlorhexidine-based chemical antiseptic. The patient is then draped in a sterile fashion. A 16 Fr urethral catheter is placed in the urethra and the balloon is inflated to facilitate the bladder neck identification. A 10 cm Pfannestiel incision is made above the symphysis pubis. Using cautery, the dissection is carried out through Camper's and Scarpa's fascia, and the anterior rectus fascia is identified. Using sharp and blunt dissection, the fascia is cleaned of the overlying fatty tissues. A scar-free area of the fascia at least 5 cm above the symphysis pubis is chosen. As described above, 1 cm × 12–16 cm fascial segment is marked with a marker pen. At the lateral aspect of the sling, the holding sutures are placed using 0-prolene sutures. The sling segment is carefully dissected from the rectus muscle, harvested, and placed in a saline solution with antibiotic. A Lone Star surgical retractor is used to retract the labia and open the vaginal introitus for better exposure. A weighted speculum is placed to retract the posterior fourchet. An Allis clamp is placed at the hymen ring along the anterior vagina and bupivacaine with epinephrine is injected 1 cm proximal to the urethral meatus toward the bladder neck, for vaginal tissue hydrodissection.

A 4 cm midline incision is made at mid urethra with the Foley balloon used as a guide. Metzenbaum scissors are used to dissect thick flaps of anterior vaginal wall epithelium in an anterolateral fashion, toward the ipsilateral shoulder, until the endopelvic fascia is reached. The Foley catheter and balloon should be constantly used as a guide to the urethra and bladder neck. At this point, with either the Metzenbaum scissors or blunt finger dissection, the endopelvic fascia is opened bilaterally. A packing sponge is placed in the vagina and attention is turned to the lower abdominal incision.

After emptying the bladder, a Stamey needle is passed through the anterior rectus fascia 2 cm above the symphysis through the retropubic space under digital guidance from the vaginal incision bilaterally and connected to the vaginal incision. As this surgical plane is being developed with ether blunt or sharp dissection, it is important to stay close to the posterior surface of the pubis to avoid blood vessel and bladder injuries. A cystoscopy is performed using a 70° lens to rule out any bladder injury. Bladder is emptied and catheter replaced. The sling is then placed under the proximal urethra and bladder neck, using two Stamey needles, the holding sutures on the lateral edges of the sling are brought to the abdominal incision through the retropubic space. Hemostats are placed on each set of holding sutures laterally. A 3-0 PDS or Vicryl suture is used to fix the midline of the sling, previously marked, to the periurethral tissue at 1 cm proximal and distal to the bladder neck. The vaginal incision is closed with 3-0 PDS suture and an estrogen cream-soaked vaginal pack is placed in the vagina.

The rectus fascia is then closed using 0 PDS sutures in a running fashion. The sling-holding sutures are tied to each other over the closed fascial incision. The tension of the sling sutures should be enough to place one finger between the rectus fascia and the sling sutures. The tension regulation is an important step to avoid recurrent incontinence (loose sling) or urinary retention (tight sling). Finally, the skin is closed with a 4-0 Monocryl suture. Based on the thickness of the subcutaneous tissue, a drain may or may not be used in the subcutaneous space before closing the incision (Figures 163.2 and 163.3).

## Postoperative care

A complete blood count is ordered on the morning of postoperative day 1. After reviewing the hemoglobin, the vaginal packing and the catheter are removed and the patient undergoes a voiding trial. If there is significant residual urine, the catheter is replaced for few more days and a voiding trial given as an outpatient. The patient is taught to perform clean intermittent catheterization if the retention persists on that visit. The patient is discharged to home with stool softeners and oral analgesics. She should be advised to avoid sexual intercourse and heavy lifting for the following six weeks. A follow-up visit at two weeks is scheduled to assess surgical outcomes and voiding pattern.

## Complications

### Intraoperative complications

Intraoperative complications such as bladder, urethral, or bowel injury are possible, but hemorrhage due to venous bleeding is the most common one. Although serious injuries and mortality associated with pubovaginal fascial sling are exceedingly uncommon, the surgeon must remain alert during and after the procedure to identify these potential issues and address them as they arise [41, 42].

### Harvest site complications

Patients undergoing rectus fascial sling are prone to develop postoperative hernias, while fascia lata sling is associated with leg pain or discomfort. There are a lack of data in the literature with regard to harvest site postoperative complications. Most of the data are case report or case series. For patients who develop symptomatic hernia, surgical repair is the recommended therapeutic approach. Postoperative leg pain should be managed initially with analgesics and physical therapy [43, 44]. Wound infection, especially in obese patients, or nonhealing of the wound in radiated patients is also reported [5].

### Urinary retention

Urinary retention can occur due to anatomic/functional outlet obstruction or bladder dysfunction, most commonly bladder hypocontractility. The prevalence of urinary retention after sling procedure is highly variable in the literature but higher than with Burch procedure or midurethral sling [5]. Clean intermittent catheterization or indwelling catheter should be recommended in the immediate or early postoperative period. Patients with persistent retention should be evaluated with UDS

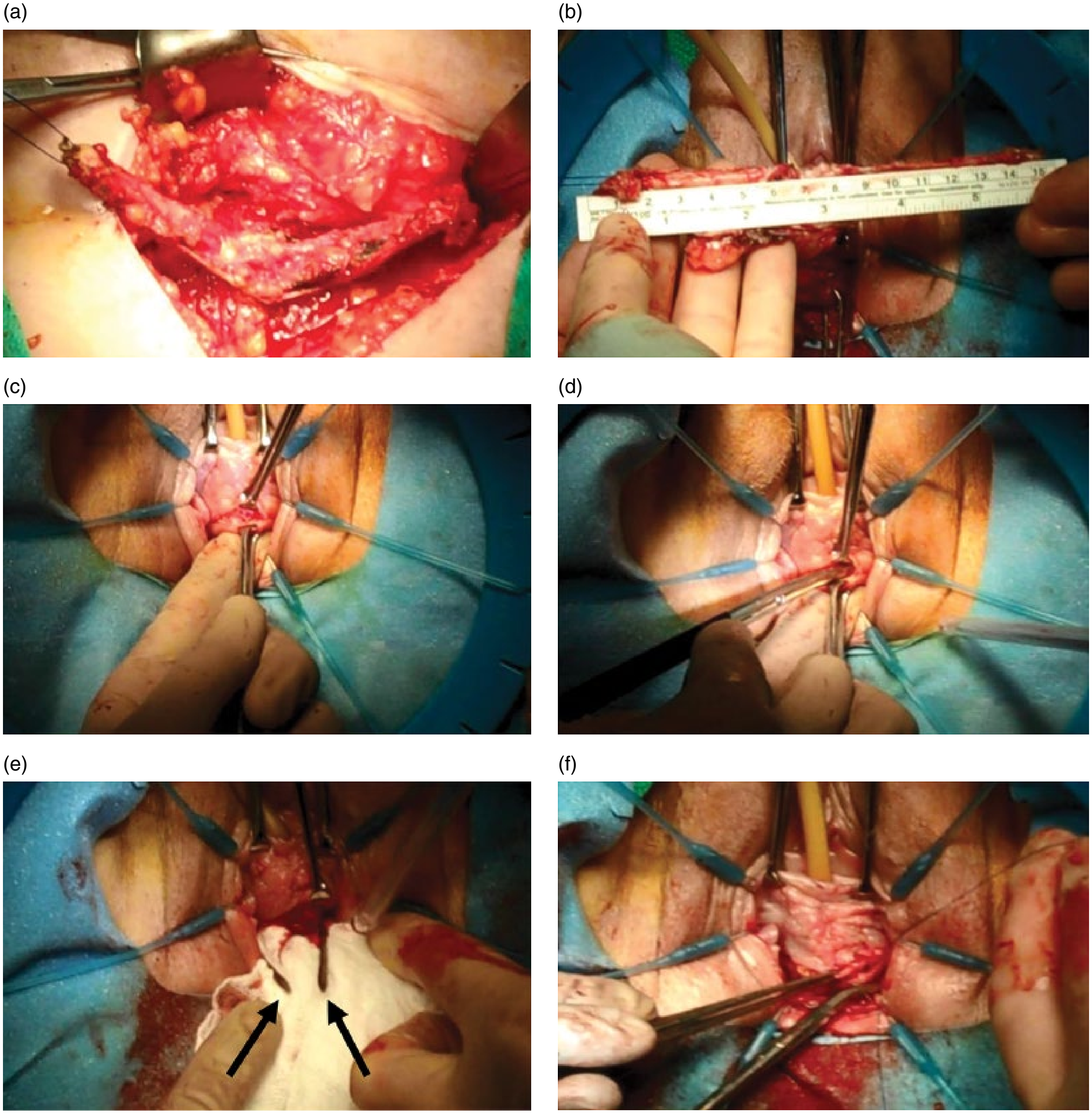

**Figure 163.2** Pubovaginal fascial sling. (a, b) Anterior rectus fascia 15 cm long. (c) Vaginal incision. (d) Dissection of the retropubic space. (e) Antigrade passage of Stamey needle (black arrows). (f) Closure of the vaginal incision.

before any further intervention. UDS findings and the patient's clinical complaints are the most important predictors to determine the therapeutic approach [45, 46].

## *De novo* urinary urgency

The incidence of *de novo* urinary urgency ranges from 5% to 40% [47]. Patients with mixed incontinence (SUI + urge incontinence) are at higher risk if compared to those with SUI only [4]. This specific group of patients should be advised about this risk before surgical intervention. If the patient develops *de novo* urinary urgency after sling placement, cystoscopy is advisable to exclude bladder perforation and obstruction needs to be ruled out [48].

The therapeutic approach depends on the patient's symptoms and how they affect their quality of life. Anticholinergic medication, pelvic floor rehabilitation, botulinum toxin, and sacral neuromodulation should be

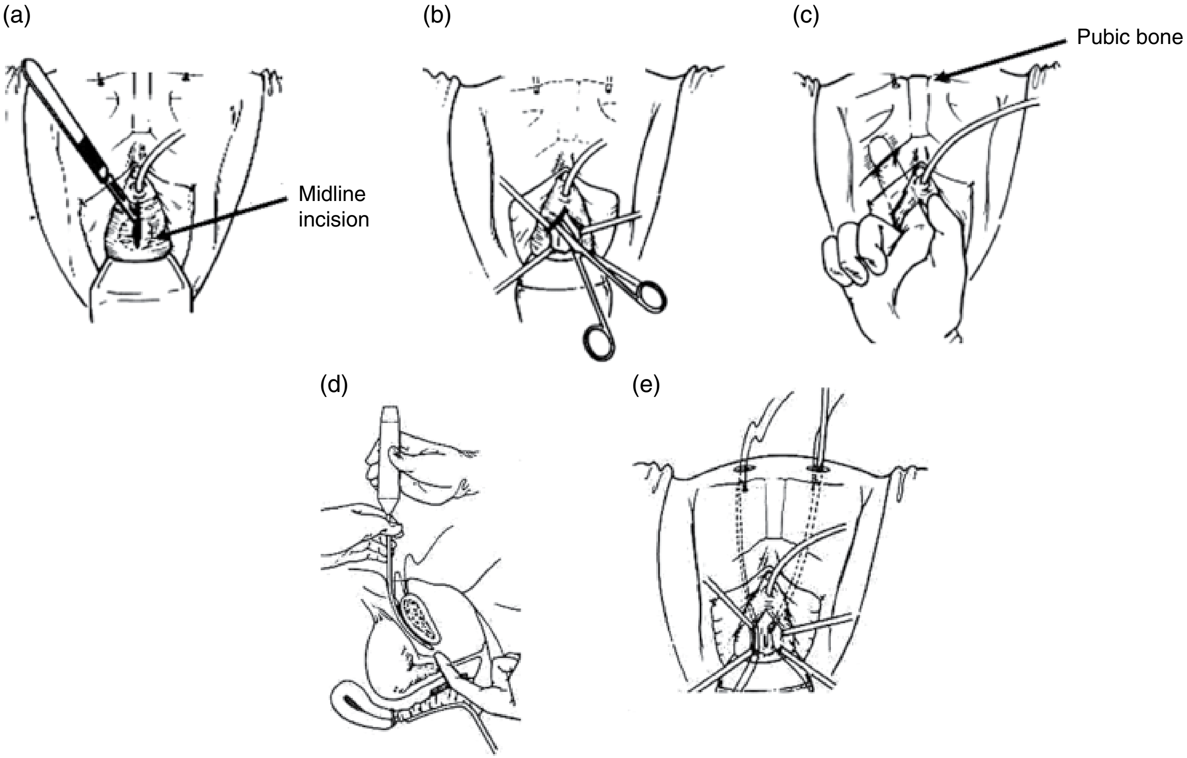

**Figure 163.3** Pubovaginal fascial sling. (a) Vaginal incision. (b) Open endopelvic fascia to access retropubic space. (c) Dissection of the retropubic space. (d) Antigrade Stamey needle passage. (e) Sling with sutures passed through the retropubic space. *Source:* Hom D, Desautel MG, Lumerman JH et al. Pubovaginal sling using polypropylene mesh and vesical bone anchors. *Urology* 1998;51(5):708–13. Reproduced with permission of Elsevier.

considered as treatment options in unobstructed patients with refractory symptoms [4].

### Persistent urinary incontinence

Persistent urinary incontinence can occur in patients with urinary incontinence secondary to intrinsic sphincter deficiency (ISD) even after a sling procedure, or can be related to sling misplacement. A careful physical exam is always recommended to exclude urogenital fistula [49]. If there is no evidence of fistula, UDS is recommended before any intervention. The therapeutic approach will depend on the diagnosis; patients with severe urinary incontinence can be managed with bulking agents, repeat autologous fascial sling, or spiral slings [49].

## Clinical outcomes

In 2007 Albo et al. published the first multicenter randomized clinical trial comparing pubovaginal fascial sling and Burch colposuspension among women with SUI [26]. The primary outcomes were overall success in terms of urinary incontinence measures, which required no episodes of urinary incontinence reported in a three-day diary, negative pad test, negative stress test, no self-reported symptoms, no retreatment for the condition, and success in terms of measures of incontinence specifically, which required only the last three criteria described above. At 24 months, success rates were higher for women who underwent the sling procedure than for those who underwent Burch for both the overall category of success (47% vs. 38%, $P = 0.001$) and the category specific to stress incontinence (66% vs. 49%, $P < 0.001$). However, pubovaginal fascial sling had greater incidence of urinary tract infection, voiding dysfunction, and postoperative urge incontinence [26]. In 2012, the same group published the 5-year follow-up after Burch procedure or pubovaginal fascial sling. The continence rate decreased from 66% to 30.8% and 49% to 24.1% for sling and Burch respectively. Satisfaction also decreased with time and remained higher in the sling group (83% vs. 73%, $P = 0.04$). Ultimately, both groups had similar adverse event rates (sling 9% vs. Burch 10%) [50].

In 2011 Rehman et al. published a Cochrane review about suburethral sling operations for urinary incontinence in women. They reported that minimally invasive slings had shorter operating time, fewer perioperative complications, less postoperative voiding dysfunction, and similar subjective cure rates when compared to traditional slings [5]. Tommaselli et al. published a systematic review about medium- and long-term outcomes following placement of midurethral slings demonstrating that pubovaginal slings had similar objective cure rates but higher subjective cure rates than transobturator midurethral slings. This analysis included 11 randomized controlled trials and 38 prospective, retrospective, and cohort studies with follow-up ranges from 36 months to 10 years [19].

In 2015, Seklehner et al. published a meta-analysis which includes 2995 patients from 17 trials. The short-term objective cure rates at 16 months follow-up were 86.8% for pubovaginal slings and 83.4% for transobturator midurethral slings. Overall, pubovaginal slings were associated with higher rates of bladder perforation and bleeding (3.2%) [1].

In 2015, Kenton et al. published a 5-year longitudinal follow-up after pubovaginal slings and transobturator midurethral slings and demonstrated an objective cure rate of 51.3% and 43,4%, respectively. In both arms of the trial, patients had a significant improvement in the first years; however, urinary symptoms and quality of life worsened in a long-term follow-up [45].

## Conclusions

Pubovaginal fascial sling is an effective treatment for patients with SUI and has a high short-term objective and subjective cure rates. Although there is a clear decrease in long-term continence rates, most women report a high level of satisfaction and better quality of life after the intervention. For these reasons, it is strongly recommended that all urologists who perform anti-incontinence procedures should be acquainted with the pubovaginal fascial sling technique and its postoperative management. It remains a bail-out procedure of choice in our practice.

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# 164

# Mesh Complications Associated with Vaginal Prolapse Surgery

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## Introduction

Surgery for the correction of pelvic organ prolapse (POP) should be individualized for each patient. By the age of 80, between 6.3% and 19% of women will undergo surgery for POP, with up to a 30% risk of requiring reoperation for recurrence [1, 2]. Given the relatively high rates of prolapse recurrence following native tissue repairs, surgeons began to use surgical implants to reinforce the native tissues and achieve improved anatomical surgical success rates. Surgical mesh has been used since the 1950s for abdominal hernia repair [3]. Allografts and xenografts have been utilized, but the success of these grafts has been reported to decrease over time [4]. A Cochrane review of randomized controlled trials comparing native tissue repairs to synthetic mesh repairs found that women with permanent transvaginal mesh (TVM) repair were less likely to have recurrent prolapse and the rate of repeat surgery for prolapse was lower in the mesh groups [5].

### Mesh kits' rise to popularity

The first synthetic mesh produced specifically for incontinence and/or prolapse treatment was introduced in 1996. Because of the recognized risks of exposure and other healing abnormalities with nonabsorbable mesh, fully absorbable meshes were introduced at the end of the 1990s. Fully absorbable meshes soon became unpopular because of their poor long-term results. Trocar-guided mesh augmentation systems, or "mesh kits" first became commercially available around 2004. The rapid growth and wide adoption of mesh kits and vaginal mesh procedures after 2005 was due in large part to aggressive marketing of the available kits. In addition, approval for prosthetic devices by the US Food and Drug Administration (FDA) Center for Devices and Radiologic Health was not as strictly regulated as for medications [6]. The desire for a surgical option with improved anatomical and functional outcomes that was implanted via a standardized and "simple" approach and that was associated with decreased rates of recurrence and reoperations increased the demand for the mesh kits. General gynecologists and urologists were taught to use the mesh kits at industry-sponsored courses. Physicians who were not subspecialty trained were taught simple techniques to implant these kits, without a demonstrated comprehensive understanding of pelvic anatomy and vaginal surgical techniques [7]. Early reports led surgeons to believe that the TVM kits were associated with higher success rates and were easy to perform [8]. Soon the mesh kits were ubiquitous, until the FDA became aware of the risks associated with these procedures.

### Official statements

In 2008, as a result of over 1500 reported adverse events in a 3-year period, the FDA issued a Public Health Notification on serious complications associated with transvaginal placement of mesh to treat POP and stress urinary incontinence (SUI). In 2011, the FDA conducted a systematic review of the literature and, based on the findings, issued an update to the previous notification. They warned that serious mesh complications for transvaginal repair of POP were not rare and that the benefits of TVM repair may not be superior to traditional nonmesh repairs. In 2016, the FDA reclassified TVM for POP repair as a class III (high-risk) device. At this time the FDA does not currently have an advisory

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against mesh repair for SUI (currently classified as class II – intermediate risk), but there is continued evaluation of the safety and effectiveness of these procedures. The FDA has maintained that patients with TVM who do not have complications should not undergo mesh removal [9–11].

## Materials

There is an ongoing search for the ideal graft material that has all of the benefits of permanent synthetic mesh without any of the associated adverse outcomes. The ideal graft would be made of an inert, noncarcinogenic, nonimmunogenic, strong, readily available, inexpensive, resistant to infection and shrinkage material while being pliable and available in various configurations [1, 6, 7, 12]. Until such a material is found, currently available, nonideal grafts are being used to a limited degree.

Biologic grafts, including autologous grafts (tissue harvested from the patient), allografts (tissue from a source other than the recipient but from the same species), and xenografts (tissue from a species other than that of the recipient), have several advantages and disadvantages when compared to synthetic materials. They undergo tissue remodeling after implantation and are less likely to cause vaginal epithelial erosion. This is likely due to their histological similarities with the native tissues. However, they are expensive, of limited availability, are of inconsistent strength between specimens, may be affected by chemical processing, and there is theoretical concern for disease transmission. In addition, autologous grafts increase the operative times and risks of donor-site morbidity [12]. Common donor sites for autologous grafts include abdominal wall rectus fascia and fascia lata. Allografts and xenografts avoid the donor-site morbidity associated with autologous grafts, but they are at risk for marked immune reaction and accelerated implant breakdown [6].

Synthetic grafts are available as absorbable and nonabsorbable materials. Both cause initial and chronic inflammatory reactions. Absorbable mesh elicits chronic foreign body reactions and promotes fibroblast activity. Once resorbed, the mesh material is replaced by collagen-rich connective tissue. The scar formed can weaken over time, which may not provide adequate long-term support [1, 6].

Synthetic mesh postimplantation behavior is not only influenced by the material that it is made from, but also by the pore size and the weave of the filaments. Pore size is important because it determines which cells can enter the mesh interstices. Macroporous mesh (pores greater than 75 μm in size) are large enough to allow entry of fibroblasts, macrophages, natural killer cells, blood vessels, and collagen fibers [13]. Allowing the entry of macrophages and natural killer cells helps prevent graft infection. Microporous mesh has an interfiber space of less than 10 μm, which only allow entry to bacteria and not to macrophages or natural killer cells. Similarly, multifilamentous mesh, which create lattices of less than 10 μm, have a similar disadvantage [6]. Under these circumstances a bacterial biofilm is laid around the mesh, not allowing mesh incorporation. Because of this, the best mesh implant is a lightweight, macroporous, and monofilamentous, or type I polypropylene mesh as described by Amid [14] (Table 164.1). Much recent laboratory and animal research has been directed at identifying the ideal synthetic mesh construction and weight.

**Table 164.1** Classification of synthetic meshes by Amid [14].

| Type of mesh | Characteristics |
|---|---|
| I | Macroporous (>75 μm) and monofilamentous. Can be further subdivided into heavy-, mid-, and lightweight materials |
| II | Microporous (<10 μm) |
| III | Macroporous with either multifilamentous or micropourous components |
| IV | Submicronic (<1 μm) |

## Complications

Immediate surgical complications related to mesh procedures, including bleeding, hematomas, and injury to adjacent organs etc. are not covered in this section as they are likely related to surgical technique and are covered in the suburethral sling chapter (Chapter 162).

The prevalence of mesh complications is difficult to determine, mostly because the true total number of patients who undergo mesh implantation and/or have mesh complications is unknown. The lack of a true denominator is likely due to a lack of systematic registration of mesh surgeries and complications and the high attrition rate of follow-up [15].

In order to better assess the nature and types of complications, it is imperative to apply specific terminology when describing mesh complications. In 2011, the International Urogynecological Association (IUGA) and the International Continence Society (ICS) convened and developed definitions as well as a standardized classification system by which mesh complications should be described. The adverse events are classified by category, time, site, and pain (Tables 164.2 and 164.3) [16].

**Table 164.2** International Urogynecological Association and International Continence Society (IUGA/ICS) definitions.

| Type of complication | Definition |
|---|---|
| Exposure | A condition displaying, revealing, exhibiting, or making accessible (vaginal mesh visualized through separated epithelium) |
| Extrusion | Passage gradually out of body structure or tissue |
| Perforation | Abnormal opening into a hollow organ or viscous |
| Dehiscence | A bursting open or gaping along natural or sutured line |
| Contraction | Shrinkage or reduction in size |
| Prominence | Parts that protrude beyond the surface (wrinkling or folding with no epithelial separation) |
| Compromise | Bring into danger |
| Separation | Physically disconnected |

Mesh-related complications can result in serious negative health impact, and frequently require surgical intervention. In a large multicenter review, about 80% of patients who had mesh-related complications underwent a surgical procedure to correct the adverse outcome. Almost 25% of patients required more than one surgical operation. Of those that were managed conservatively with medication and physical therapy, approximately 60% ultimately required surgery [17].

The Manufacturer and User Device Experience (MAUDE) database is a collection of medical device reports that are reported from physicians, manufacturers, and patients to the FDA regarding suspected device-associated complications, deaths, injuries, or malfunctions. A review of the MAUDE database from 2005 through 2010 revealed over 1700 TVM-related complications; in descending order of frequency these were mesh erosion or exposure, pain, infection, bleeding, dyspareunia, organ perforation, urinary problems, vaginal scarring or mesh contraction, neuromuscular problems, recurrent prolapse, and fistula formation [2].

Mesh exposure through the vaginal epithelium is one of the most common and well-known complications associated with TVM repair for POP (Figure 164.1). Other terms for this condition include erosion, extrusion, and rejection. The initial literature quoted the incidence of exposure to be between 0 and 33%. According to more recent review articles, the rate of mesh exposure is between 10% and 12% when implanted vaginally for repair of prolapse [5, 18]. Other reviews of level 1 evidence place the rates of exposure as high as 19% [2, 19]. Interestingly, short-term mesh exposure rates following abdominal sacrocolpopexy are significantly lower, ranging from 3% to 5%. Long-term follow-up data on sacrocolpopexy report an exposure rate of 10.5%, but about half of the mesh used in that study was made of non-type 1 mesh with known higher risk of exposure [20]. The risk of mesh exposure is higher when concomitant total laparoscopic hysterectomy is performed, reaching as high as 23%, likely secondary to the electrocautery used during the colpotomy. However, the risk drops to less than 5% if a supracervical hysterectomy is performed [21, 22]. A similar phenomenon is found with vaginal implantation, with exposure rates of up to 11.6% after six months, 17.4% after 1 year, up to 20% by 3 years, and 21% by 5 years when a vaginal hysterectomy is performed along with a TVM [23, 24].

It is crucial to understand the risk factors that are associated with mesh exposure so that patients can be appropriately counseled regarding their risks of adverse outcomes. Patients over 60 years old have a 2.2-fold increased risk, smokers a 3.7-fold increased risk, and patients with a body mass index (BMI) greater than 30 have a 30-fold increased risk of a mesh exposure [25]. Other significant factors that increase the risk of exposure include total mesh volume, experience/technique of the surgeon, severity of vaginal atrophy, concomitant hysterectomy, early resumption of vaginal sexual intercourse, diabetes, excessive mesh tension, hematoma formation, inflammation/cellulitis, infection, steroid use, placement of the mesh over a fascial plication, and an inverted “T” colpotomy [1, 4, 18, 26–28].

Pelvic pain and dyspareunia are difficult to quantify due to their subjective nature. Rates of pain anywhere from 0 to 28% are quoted [2, 19, 29], although it should be noted that studies exist showing just the opposite. Nieminen et al. found a significant reduction in dyspareunia in patients who underwent TVM repairs for anterior prolapse compared to traditional anterior colporrhaphy [30]. Mesh contraction typically presents as focal or diffuse tenderness, dyspareunia, or as prominent bands under the vaginal mucosa due to increased mesh tension. Studies have shown that polypropylene mesh can shrink up to 50% of its original length over a short period of time [31]. Regardless of the nature of the pain, the large majority of patients who undergo transection or excision of the contracted mesh segment(s) report their pain significantly reduced or resolved [2, 19].

There is approximately a 10% risk of lower urinary tract complications as a result of surgery for POP in general. When comparing prolapse repair with mesh versus native tissue repairs there is a significantly higher rate of bladder perforation (3.5% vs. 0.5%) and SUI (12.3% vs. 6.3%) in the mesh group [2, 32].

**Table 164.3** International Urogynecological Association and International Continence Society (IUGA/ICS) classification.

| Category | | | | |
|---|---|---|---|---|
| **General Descrption** | **A (Asymptomatic)** | **B (Symptomatic]** | **C (Infection)** | **D (Abscess)** |
| **1 Vaginal:**<br>no epithelial separation, including prominence or contraction | **1A:**<br>Abnormal graft finding on clinical exam | **1B:**<br>Symptomatic (discomfort, pain, dyspareunia in either partner, bleeding) | **1C:**<br>Infection (suspected or actual) | **1D:**<br>Abscess |
| **2 Vaginal:**<br>less than or equal to 1cm exposure | **2A:**<br>Asymptomatic | **2B:**<br>Symptomatic | **2C:**<br>Infection | **2D:**<br>Abscess |
| **3 Vaginal:**<br>Greater than 1cm exposure, or any extrusion | **3A:**<br>Asymptomatic | **3B:**<br>Symptomatic | **3C:**<br>Infection | **3D:**<br>Abscess |
| **4 Urinary Tract:**<br>Compromise or perforation, including fistula and calculus | **4A:**<br>Small intraoperative defect (bladder perforation) | **4B:**<br>Other lower urinary tract complication or urinary retention | **4C:**<br>Ureteric or upper urinary tract complication | |
| **5 Rectal or Bowel:**<br>Compromise, perforation, or fistula | **5A:**<br>Small intraoperative defect | **5B:**<br>Rectal injury or compromise | **5C:**<br>Small or large bowel injury or compromise | **5D:**<br>Abscess |
| **6 Skin and/or Musculoskeletal:**<br>Complications including discharge, pain, lump or sinus tract formation | **6A:**<br>Asymptomatic, abnormal finding on clinical exam | **6B:**<br>Symptomatic (discharge, pain, lump) | **6C:**<br>Infection (sinus tract formation) | **6D:**<br>Abscess |
| **7 Patient:**<br>Compromise, including hematoma or systemic compromise | **7A:**<br>Bleeding complication | **7B:**<br>Major degree of resuscitiation or intensive care | **7C:**<br>Mortality | |

| Time [clinically diagnosed] | | | |
|---|---|---|---|
| **T1**<br>Intraoperative to 48 hours | **T2:**<br>48 hours to 2 months | **T3**<br>2 months to 12 months | **T4:**<br>Over 12 months |

| Site | | | | |
|---|---|---|---|---|
| **S1:**<br>Vaginal area of suture line | **S2:**<br>Vaginal area away from area of suture line | **S3:**<br>Trocar passage<br>Exception: intra-abdominal (S5) | **S4:**<br>Other skin or musculoskeletal site | **S5:**<br>Intra-abdominal |

| Pain | | | | | |
|---|---|---|---|---|---|
| **U:**<br>Unspecified | **a:**<br>Asymptomatic or no pain | **b:**<br>Provoked pain only | **c:**<br>Pain during sexual intercourse | **d:**<br>Pain during physical activities | **e:**<br>Spontaneous Pain |

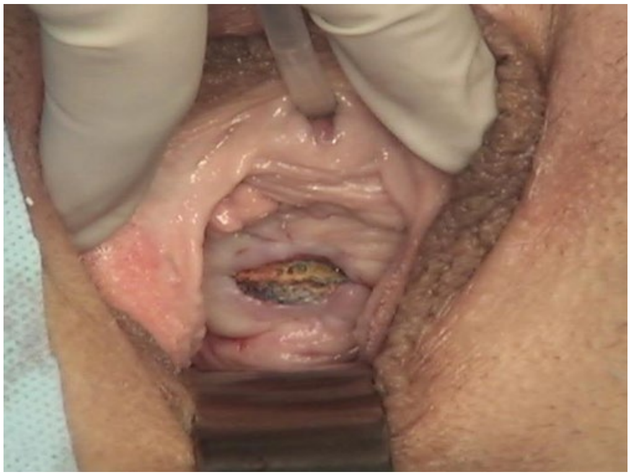

**Figure 164.1** Vaginal mesh exposure.

## Clinical presentation and evaluation

The presentation of mesh exposure can vary greatly, from detection in an asymptomatic patient on a routine exam to dyspareunia, partner discomfort during intercourse, pelvic pain, vaginal bleeding or discharge, urgency, frequency, urinary tract infections, hematuria, dyschezia, or incontinence. The first step in any evaluation should always be a careful and detailed history. Patients do not always return to the physician who performed the initial surgery, and in such cases reviewing previous operative reports is imperative. The physician should determine the full extent of the mesh-related complication, as there may be more than one defect, implant, or complaint [29, 33].

A thorough pelvic exam should be performed, not only focusing on the area that the patient notes is the problem area. The entire pelvis should be evaluated for other possible abnormalities, of which the patient may be unaware. For patients with significant pain, a vaginoscopy may be necessary to adequately visualize the vagina for any small protruding mesh fibers. The entirety of the vagina should be palpated with one or two fingers, as the physician may be able to identify small mesh fibers from an exposure, contractures or strictures that may not be visible on speculum exam. The pelvic floor muscles should also be evaluated for focal pain or spasms. A pelvic organ prolapse quantification (POP-Q) exam should be performed to identify recurrent prolapse, shortening of the vaginal length, or vaginal stricture formation. A rectal exam should be performed in patients who underwent posterior augmentation, and office cystoscopy should be considered for those with urinary symptoms or hematuria. Polypropylene mesh can be visualized on ultrasound as a discrete echogenic area. The use of perineal or intracavitary 2D and 3D ultrasound can be crucial in the diagnosis and preoperative planning for some patients as it can identify the exact location of the mesh or if it is folded or twisted (Figure 164.2) [29, 33, 34].

It is crucial to document all the findings of an exam. While the IUGA/ICS classification system is one of the most comprehensive grading systems currently available, it is not perfect and has been criticized for being too complex and having poor interrater reliability. A standardized formula for describing and grading the severity of complications is important for interphysician communication, to allow for better assessment of the safety of the procedures, and for research purposes [33, 35].

## Prevention of mesh-related complications

The most appropriate way to manage mesh complications is to focus preoperatively on prevention. Given all of the above noted complications related to mesh, it is critical to only use mesh in the most appropriate patients and situations. Prevention starts with choosing a suitable patient, who would not otherwise benefit from a vaginal native tissue repair, biologic grafts, or an abdominal repair. There are methods by which physicians can improve their surgical outcomes preoperatively. Pessaries should be removed at least two weeks prior to surgery to reduce inflammatory reaction and improve epithelial integrity. A pelvic exam should be performed to visualize any ulceration. Preoperative administration of local vaginal estrogen cream enhances tissue integrity and can decrease risk of mesh-related complications in patients with vaginal atrophy [26, 36].

Perioperative methods to decrease risk of mesh complications start with the surgeon using optimal surgical technique. Hemostasis for prevention of hematoma-related suture line disruption is of utmost importance to prevent mesh exposure. The surgeon should consider hydrodissection of appropriate tissue planes with a hemostatic solution, maintain hemostasis throughout the procedure with sutures or minimal electrocautery use, and employ the use of vaginal packing postoperatively to minimize the risk of hematoma formation. Submucosal abscesses, for which hematomas may serve as a nidus for the infection, are also risk factors for mesh exposure. Prophylactic intravenous antibiotics should be administered at the onset of every urogynecological procedure. The volume of mesh implanted should be limited to minimize folding over and impaired tissue incorporation. The length of the incision of the vaginal epithelium should be minimized and should be closed with a full-thickness closure without tension in a nonlocking manner to allow for adequate revascularization and healing [18, 26, 36].

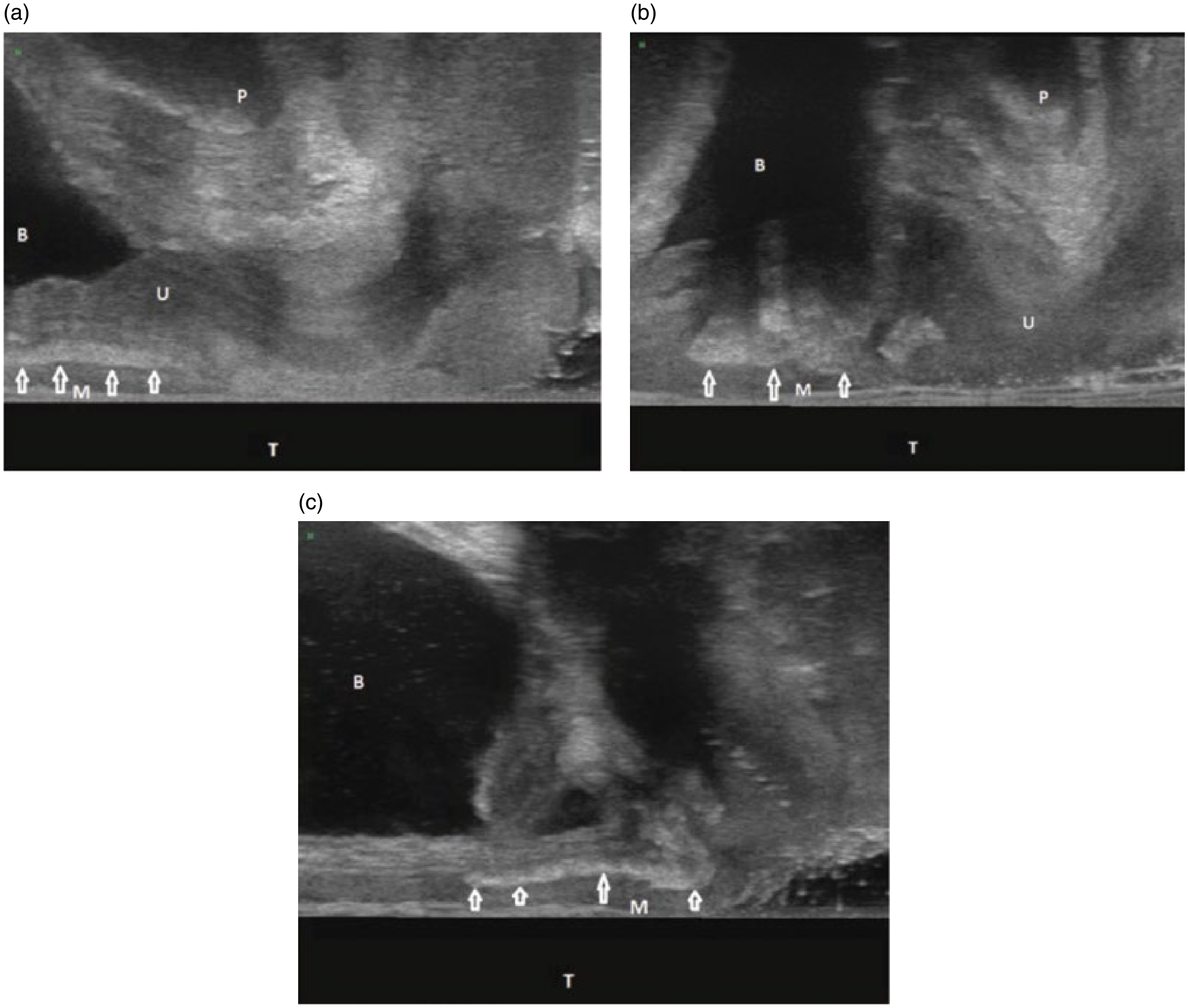

**Figure 164.2** Three-dimensional ultrasound image of sling. (a) 180° scan of the anterior compartment: mesh in the anterior vaginal wall. (b) 180° scan of the anterior compartment: mesh in the anterior vaginal wall associated with edema mesh in the anterior vaginal wall. (c) Transperineal ultrasound: mesh in the anterior vaginal wall detached from the apex. B, bladder; P, pubic symphysis; U, urethra; M, mesh; T, probe.

Finally, patients should be observed during several short-interval follow-up appointments to assess for initial signs of mesh-related complications. Early identification can help to minimize the extent of the complications. Patients should also be instructed to limit exertional physical activity for at least six weeks, including pelvic rest [36].

## Management of mesh-related complications

The management of mesh-related complications depends upon the complication, its location, severity, and impact on the patient. Mesh complications can occur in the short term, as well as many years later, so long-term follow-up is important for patients with mesh implants [15].

Conservative management with vaginal estrogen and in-office trimming is most appropriate for small exposures (<0.5 cm), if the exposure is easily reachable. With topical local anesthetic administered, the exposure should be identified and sharply excised to ensure adequate elimination of as much of the mesh as possible from the exposed area. Bleeding is typically minimal, but silver nitrate cautery can be used as needed in the office [26].

Larger (up to 4 cm) exposures are unlikely to heal with conservative management and will require outpatient surgical excision. The vaginal tissue should be prepared preoperatively with local estrogen cream to help with tissue dissection. The tissue surrounding the exposed mesh should be infiltrated with 1% lidocaine with epinephrine. Using a scalpel, the exposed area should be circumscribed with a 5 mm margin of vaginal epithelium. Dissection should continue circumferentially, undermining and mobilizing the surrounding healthy 1 cm of vaginal epithelium. The mesh, along with the 5 mm vaginal epithelial margin, should be excised with Mayo scissors. During the excision, careful attention should be paid to the mesh attachments to the underlying tissues (i.e. bladder or rectum). Depending on the width of the exposure, reapproximation of the cut mesh edges to close the defect could be attempted, with care taken to avoid creating strictures or bands. The edges of the remaining vaginal epithelium should be reapproximated without tension after ensuring hemostasis in a manner that minimizes the creation of vaginal strictures [26, 37].

Exposures that are greater than 4 cm are uncommon, most likely due to patients seeking medical care as a result of associated pelvic symptoms. However, when exposures of this size occur, it is frequently due to devascularized sloughing of segments of vaginal epithelium. The exposed mesh should be excised in a similar manner as described previously; however, it is possible that the vaginal epithelial edges may not be able to be reapproximated without affecting the vaginal length or diameter. Proposed options for closure of this sizeable defect include the use of biologic grafts to aid in re-epithelialization or creation of a vulvar skin graft [26, 37, 38].

Erosions into adjacent viscera are more challenging to manage. These require surgical intervention and may necessitate coordination and collaboration with urologic or colorectal surgeons. These types of erosion involve removal of mesh segments within the surrounding visceral walls. Rectal erosions can be managed with the use of an anoscope (Figure 164.3). Posterior vaginal mesh may sometimes impinge upon the rectum without eroding through the mucosa, and may lead to defecatory symptoms. In these situations, the mesh may be transected or removed through a transvaginal approach. Close attention is needed to prevent the development of a recto-vaginal fistula (RVF). If an RVF has developed, the mesh in that area should be carefully dissected out and the fistula should be repaired in the usual fashion [26].

Mesh erosion into the bladder may be managed vaginally, cystoscopically, or laparoscopically through a cystotomy. Cystoscopic surgery can be performed with cystoscopic graspers as well as with a 5 mm laparoscopic trocar placed suprapubically into the bladder for placement of laparoscopic graspers and/or scissors. Cystoscopic surgery should be limited to small exposures, such as following a midurethral sling, where suturing is not necessary. Cystoscopy should be repeated a few months later to visualize and document any recurrence of exposure. Benefits of cystoscopic surgery allow for the removal of exposed mesh, and prevention of further damage, without requiring an actual cystotomy. Erosion into the urethra can be managed with a pediatric nasal speculum to allow for circumferential visualization of the mesh fibers. Attempts should be made to avoid cutting into the urethra if possible, as well as avoiding the development of intrinsic sphincter deficiency or a urethrovaginal fistula [26, 39]. If there is concern for ureteral involvement, the placement of ureteral stents may aid in detection of ureteral injury or involvement [15].

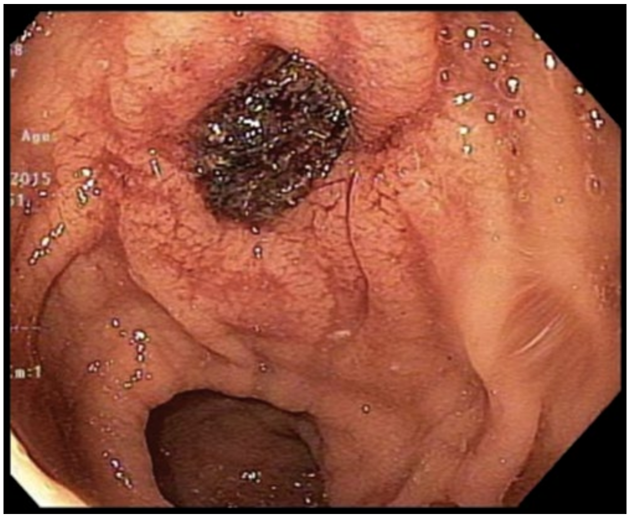

**Figure 164.3** Rectal erosion.

Mesh infection has occurred with and without mesh exposure and the incidence ranges from 0 to 8%. The various bacteria cultured have included Gram-negative and Gram-positive as well as aerobic and anaerobic subtypes. These types of complications were associated with multifilament non-type I meshes, and so have become more rare [18].

For patients with urinary retention from bladder outlet obstruction due to excessive tensioning, midline sling transection should be considered. If left untreated, irreversible scarring of the urethral lumen, voiding dysfunction and bladder remodeling may occur. Patients who present with new-onset urgency complaints should have the sling tension evaluated for possible mesh contraction. The use of 3D ultrasound may be useful in such situations [15].

Dyspareunia or pelvic pain following mesh POP surgery can be difficult to manage. The surgeon should ascertain that the pain is directly related to the implanted mesh, and not due to another condition such as levator spasm, interstitial cystitis, or trigonitis. If there is concurrent vaginal mesh exposure, mesh excision may be helpful. However, in the absence of mesh exposure, patients should be counseled extensively that even with removal of a portion or the entire mesh, their symptoms may not abate and the prolapse may recur [15]. For contracted mesh that leads to palpable focally painful vaginal segments, the mesh arms should be transected as lateral as possible, and the contracted sections should be removed entirely [31].

## Outcomes

Patients must be counseled appropriately before undergoing any surgery or treatment for mesh complications. Patients should be given realistic expectations with regard to possible outcomes, including persistent symptoms, further complications, or worsening of symptoms. Referral of patients to tertiary centers that have experience treating mesh complications should be considered. Outcomes from treatment of mesh-related complications, from conservative therapy to complete mesh removal, can vary tremendously by patient and complication. Success rates have been reported ranging from 25% to 100% for all complications by subjective improvement or cure with varying lengths of follow-up. In addition, several studies report a significant number of patients who have no improvement and a percentage of patients whose symptoms worsened after the second procedure. Of note, excision of mesh for exposure tends to have higher success rates, whereas mesh excision for pelvic pain or dyspareunia is associated with higher persistence rates. With regard to pain, the reported rates of improvement range from 50% to 78%, but persistence of pain is well recognized in the literature. One study, with long-term follow-up of patients who underwent surgical excision of mesh-related complications, 74% of patients reported their pain was improved and 14% reported worsening of symptoms. In that study, it was ascertained that half of the patients reported not being bothered by their residual mesh-related symptoms, whereas just under half reported continued problematic pain. More than half of the patients underwent additional treatments for their complications. Patients with chronic pain disorders (such as fibromyalgia) are three times more likely to have continued (or worsened) pain after mesh implantation and/or removal than those without a chronic pain disorder. However, when pain is associated with mesh erosion or contraction of the mesh, outcomes are much better [15, 19, 31, 40, 41].

## Recommendations for appropriate use

Despite all of the associated complications previously described, vaginal mesh is still an important tool in a pelvic surgeon's armamentarium, and should be considered for certain specific indications. As with any surgery, patients should be counseled extensively regarding the risks of the procedure, all possible alternatives, and their informed consent should be documented in the medical record [3].

Regulatory bodies in Europe and the United States have released recommendations for the use of synthetic mesh for treating POP. Numerous American and international professional societies, including the American College of Obstetricians and Gynecologists, the American Urogynecology Society, and the International Urogynecological Association have released guidelines for patients and healthcare providers regarding TVM for POP repair. They recommend that TVM should be reserved for high-risk patients, in whom the benefits justify the risks. Examples of such patients include those with recurrent POP and large cystoceles, while posterior vaginal compartment prolapse, younger women, primary repairs, and those with underlying pain syndromes likely do not have a demonstrable benefit, and may have a greater risk for complications. The regulations and guidelines are continually changing in this evolving field. It is imperative that physicians are specifically trained in the placement and management of these devices, have a comprehensive understanding of pelvic anatomy, stay current on the research and recommendations, and appropriately counsel patients regarding the risks and benefits of each procedure. A registry should be developed for surveillance of all outcomes [42–45].

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## 165

# Male Slings for Treatment of Post-prostatectomy Incontinence

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## Epidemiology

Prostate cancer is the most prevalent malignancy among men in the United States, and surgical options include open retropubic or robot-assisted laparoscopic radical prostatectomy. Oncologic outcomes are overall favorable, and much attention has been paid to quality of life among men treated surgically for prostate cancer. Urinary incontinence is a significant quality-of-life issue affecting a large proportion of the population [1]. It is estimated that approximately 22.6 million men in the United States are affected by urinary incontinence, and 8.2 million have moderate to severe incontinence [2]. Pure stress urinary incontinence (SUI) accounts for only a subset (12.5%) of these patients, yet it remains a substantial problem. In the era of robot-assisted laparoscopic prostatectomy, the incidence of urinary incontinence at 12 months varies between 4% and 31%. Of these, only 6–9% are bothered enough to elect surgical treatment for their incontinence [3, 4]. In addition, men with prostate cancer who choose radiation therapy, androgen ablation, or even watchful waiting may also develop urinary incontinence with rates of up to 12%, 11%, and 3%, respectively [5, 6].

## Pathophysiology of male continence and post-prostatectomy incontinence

In the male, two sphincteric mechanisms work in concert to provide urinary continence. The proximal sphincter, composed of smooth muscle fibers at the bladder neck extending to the bulbar urethra [7], is under autonomic control; in contrast, the distal sphincter is composed of both striated and smooth muscle fibers extending from the verumontanum to the bulbar urethra [8] and is innervated by both unmyelinated autonomic and myelinated somatic nerves [9]. Magnetic resonance imaging (MRI) and cadaveric dissection studies have demonstrated the length of the distal sphincter to range from 1.4 to 2.4 cm [8, 10, 11]. The smooth muscle fibers of the distal sphincter lie internal to the striated fibers and are contiguous with the smooth muscle fibers of the proximal sphincter [7]. Myers suggested that this rhabdosphincter complex should be thought of as the "sphincteric urethra" (Figures 165.1 and 165.2) [8, 12]. In the physiologically normal male, the intrinsic component of the distal sphincter mechanism is responsible for passive continence, and the extrinsic component of the distal sphincter mechanism is responsible for providing active continence.

Urinary incontinence following surgical prostatectomy may be influenced by a variety of factors, including insufficient sphincteric activity, detrusor overactivity, age, functional urethral length or anatomic abnormalities involving the bladder or vesicourethral anastomosis [13]. In patients who undergo surgical prostatectomy, destruction of the proximal sphincteric mechanism may occur. Many of these patients retain urinary continence solely by action of the distal sphincteric complex. At rest, this is maintained by apposition of urethral tissues. Resting tone is provided by slow-twitch striated fibers, while fast-twitch fibers within the sphincteric complex provide continence during physical exertion or increased intra-abdominal pressure. In response to increases of abdominal or detrusor pressure and during voluntary inhibition of flow in these patients, voluntary activity of the rhabdosphincter fibers may occur in conjunction with associated contraction of levator ani fibers, in order to maintain urinary continence [13, 14]. SUI related to deficiency of

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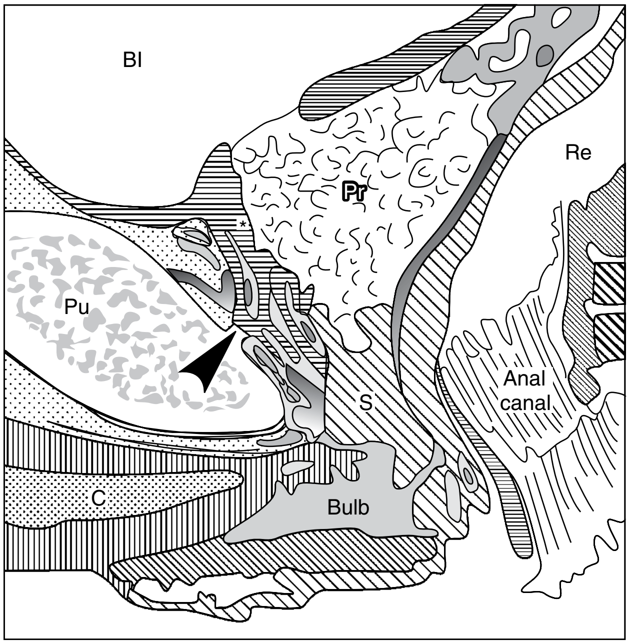


Figure 165.1 Structural anatomy of the striated urethral sphincter (S) and spatial relationship to the prostate (Pr), bladder (Bl), pubis (Pu), pubovesical ligament (arrowhead), bulbous urethra (Bulb), corpus cavernosum (C). Re, rectum. *Source:* Mayo Foundation for Medical Education and Research Minnesota, USA. Reproduced with permission of the Mayo Foundation for Medical Education and Research.

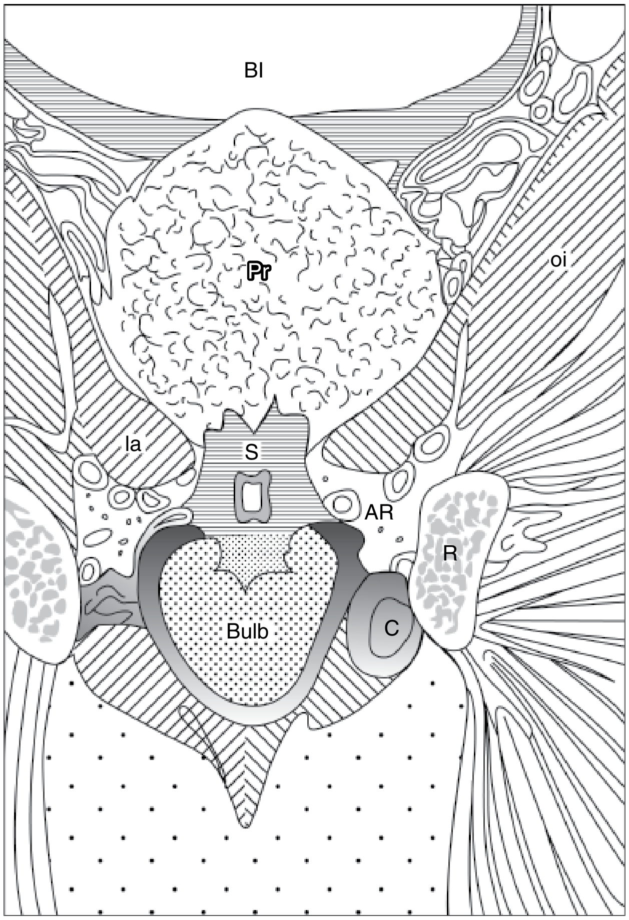


Figure 165.2 Structural anatomy of the striated urethral sphincter (S) and spatial relationship to the prostate (Pr), levator ani (la), bulbous urethra, corpus cavernosum (C), ischiopubic ramus (R), and anterior recess of ischioanal fossa (AR). Bl, bladder. *Source:* Mayo Foundation for Medical Education and Research Minnesota, USA. Reproduced with permission of the Mayo Foundation for Medical Education and Research.

the external sphincteric mechanism is the most frequent type of incontinence following radical prostatectomy. Several studies have demonstrated urodynamic evidence of intrinsic sphincter deficiency (ISD) in the majority of patients with post-prostatectomy incontinence, ranging from 83% to 90% [15–17]. In up to 60% of patients, this may be the only urodynamic finding to account for incontinence [18]. Thus, clinical and urodynamic evidence supports SUI caused by sphincter deficiency as the most common cause of incontinence following radical prostatectomy. It is important, however, to note that transient urodynamic detrusor overactivity may be experienced in 2–77% of men following radical prostatectomy and may persist for up to 1 year [19, 20].

## Management

Active conservative management is often recommended for the first 6–12 months after prostatectomy. In the early postoperative period, reassurance as well as conservative therapy, including pelvic floor muscle strengthening exercises, timed voiding, and avoidance of dietary bladder irritants, may be helpful. Randomized prospective trials have reported quicker return to continence in patients who have undergone pelvic floor strengthening exercises [21, 22]; however, others have reported that this has not been true for patients with severe incontinence and may not extrapolate to long-term continence outcomes [23]. In addition, patient factors including age, comorbidity, preoperative voiding dysfunction, and neurovascular bundle preservation during prostatectomy may influence postoperative return to continence. Unfortunately, pharmacotherapeutic agents for managing male stress incontinence have not been efficacious, nor have they been approved by the US Food and Drug Administration (FDA). Urethral bulking agents may be considered for mild urinary leakage, but success rates are generally low, with fewer than half of patients achieving satisfactory continence [24].

Periodic evaluation of urinary incontinence should be performed at regular follow-up visits during the first year after prostatectomy. Patients with bothersome persistent post-prostatectomy incontinence despite pelvic floor muscle strengthening exercises may be considered for surgery. Contemporary surgical options for post-prostatectomy incontinence include the artificial urinary sphincter (AUS) and the male urethral sling. The AUS was introduced in 1973 [25] and has long been considered the gold standard for the surgical treatment of post-prostatectomy incontinence. The current model, the AMS 800 AUS (American Medical Systems Inc., Minnetonka, MN, USA), has been associated with high success rates (61–96%) [26, 27] and high patient satisfaction in appropriately selected patients [28]. The present chapter focuses on the role of male urethral slings in the treatment of post-prostatectomy incontinence, while more extensive discussion of AUS is provided elsewhere.

## Male urethral sling

The male sling procedure is based upon the theory of passive compression along the ventral urethral surface to maintain continence [29]. The concept of urethral compression by male sling is not new, and before the AUS was introduced, a variety of urethral compression procedures were investigated in an attempt to control urinary incontinence. Most notable were the Kaufman procedures in the 1970s, which included a crural crossover (Kaufman 1) [30], later modified to involve a prosthesis using silicone gel to compress the ventral urethra (Kaufman 2) [31], but it soon fell out of favor. In 1998 Schaeffer et al. described a male sling using three tetrafluoroethylene (Dacron) bolsters beneath the bulbar urethra [32]. A Stamey needle was used to transfer the sutures in the suprapubic area, which were tied across the rectus fascia. Intraoperative resting urethral pressure and abdominal leak point pressures were measured for sling tension. Despite a reasonable short-term success and patient satisfaction [33], this sling was abandoned due to a high rate of complications or reintervention, including bolster removal (6%), sling removal (10%), and severe perineal pain (26%). Since that time, a variety of mechanisms have been employed by which to apply passive external urethral compression with male slings. A primary advantage of using male urethral slings for post-prostatectomy incontinence over the AUS is its minimally invasive nature. They are also less expensive than AUS devices, and unlike the AUS, slings provide fixed urethral resistance and/or repositioning that potentially enables better physiologic voiding [34]. Furthermore, slings avoid the need for manipulating the device and provide an alternative surgical option for patients with mild to moderate incontinence or who refuse to have an AUS.

Recently, Liu et al. [35] evaluated the trend of male sling surgery in relation to AUS in the United States. They reported an overall increased rate of slings from 32.7% in 2004 to 45% in 2013 ($P < 0.001$), with a peak in 2011 when sling placement was 1.6 times more frequently performed than AUS (sling 62.2% vs. AUS 37.8%). There are many types of male slings, including the bone-anchored sling, transobturator sling, and quadratic sling.

### Bone-anchored sling

The InVance™ (American Medical Systems Inc.) bone-anchored male sling (BAMS) represented a major improvement in technique, minimizing invasiveness via a purely perineal approach. With BAMS, a silicone-coated polypropylene sling is secured to the descending pubic rami using 5 mm titanium bone screws. A disposable battery-powered inserter is used to insert a total of six bone screws which are preattached with no. 1 Prolene suture. The silicone-coated mesh is then anchored to the pubic rami, providing the urethral compression. Comiter first reported using BAMS in 2002 [36]. The author reported their experience in patients with both mild to moderate and severe incontinence. They found that patients with mild to moderate incontinence (<5 pads) had a significantly better outcomes compared to those with severe incontinence (>5 pads). Sling failure rates correlated well with the type of material used and the severity of incontinence [37]. Similarly, in a study by Castle et al in 38 patients, none of the patients with severe incontinence were dry after BAMS [38].

Similar results with the InVance BAMS were reported by Rajpurkar et al., who reported overall success rates of 74% and a patient satisfaction of over 70% at a mean follow-up of 24 months [39].

Long-term results with the InVance BAMS were recently reported by Carmel et al. [40]. In their study, 45 patients with post-prostatectomy incontinence underwent InVance sling placement with a median follow-up of 36 months. They underwent regular follow-up at 2, 6, 12 months, and yearly thereafter with pad testing, urodynamics, history, and UCLA/RAND and American Urological Association (AUA) symptom score data. Thirty-six percent of patients were dry, 40% improved, and 24% reported failure. The vast majority of patients (86%) considered themselves cured or almost cured, and 72% were satisfied or very satisfied with the procedure. Complications included temporary perineal numbness lasting 1–3 months in 22%, temporary urinary retention in 7%, overactive bladder in 4%, and mesh infection necessitating removal in one patient.

Similarly, a recent French multicenter study described treatment success and predictors of failure among 84 patients treated for incontinence with InVance male slings [41]. In this study, at a mean of 20 months, 45% of patients were dry, 26% improved, and 29% had treatment failure. Univariate analysis identified three features as predictors of treatment failure: severe urinary incontinence, urodynamic instability, and a history of bimodal therapy for prostate cancer including radiation therapy. Failure rate was 67% if two or more of these factors were present versus 25% if one or none was present ($P = 0.013$). Bimodal therapy was the sole independent predictor of failure in multivariate analysis in this study [41].

In our 5-year experience with BAMS in 87 patients published in 2007, we found that only 52.8% of patients were cured and another 25.2% significantly improved of their incontinence, while 21.8% failed the sling procedure [42].

Fischer et al. used a risk analysis model to predict success in 62 men treated for post-prostatectomy incontinence with BAMS and found that among several factors (time from prostatectomy, age, abdominal leak point pressure, pad weight testing, maximum bladder capacity, detrusor overactivity, International Prostate Symptom Score (IPSS), and Urinary Distress Inventory (UDI-6)), only preoperative pad weight of less than 423 g/day was a predictor of success. Patients with less than 423 g/day leakage had a 71% chance of success and were six times more likely to have success as defined by perception of very much or much better on Patient Global Impression of Improvement (PGI-I) questionnaires [43].

Complications reported with BAMS included transient retention in 2%, overactive bladder in 5%, mesh erosion in 2%, infection in 2%, and perineal pain in 15% [44].

Because of the potential risk of bone infection and bone pain from the bone screws, this male sling has been removed from the market and is no longer available for implantation.

## Transobturator sling

Whereas BAMS function by fixed urethral compression, transobturator slings were subsequently developed based on the concept of proximal relocation of the sphincteric urethra. Rehder and Gozzi described a novel technique for placement of a polypropylene tape beneath the bulbar urethra using the transobturator approach in a series of four cadaveric and 20 human male patients [45]. The middle part of the tape was fixed distally to the bulb and proximally to the perineal body, and when tension was applied to the ends of the tape, the proximal anterior urethra was relocated proximally by a distance of 3–4 cm, effectively lengthening the membranous urethra. Baseline and postoperative video urodynamics in their clinical series confirmed that at rest, the bladder neck and posterior urethra were more occluded, and the bladder neck was closed and more elevated than at baseline. In addition, postoperative video urodynamics demonstrated a more elongated membranous urethra during micturition, having increased from a mean of 3 mm to a mean of 17 mm following placement of the tape. Urethral pressure profilometry in the same series demonstrated an improvement of supine mean urethral closing pressure at rest from 13.2 cmH$_2$O preoperatively to 86.4 cmH$_2$O postoperatively.

The rationale for treating post-prostatectomy male incontinence by transobturator tape is based on the theory that post-prostatectomy men with partially intact external sphincteric complexes may develop incontinence due to urethral hypermobility, resulting in urethral subluxation or perineal descent from the pelvis, possibly associated with coexistent levator laxity; hence proximal relocation of the sphincteric urethra may result in improved continence [45, 46].

Gozzi et al. reported continence results among 67 post-prostatectomy patients treated with transobturator urethral slings [47]. At three months postoperatively, 52% were cured (no pads) and 38% had improvement of incontinence (1–2 pads/day). Complications included persistent incontinence requiring sling replacement in five patients (7%), suprapubic drainage for postoperative retention in 11 patients (16%), and subsequent placement of AUS in two patients (3%). A recent prospective multicenter trial by Cornel et al. examined pad weight test results at three months and 1 year following AdVance™ (American Medical Systems Inc.) transobturator sling suspension in 37 men with incontinence following radical retropubic prostatectomy (RRP) and transurethral resection of the prostate (TURP) [48]. The overall cure rate was 14.3% at three months and 9% at 1 year. Improvement was noted in 42.8% at three months and 36.5% at 1 year. Pad testing demonstrated worsening incontinence in 14.2% of patients postoperatively. In addition, urinary bother recorded by the visual analog scale (VAS) was improved at three months postoperatively, but was not significantly different at 1 year. VAS score correlated with objective cure or improvement on pad weight testing. Interestingly, cure as defined by pad weight testing occurred only in the RRP group, with no patients cured who had TURP or radiotherapy in addition to RRP. Preoperative incontinence using pad weight cutoffs of 200 and 400 ml/day, or fewer or greater than 5 pads/day, was not significantly associated with pad testing or VAS improvement. The results in the report by Cornel et al. [48] are less favorable than in those by Gozzi et al.'s series [47]. The reason for the discrepancy between the series is unclear, but Cornel et al.'s study does suggest that patients who have had TURP or radiotherapy may not benefit from transobturator sling placement based on the definitions used for successful outcome in their study. In addition, it is important to note that when compared to continence results with

AUS, outcomes reports with male slings have been widely variable and difficult to interpret owing to small, single-center studies with short follow-up periods and variable definitions of success.

Recently, Rehder et al. [49] reported outcomes at 3 years with 53% cured, 23.8% improved, and 23% failed after sling. There was higher success in mild to moderate incontinence as compared to severe incontinence. Clinical outcomes were also compared in "ideal" versus "non-ideal" patients by Sturm et al. [50]. Six patient selection criteria were established:

- Less than four pads/day or <300 g daily pad weight
- Intact-appearing external urinary sphincter on cystoscopy
- No history of pelvic radiation
- No history of previous surgical procedure to treat incontinence
- Volitional detrusor contraction when voiding
- Postvoid residual urine volume <100 ml.

It was noted that there was significant reduction in both pad usage (77% vs. 46%) in patients who met all six criteria when compared to patients did not meet all criteria. Similarly, pad weight reduction was significantly lower in the group who met all six criteria (88% vs. 61%) when compared with the group who did not meet all criteria.

A new modified transobturator sling (AdVance® XP, American Medical Systems Inc.) has been introduced recently by the same manufacturer. It obtained FDA approval in Canada in 2011 but has not yet been approved in United States. The enhancements include new mesh design, longer arms, Tyvek sleeve liner, and Chevron anchoring mechanism to increase the holding power and consistent displacement of load.

Available data in the literature comparing AdVance XP to conventional AdVance slings showed similar cure rates of 63% versus 59% in Advance and Advance XP slings, respectively. Similarly, 16% in the AdVance group and 17% in the AdVance XP group improved significantly. Failure rates were comparable (21% for AdVance versus 24% for AdVance XP) [51].

In another recent long-term prospective trial by Kretschmer et al. comparing AdVance and AdVance XP slings [52], higher cure rates were reported in the AdVance XP group (64.3% vs. 46.2%), while higher failure rates were reported in the AdVance group (30.8% vs. 7.1%).

Surgical treatment of male stress incontinence with urethral slings raises the question of *de novo* obstruction or associated urodynamic changes. This question was evaluated by Davies et al., who performed baseline and three-month postoperative urodynamic testing on 13 patients undergoing placement of AdVance male urethral slings for post-prostatectomy incontinence. At three months postoperatively, Valsalva leak point pressure (VLPP) significantly improved from 29.3 to 46.6 $cmH_2O$ ($P = 0.03$), but there was no difference in baseline and postoperative detrusor voiding pressure, maximum or average flow rates, or postvoid residual volume [53].

### Quadratic sling

The newest addition to the repertoire of male slings is the quadratic sling from Coloplast Corporation (Minneapolis, MN, USA). It is designed to provide a broad area of urethral compression *and* to achieve proximal relocation of the membranous urethra. Quadratic fixation is achieved with both transobturator (TO) and prepubic (PP) components. The Virtue® sling is a synthetic, monofilament polypropylene knitted mesh that measures 5.5 cm × 7 cm, with 1.5 cm × 25 cm superior extensions and 1.5 cm × 22.5 cm inferior extensions.

By combining the mechanisms of action of the bone-anchored and transobturator retroluminal slings, the quadratic device can increase urethral resistance more than a purely perineal or TO approach. This was confirmed in a cohort of 22 men with post-prostatectomy incontinence undergoing Virtue sling placement. The mean urethral resistance increased from a baseline retrograde leak point pressure (RLPP) of $33.4 \pm 8.8$ $cmH_2O$ to a mean post-tension RLPP of $68.8 \pm 6.0$ $cmH_2O$ [54].

Another multicenter trial involving 31 incontinent men managed with quadratic sling was recently reported by Comiter et al. [55]. The cohort included 43.3% patients with mild, 23.3% with moderate, and 33.3% with severe incontinence. Median percent reduction in pad weight for the cohort was 89.3% at 6 weeks and 88.3% at 12 months. This did not differ significantly among the subgroups based on baseline pad weight. For those with mild leakage, percent reduction in pad weight at 12 months was 89.7%, 89.6%, and 72.2% in the mild, moderate, and severe groups, respectively.

Complications reported were mild overall and included mild genital paresthesias (19.4%) and mild perineal pain (12.9%). There were no instances of infection or erosion. It was also noted that the success rate was no different in the 19% of patients who underwent adjuvant radiation compared to those who did not. This is in contrast to other male slings, which traditionally have poorer outcomes in patients who have undergone radiation.

## Patient selection and evaluation

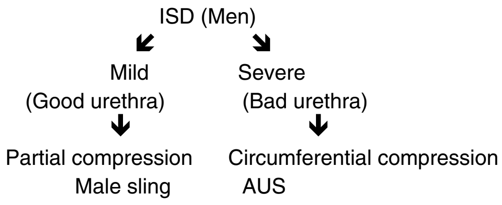
Careful evaluation and patient selection is important when pursuing slings to treat male urinary incontinence. Ideally candidates should be at least 6–12 months post-prostatectomy and exhibit mild-to-moderate incontinence.

Features that might be predictive of failure should be considered, including high-volume incontinence, comorbidity status, and mixed or urge-predominant incontinence. Caution should be exercised when considering slings in patients who have undergone radiation therapy. History of prior incontinence procedures, patient age, manual dexterity, and patients' preferences should also be taken into account. Careful history-taking is paramount. Physical examination, for example with a standing cough test, should be performed for documentation and gross quantification of stress incontinence. Cystoscopy should be performed on all candidates to confirm the presence of some sphincteric coaptation and to rule out urethral stricture or bladder neck contracture. When history suggests mixed incontinence with urgency or if neurologic disease coexists, urodynamics evaluation should be considered to evaluate detrusor activity. As with all interventions for incontinence, caution should be used when patients have detrusor overactivity.

Detrusor hypocontractility is a contraindication for sling placement, whereas an AUS may still be appropriate in this setting. In addition, patients who have previously undergone incontinence surgery with either a sling or AUS may be more likely to benefit from AUS than a repeat sling [56]. Patients with risk factors for sling failure, including severe stress incontinence or history of radiation therapy, may be better served by AUS than a sling. Despite these risk factors, however, male slings may be indicated in otherwise appropriately selected patients with poor dexterity to operate an AUS.

Kumar et al., interestingly, found that when faced with a choice of AUS versus male sling, 25% of patients preferred to have a sling in spite of their urologist's recommendation to pursue AUS instead [57]. Furthermore, when given a choice, 92% of patients chose sling over AUS. The primary reason for these findings appears to be the desire of many patients to avoid a mechanical device that would require manipulation.

We propose the following surgical treatment algorithm to stratify patients based on their degree of ISD:



In the absence of risk factors for sling failure, many patients may benefit from either a sling or AUS and should understand the merits of each in the process of making an informed decision. It is also important for patients undergoing incontinence procedures to have realistic expectations concerning outcomes.

## Surgical technique

Placement of bone-anchored slings is described, but emphasis is given to the placement of the more commonly used transobturator male slings.

### InVance bone-anchored slings

The patient is positioned in the high dorsal lithotomy position under general anesthesia with the perineum prepped and draped. A 14 Fr urethral catheter is placed for bladder drainage and urethral identification during the procedure. A 4 cm midline perineal incision is made over the urethra after palpating the catheter and ischial tuberosities. Dissection is carried down over the urethra, leaving the bulbospongiosus muscle intact. Dissection is directed laterally to the pubic tubercle, and descending pubic rami are identified. The inferior aspects of the pubic rami are identified. A Scott/Wilson or similar retractor is placed into the incision for exposure. The applicator is used to insert six 5 mm titanium screws as bone anchors into the pubic rami. Three bone anchors are placed 1 cm apart into each descending ramus, just inferior to the pubic symphysis. The most inferior bone anchor should be placed no more inferiorly on the descending ramus than at the level of the bulbar urethra. Each bone anchor is preattached to a no. 1 Prolene suture. An audible change in pitch indicates that the anchor has been inserted to the appropriate depth. The sling is a 4 × 7 cm sheet of pliable mesh composed of silicone-coated multifilament polyester known as InteMesh. The mesh may be trimmed to fit the patient in some cases. One side of the mesh is first tied down snugly with the Prolene sutures attached to the bone anchors in one pubic ramus. Sutures should be placed at least 1 cm medially from the edge of the mesh to provide optimal strength. The second side of the mesh is similarly tied down tightly using the Prolene sutures attached to bone anchors on the second pubic ramus. The mesh should be tied down as tightly as possible to provide maximum tension. An alternative involves intraoperative leak point determination to determine the appropriate mesh tension prior to tying down the second side of the mesh. The perineal incision is closed in three layers using two layers of 3-0 Vicryl and skin with 4-0 chromic suture to complete the procedure.

### AdVance transobturator slings

The patient is positioned in high dorsal lithotomy position under general anesthesia. The anal area is covered and isolated from the surgical field by using a sterile towel. A 14 Fr urethral catheter is placed for bladder drainage and urethral identification. A midline perineal incision is made (Figure 165.3) and carried down to the

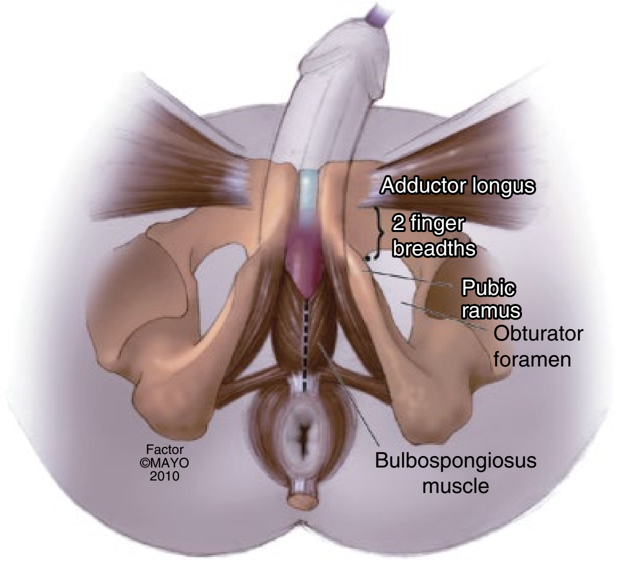


**Figure 165.3** Relevant pelvic anatomy for placement of a transobturator male sling. A midline perineal incision is made. Bilateral stab incisions are made two fingerbreadths posterior to the adductor longus tendon at the level of the base of the penis. *Source:* Dr. Ajay Nehra. Reproduced with permission of Dr. Ajay Nehra.

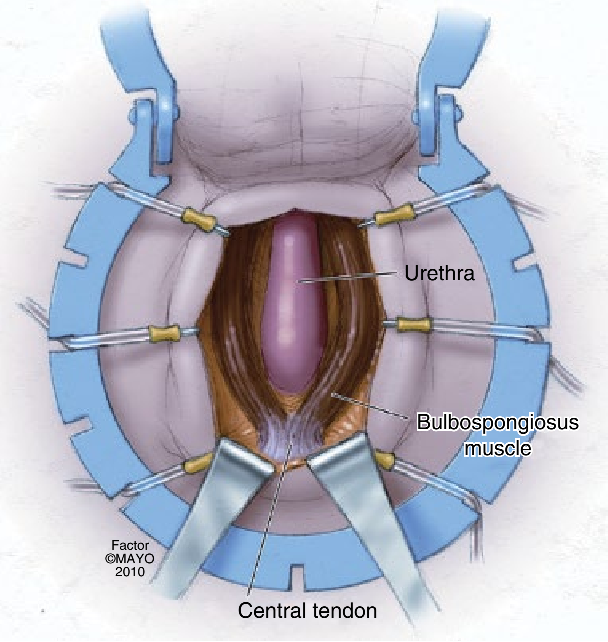


**Figure 165.4** Urethra is identified within the midline perineal incision. The bulbospongiosus muscle is spared. A self-retaining retractor is placed into the incision for exposure. *Source:* Dr. Ajay Nehra. Reproduced with permission of Dr. Ajay Nehra.

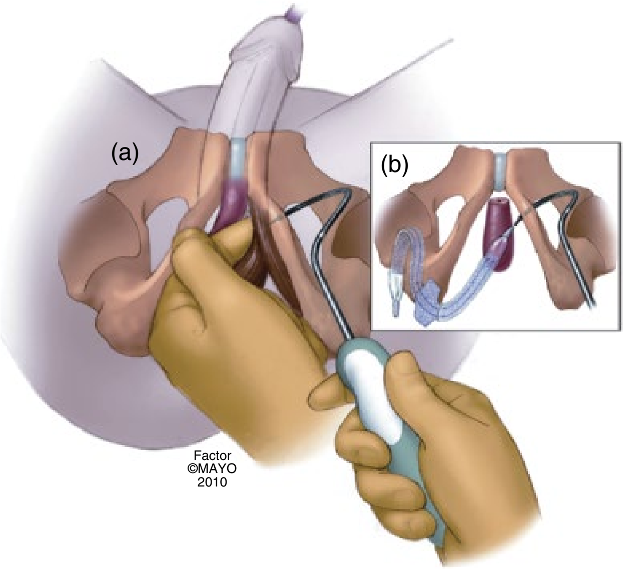


**Figure 165.5** (a) A curved trocar is placed through the stab incision. The descending pubic ramus is encountered and the trocar then angled laterally and passed through the obturator ring with index finger guidance. The trocar follows the index finger into the perineal incision. This process is then repeated on the contralateral side. (b) Each end of the AdVance sling is then attached to a trocar eye and brought out through the stab incision. *Source:* Dr. Ajay Nehra. Reproduced with permission of Dr. Ajay Nehra.

bulbar urethra, which is identified by palpation of the catheter. The bulbospongiosus muscle is left intact (Figure 165.4). A self-retaining Scott/Wilson retractor is placed into the incision for exposure. The perineal body is only partially dissected during mobilization of the bulbar urethra. Two separate stab incisions are made bilaterally 1 cm inferior to the adductor longus tendon, in the groin area. An introducing trocar is passed through one of the stab incisions using an outside-to-inside approach. The tough obturator membrane is then perforated with the trocar, which is advanced medially and passed through the obturator membrane and ring. An index finger is used through the perineal incision to guide the trocar out through the perineal incision. This finger also protects the urethra simultaneously from any inadvertent injury. A second trocar is then passed through the contralateral stab incision in the same manner. The distal ends of the sling are passed through the eye of each trocar and brought out with each trocar through the stab incisions (Figure 165.5). The mesh at the center of the sling is placed flatly against the sphincteric urethra. Cystoscopy is performed to exclude urethral or bladder injury. Tension on the sling is adjusted under direct vision using urethroscopy so that acoaptation is noted at the sphincteric urethra without obstruction of the lumen (Figure 165.6). The mesh is then fixed to the bulbospongiosus muscle overlying the bulbar urethra using one 3-0 Vicryl suture at each corner. Sleeves are removed from the ends of the mesh and, using a right angle, the distal ends of the sling and attached suture are tunneled out of separate stab incisions approximately 2 cm inferomedial to the initial stab incisions bilaterally. Sleeves are removed from the arms of the sling, and the excess mesh is excised (Figure 165.7). Stab incisions are closed with simple 4-0 Vicryl suture. The perineal incision is then closed using two layers of 3-0 Vicryl and skin using 4-0 chromic suture (Figure 165.8). Oral antibiotics are prescribed for one week, and strict activity restrictions are implemented, including no hard chairs, biking, sexual activity, or lifting more than 5 kg for 2–3 months.

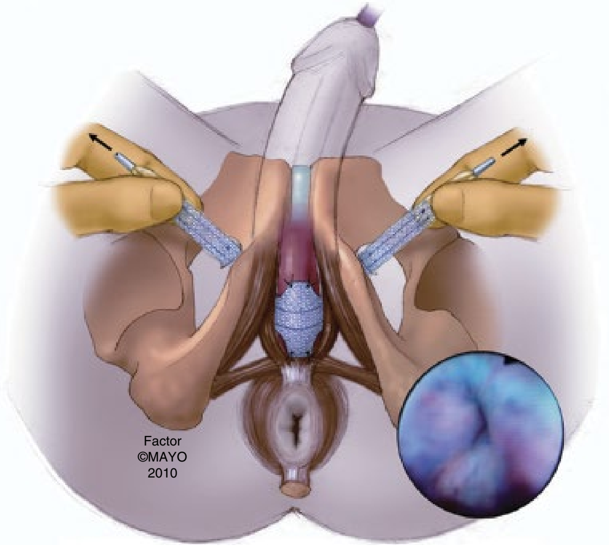


**Figure 165.6** Mesh is placed flatly against the urethra and anchored in four corners with 3-0 Vicryl suture. Urethroscopy is performed, and tension is applied to the ends of the mesh under urethroscopic vision to confirm appropriate coaptation of the sphincteric urethra. *Source:* Dr Ajay Nehra. Reproduced with permission of Dr Ajay Nehra.

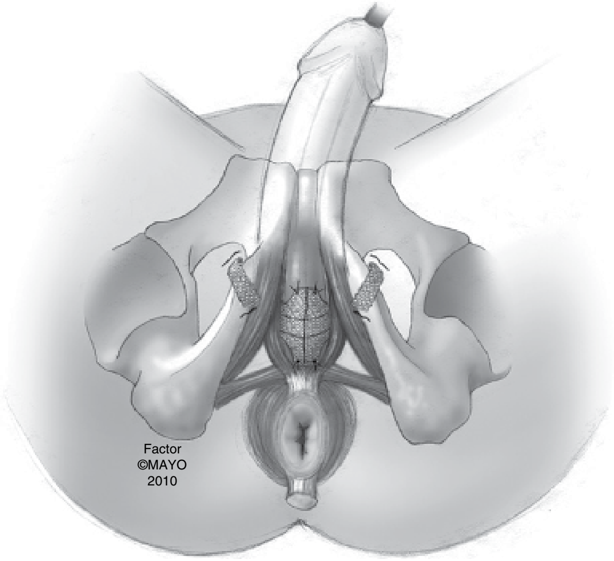
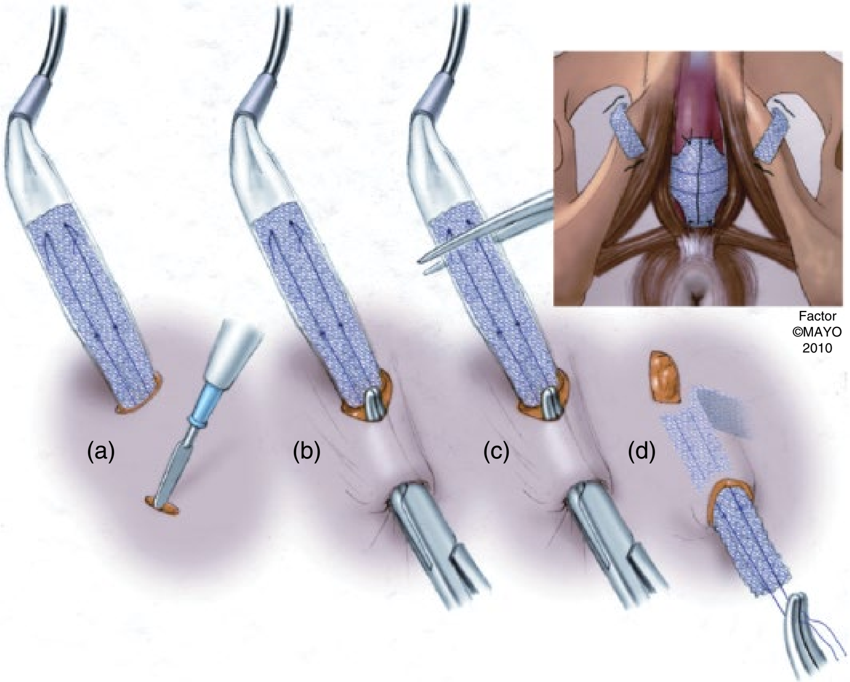


**Figure 165.8** Stab incisions are closed with simple interrupted absorbable suture and the perineal incision in three layers with running absorbable suture. *Source:* Dr. Ajay Nehra. Reproduced with permission of Dr. Ajay Nehra.

**Figure 165.7** (a, b) A superficial stab incision is made 2 cm inferomedial to the stab incision bilaterally. (c) Sleeves are removed from each side of the mesh. (d) A right angle is used to create a tunnel and bring the mesh ends out through the inferomedial stab incisions. Excess mesh is trimmed at skin level. *Source:* Dr, Ajay Nehra. Reproduced with permission of Dr, Ajay Nehra.



## Coloplast Virtue male sling

The Coloplast Virtue sling involves mesh that employs two prepubic arms and two transobturator arms in order to provide quadratic fixation of the bulbar urethra (Figure 165.9). This system is designed to provide both urethral elevation and compression, combining properties of both bone-anchored and transobturator slings in order to improve post-prostatectomy continence.

The patient is positioned in dorsal lithotomy under general anesthesia. The anal area is covered and isolated from the surgical field by using a sterile towel. A 14 Fr catheter is placed to help identify the urethra, and a vertical midline perineal incision is made and carried down to the bulbar urethra. A self-retaining Scott/Wilson retractor is used for adequate exposure. The urethra and descending pubic rami are exposed bilaterally, while leaving the bulbospongiosus muscle intact. Using sharp dissection, the bulbous urethra is partially detached from the central tendon to the perineal body, thereby allowing mobility of the bulbar urethra. Two separate stab incisions are made bilaterally 1 cm inferior to the adductor longus tendon, in the groin area.

For the TO arms of the sling, the semilunar trocars are passed in an inside-to-out fashion, from the perineal incision out through groin stab incisions. The urethra is protected while passing the trocar. The obturator membrane is encountered as a tough structure and is perforated with the tip of the trocar. The trocar tip should exit from groin approximately 1 cm inferior to the insertion of the adductor longus tendon, which is easily palpable. The suture attached with the TO arm of the sling is looped into the eye of the trocar. Skin overlying the trocar tip is incised, and both the tip of the trocar and the attached suture are exposed. The arm of the sling and the attached suture are pulled out through the groin incision.

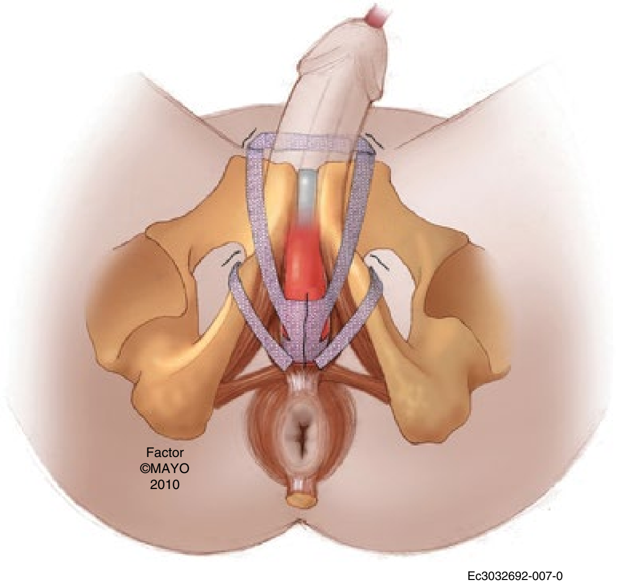


**Figure 165.9** Coloplast Virtue male sling. *Source:* Dr. Ajay Nehra. Reproduced with permission of Dr. Ajay Nehra.

Next, attention is diverted to the prepubic area to place the prepubic arms. The semilunar trocar for the prepubic arms of the Virtue sling is passed in an out-to-in fashion in the subcutaneous tissue plane anterior to the pubic bone. Two stab skin incisions are made 2–3 fingerbreadths lateral to midline overlying the pubic symphysis. The semilunar trocar is then passed from the pubic incision, anterior to the pubic bone out through the perineal incision guided with the index finger of the contralateral hand. The perineal incision may be retracted cephalad to assist with the trocar passage. The suture loops from the prepubic arms are then attached to the ends of the semilunar trocar, and the prepubic extensions of the sling are transferred through the pubic incision. Sling arms are then progressively and symmetrically tensioned such that the transobturator arms elevate the bulbar urethra by 2–3 cm, and the prepubic arms provide compression of the bulbar urethra. The mesh is laid flat in this fashion opposite the bulbar urethra. Next the Foley catheter is removed. To confirm appropriate sling tension, an RLPP is obtained by inserting a small catheter into the fossa navicularis and then connecting this to a saline bag with the drip chamber set at a water height of 60 cm above the pubic symphysis. For sling tension, the saline is allowed to flow, and progressive sling tension is applied to the transobturator arms until the drip chamber flow starts to slow. Next progressive tension is then applied to the prepubic arms until the drip chamber flow completely stops. This indicates that urethral pressure of 60 $cmH_2O$ has been achieved.

Once the appropriate sling tension has been achieved, the distal aspect of the sling adjacent to the prepubic arms is secured to the underlying periosteum using a 2-0 Prolene suture. The TO arms are then tunneled subcutaneously back through the perineal incision using a hemostat, and then the overlapping transobturator arms are fixed to each other in the midline using 2-0 Prolene suture. The excess sling arms are transected below the skin level. Likewise, for the prepubic arms, once properly fixated, the plastic sleeves of the prepubic arms are removed and the arms trimmed below the skin level. Incisions are then irrigated with antibiotic solution. The stab wounds and the perineal wound are closed in multiple layers. A 14 Fr catheter should be left in overnight, followed by a trial of voiding on postoperative day 1. Patients are advised to avoid lifting objects heavier than 5 kg for at least six weeks following surgery. They should also refrain from strenuous activity that might place excess stress on the perineum, including running, squatting, bicycle riding, and sexual activity.

## Conclusions

Advances in the diagnosis, management, and treatment of men with SUI have resulted in various surgical options. A meticulous preoperative evaluation and long-term analysis of outcomes and results will provide insights into success following sling surgery. Male sling surgery has emerged as a safe and efficacious alternative to AUS placement in properly selected men with post-prostatectomy incontinence. Slings are preferred by most patients over the AUS, as the need to manipulate a scrotal pump to permit bladder evacuation can be avoided. Patient selection remains the key to success in any male sling surgery. In particular, in patients with mild to moderate SUI with normal bladder contractility, intermediate-term results with sling surgery appear equivalent to those for AUS placement. Similarly, patients with history of prior radiation and/or prior incontinence procedures should not be offered male sling. There are limited data available for the newer quadratic slings, and long-term data are presently lacking for male slings. Patients should be counseled appropriately and provided with realistic expectations.

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# Neuromodulation

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## Introduction

Chronic urinary frequency, urgency, and urge incontinence, collectively referred to as overactive bladder (OAB), are a common cause of voiding dysfunction and a frequently seen problem in the urologist's practice. Approximately 30 million people in the United States have OAB, leading to significant impairment in quality of life, a higher risk of falls, lower self-esteem and health perception [1]. Annual cost associated with OAB, including direct care, health consequences, and lost productivity, is estimated at more than US$10 billion [2].

For patients with OAB, first-line treatment options include conservative therapies, such as behavioral interventions, pelvic floor exercises, and biofeedback, followed by pharmacologic therapy. Although many patients find relief with these therapies, up to 40% of patients are either refractory to primary management or have an unsatisfactory response [3], and other options must be considered. Currently, several options exist for these patients, ranging from intradetrusor injection of botulinum toxin to irreversible surgical therapy, including detrusor myomectomy, augmentation cystoplasty, and urinary diversion. Unfortunately, these procedures are also associated with significant morbidity. Bladder botulinum toxin injection recently received US Food and Drug Administration (FDA) approval for use in patients with neurogenic and idiopathic OAB. Although results have been promising, there is a need for repeat injections and data on long-term results are lacking. Sacral nerve stimulation (SNS) as well as percutaneous tibial nerve stimulation (PTNS) offer attractive alternatives which are state-of-the-art, minimally invasive, and reversible treatments with a high rate of success for patients with voiding dysfunction (urinary retention or OAB) for whom conservative therapies have failed prior to consideration of more invasive and irreversible treatment modalities.

In this chapter we review the history of these novel techniques, as well as the current state of electric neuromodulation (sacral and tibial) for the treatment of refractory voiding dysfunction, including a detailed description of the therapies, possible mechanisms of action, indications for the procedures, patient selection, surgical techniques, efficacy/outcomes, risks/benefits, and cost considerations.

## Historical perspective

Neuromodulation therapy for voiding dysfunction and urinary incontinence represents a recent step in the long history of the use of electrical stimulation for medical purposes. Caldwell [4] reported (in 1963) the use of electrical stimulation of the pelvic floor by implanted electrodes to control stress urinary incontinence and attempted to treat neurogenic incontinence with an implantable stimulator. The instruments in that era were rudimentary; however, with advances in cardiac pacing and improved understanding and miniaturization of electronic instruments, interest in neuromodulation of bladder function was revived in the 1970s and 1980s. Most of the credit for laying the foundation of neuromodulation as it is performed today goes to Drs. Schmidt and Tanagho [5, 6] who did many of the early studies at the University of California, San Francisco. Their work was instrumental in advancing the use of SNS for the treatment of refractory voiding dysfunction. They demonstrated that by using an electrode connected to an implanted pulse generator to provide continuous stimulation of sacral root S3, detrusor and sphincter activity

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could be modulated and micturition reflexes stabilized. Further research in understanding the mechanism of neuromodulation was done by Drs. Craggs and Fowler in London and Drs. de Groat and Chancellor at the University of Pittsburgh in the mid-1990s [7, 8].

Initially, SNS was performed as a two-stage procedure, and the quadripolar lead electrode was placed through an open sacral incision; the implantable pulse generator (IPG) was placed in the abdomen. The procedure was relatively involved and took approximately 2 hours to perform. The first major change was placement of the IPG in the upper buttock region. This helped decrease both the time needed to perform the procedure and the rate of infection. The next major change was the development of the tined lead, allowing percutaneous lead placement under fluoroscopy. This change made the procedure less invasive and further decreased the time needed to perform it.

The initial large-scale trials were performed in the mid-1990s when Medtronic Incorporated bought the technology from a struggling startup company and completed FDA trials, leading to the approval of SNS for the treatment of urge incontinence in 1997 and for frequency/urgency as well as nonobstructive urinary retention in 1999. Since then, SNS has been used successfully in over 26 000 patients for lower urinary tract dysfunction [9].

## Mechanism of action

The mechanism of action of neuromodulation on voiding dysfunction has not been fully elucidated. In general, neuromodulation works on the principle that activity in one neural pathway can influence activity in another neural pathway. The S2–S4 nerve roots provide the primary autonomic and somatic innervation to the bladder, urethra, and pelvic floor. It is known that contractions of the pelvic floor and voluntary external sphincter can abolish unstable bladder contractions. This may represent one of the mechanisms whereby stimulation of the S3 or S4 nerve root results in strengthening of the pelvic floor and sphincter, resulting in a more appropriate relaxation of the pelvic floor and urethra with less bladder instability.

Chancellor and de Groat [10, 11] have suggested SNS improves somatic afferent inhibition of sensory processing in the spinal cord, playing an important role in modulating abnormal micturition. Schmidt et al. [12] noticed significant improvement in voiding dysfunction through the strengthening of the pelvic floor and external sphincter through efferent-mediated augmentation of the guarding reflex. Fowler and colleagues [8] suggested that neuromodulation affects afferent pathways through changes in the spino-bulbospinal pathways to the pontine micturition center. Gronewald et al. [13] have noted that the beneficial effect of SNS can occur without efferent activation of muscle fibers. It is likely that both efferent and afferent mechanisms play a role, with patients primarily with frequency and urgency helped more through afferent sensory mechanisms, and those with primarily urge incontinence improving as a result of increased efferent activity.

Chronic SNS has been shown to lead to augmented somatosensory cortical responses to evoked potentials along the pudendal and posterior tibial nerves [14]. Furthermore, through positron emission tomography studies, additional neural plasticity is observed over the course of neuromodulation in cortical areas associated with motor learning and with pelvic floor and abdominal musculature [15]. Suffice it to say that modulation of the sacral nerve toots restores a more normal relationship between the excitatory and inhibitory urinary control systems, helping the two extremes of voiding dysfunction/urinary retention and urge incontinence.

## Indications and efficacy of sacral neuromodulation

All patients considered for SNS should have a complete history and physical examination, including a genital, rectal, and neurological examination. These patients should perform accurate voiding diaries and generally undergo urodynamic studies to confirm the diagnosis and ascertain whether they are suitable candidates.

### Overactive bladder

The first American Urological Association (AUA) guidelines on OAB released in 2009 focused on 13 studies in the literature of largely single-group observational designs, which evaluated the efficacy and adverse events of SNS in patients with severe refractory OAB symptoms, many of whom had failed multiple other therapies. Greater than 50% improvement was observed at 5 years in 68% of patients with urgency incontinence and in 56% of those with frequency urgency in those who initially had success with the external testing and went on to pulse generator implantation [16].

The updated literature review, and most recently updated AUA guidelines on OAB (May 2014) examined an additional 16 relevant treatment studies, including one prospective randomized multicenter trial, one crossover study, and another 14 observational studies. These recent studies corroborated similar efficacy reported in the prior guidelines [17]. The guidelines concluded that clinicians may offer sacral neurostimulation (SNS) as *third-line* treatment in a carefully selected patient population characterized by severe refractory OAB symptoms or patients who are not candidates for second-line therapy and are willing to undergo a surgical procedure. Given its lower side-effect profile, some experts argue that SNS should be offered as first-line therapy for OAB in the elderly, who may experience significant mental status changes with anticholinergic therapy.

## Nonobstructive urinary retention

Prior to the introduction of neuromodulation many of the patients with this disease entity were managed with intermittent catheterization and/or indwelling catheter, given that no pharmacologic therapy was found to be sufficiently efficacious to treat these patients. Recent studies have shown that a significant number of patients with nonobstructive urinary retention who have undergone SNS treatment have been able to eliminate catheterization in six months (50–69%) as well as decrease catheterization volumes (PVR) (70–80%) [18–20]. SNS has even been shown to be particularly efficacious in patients with Fowler's syndrome (young women with idiopathic retention and specific EMG findings) [21].

## Expanding indications

Since the introduction of SNS for OAB and nonobstructive urinary retention, there has been growing recognition of the potential benefit of SNS for a broader range of pelvic disorders that may involve some OAB symptoms. Although some these applications are investigational and represent off-label use, research is ongoing into the potential use of SNS for interstitial cystitis/painful bladder syndrome (IC/PBS)/pelvic pain, neurogenic voiding dysfunction, and sexual dysfunction. Early evidence suggests that some patients with these conditions may also benefit from sacral neuromodulation, potentially further expanding the indications for SNS.

## Interstitial cystitis/painful bladder syndrome

Urinary symptoms in patients with IC/PBS may respond better to SNS than do pain symptoms. Multiple small series have demonstrated at least significant short-term efficacy [22, 23]. The highest response rates were reported by Comiter [22] for carefully selected patients who underwent a successful period of test stimulation. In this study, only 27 of 39 patients progressed from test stimulation to permanent implantation, but the rate of success was 94% among those patients undergoing permanent implantation. Given the increasing evidence of the efficacy of sacral neuromodulation in patients with IC/PBS this treatment is currently considered part of the AUA and European Association of Urology (EAU) guidelines for the management of IC/PBS [24, 25].

## Fecal incontinence

The FDA recently approved sacral neuromodulation for the treatment of refractory fecal incontinence. Several prospective studies have reported on the efficacy of SNS for the treatment of refractory fecal incontinence with or without sphincter defects [26, 27]. Wexner et al. [27] reported on outcomes of a large prospective cohort of 120 women with refractory fecal incontinence and showed a significant reduction in incontinence episodes from nine episodes at baseline to two episodes at 1 year. They also reported significant clinical improvements in Fecal Incontinence Severity Index scores, Fecal Incontinence Quality of Life Questionnaire, use of pads and other forms of protection, and overall self-perception of bowel health.

## Neurogenic bladder

Lombardi and Del Popolo [28] studied the efficacy and safety of SNS in patients with incomplete spinal cord injury suffering from neurogenic lower urinary tract symptoms with a mean follow-up of 61 months. Those patients with urinary retention reported a 50% improvement in baseline voiding parameters, with a significant decrease in the number of catheterizations and a significant increase in the frequency of voids and voided volume. Furthermore, at the conclusion of the study, 38% of patients no longer required catheterization for bladder emptying. A major practical limitation of SNS for neurologic disorders (spinal cord injury and multiple sclerosis patients) is the need of many of these patients to undergo magnetic resonance imaging (MRI) studies. MRIs have been shown to cause heating of the leads, and may damage the IPG [29, 30]. It is contraindicated to perform a MRI in a patient who has undergone SNS with an IPG, with the exception of brain MRI. As such, it is important that the patient's neurologist be informed and be part of the decision-making process prior to performing SNS.

## Sexual dysfunction

Improvement in female sexual function after SNS treatment has been suggested in recent studies in the literature in a subset of patients suffering from idiopathic and neurogenic detrusor overactivity. Statistically significant improvement has been noted in terms of desire, lubrication, orgasm, satisfaction, and pain [31]. Furthermore, studies have also reported improvement in Female Sexual Function Index (FSFI) and Female Sexual Distress (FSDS) scores [32, 33]. It is hypothesized that the mechanism of action of SNS on improvement of sexual dysfunction relies on pudendal nerve integrity [31]. However, this remains a debated topic in the literature, and large multicenter prospective controlled trials are needed to provide good-quality results and demonstrate a possible direct effect of SNS and improvement in sexual dysfunction.

## Sacral neuromodulation test procedure

A test procedure provides a short-term trial of 3–7 days of SNS and is important to patient selection before permanent implantation of an IPG. This is sometimes referred to as percutaneous nerve evaluation (PNE). It lets the patient and physician decide whether the benefits of permanent IPG implantation are worthwhile while weighing the benefits, risks, and costs of the therapy. The test procedure can be performed in the office under straight local anesthesia using fluoroscopy guidance; alternatively, a test procedure using permanent tined leads can be performed in the ambulatory surgery unit or operating room. The patient should complete a 2- to 3-day voiding diary before the test procedure.

### Percutaneous nerve evaluation

The patient is placed in the prone position with one or two pillows under the lower abdomen to improve the sacral approach. The sacrum, buttocks, and perineum are sterilely prepped with antiseptic solution and the sterile drapes are placed to allow for visualization of the buttocks and gluteal crease, as well as the patient's feet and toes, during the procedure (Figure 166.1). The sacral notches and coccygeal drop-off are identified by palpation or fluoroscopy. S3 usually is located 1.5–2 cm lateral to the midline at the level of the sacral notches, or about 9 cm above the coccygeal drop-off. Local anesthesia is achieved from S2 to S4 over the underlying skin and subcutaneous tissue, making certain not to enter the foramen. Insulated foramen needles are inserted percutaneously into the foramen at a 60° angle relative to the skin in the S3 and S4 foramens, using the previously mentioned landmarks and fluoroscopic guidance (with primarily lateral imaging). The test stimulator is connected to the foramen needle via the test stimulation cable, and stimulation is applied (Figure 166.2).

With electrical stimulation applied, the clinician observes for appropriate sensory and motor responses to stimulation. If the appropriate responses are not observed, the needle may be adjusted up and down to change the depth, or a second foramen needle may be placed on the contralateral side. If the sensory and motor responses are inconsistent with sacral nerve S3 response, then the needle must be reinserted into a different foramen and retested. If the desired responses are seen, the temporary test stimulation lead (wire) is inserted into the foramen needle until the lead electrode exits the needle tip (determined by markings on the lead). The lead is retested for appropriate responses, and if confirmed, the foramen needle is removed over the lead, leaving the lead in place in the S3 foramen. The patient can try out left and right sides or S3 and S4 and decide on the best response. Sacral radiographs are used to document the position of the wire electrode immediately after the procedure (Figure 166.3). Once the wires are attached to an external stimulator and secured the patient is sent home.

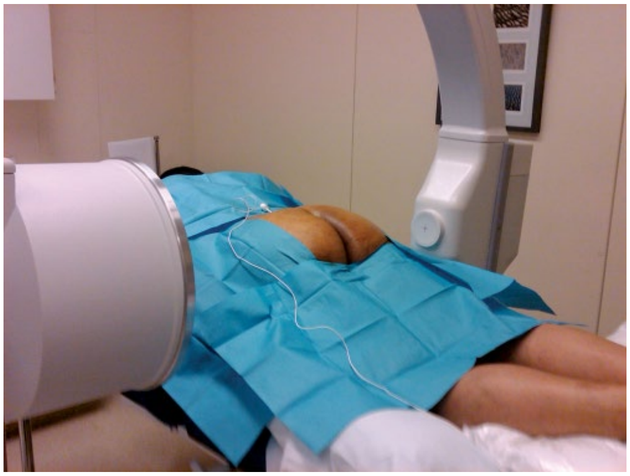

**Figure 166.1** Office-based percutaneous nerve evaluation (PNE) test. The patient is placed in the prone position with one or two pillows under the lower abdomen to improve the sacral approach with slight flexion at the hips. The patient's shoes and socks are removed to allow observation of the feet and toes. The sacrum, buttocks, and perineum are sterilely prepped with antiseptic solution and the sterile drapes are placed to allow visualization of the buttocks and gluteal crease area during the procedure.

The test period lasts for a few days up to one week. The patient maintains stimulation at a comfortable level and completes a 2–3 day voiding diary to provide objective data. The wire is then removed at 3–7 days by withdrawing the lead with gentle traction. A voiding diary is repeated a week later to make certain the patient returns to baseline voiding. The diaries are compared with the patient's pretest diary and, based on the patient's results, a final decision is made to proceed or not to proceed with permanent implantation. Usually, the patient needs to exhibit significant subjective improvement, and the voiding diary should show at least 50% improvement in voiding parameters (such as number of urge incontinence episodes) to warrant proceeding to implantation

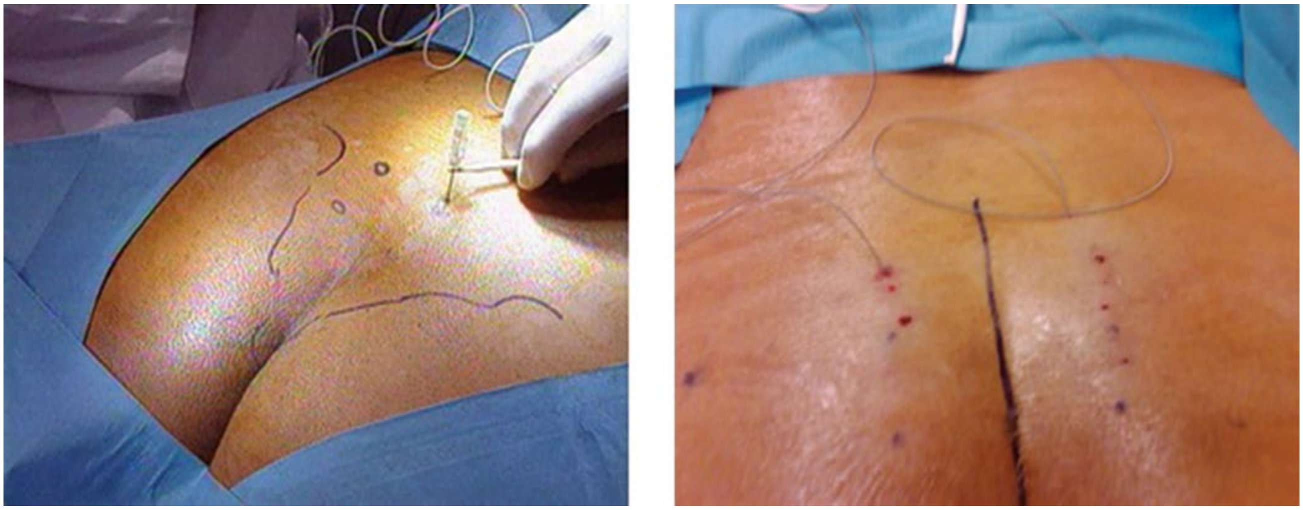

**Figure 166.2** Placement of the foramen needle. The sacral notches and coccygeal drop-off are identified by palpation or fluoroscopy. S3 is usually located 1.5–2 cm lateral to the midline at the level of the sacral notches, or about 9 cm above the coccygeal drop-off. Insulated foramen needles are inserted percutaneously into the foramen at a 60° angle relative to the skin in the S3 and S4 foramens under fluoroscopic guidance. The test stimulator is connected to the foramen needle via the test stimulation cable and stimulation is applied. The patient can try out left and right sides and decide on the best response. Bilateral test stimulation may be helpful for some patients who fail an initial trial with unilateral placement.

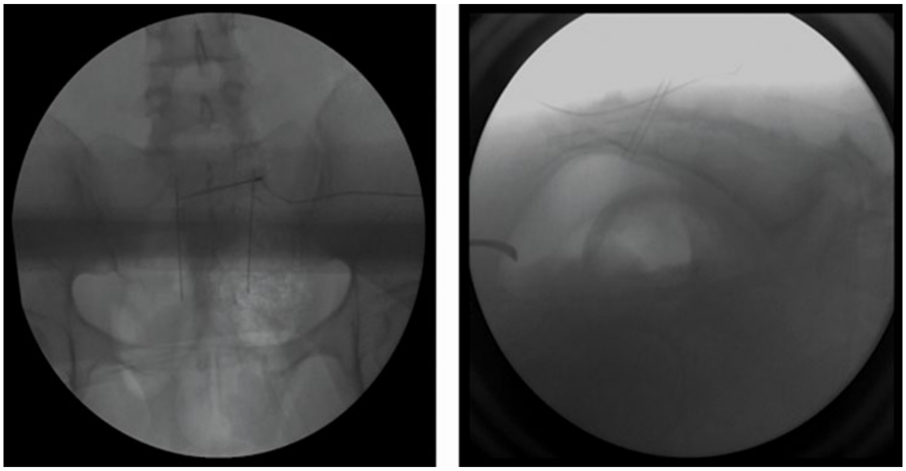

**Figure 166.3** Fluoroscopic images of foramen needles bilaterally at S3. Anterior–posterior and lateral views shown.

of the IPG. After an interval of two weeks or more, the patient is brought back to the operating room and a tined quadripolar lead electrode is placed with implantation of the IPG.

## Staged lead placement (first and second stage)

In equivocal cases, or if the insulated wires move or migrate, a trial can be carried out with a quadripolar tined electrode before making a final decision. In patients in whom sacral spinal anatomy may be distorted (i.e. congenital malformations, trauma, or surgery), or those who may not tolerate an office test stimulation, placement of a tined, quadripolar lead as a staged procedure under anesthesia (sedation or general) is recommended.

The initial procedure (first stage) is similar to the test stimulation described but is performed in the operating room under light sedation. During the surgery, prophylactic broad-spectrum antibiotics are provided and strict antiseptic precautions are maintained. While lying in the prone position, the patient is prepped with multiple layers of povidone-iodine, and again surgical drapes are positioned to allow for visualization of buttocks and gluteal crease area during the procedure as well as the patient's feet and ankles, which are left undraped to allow

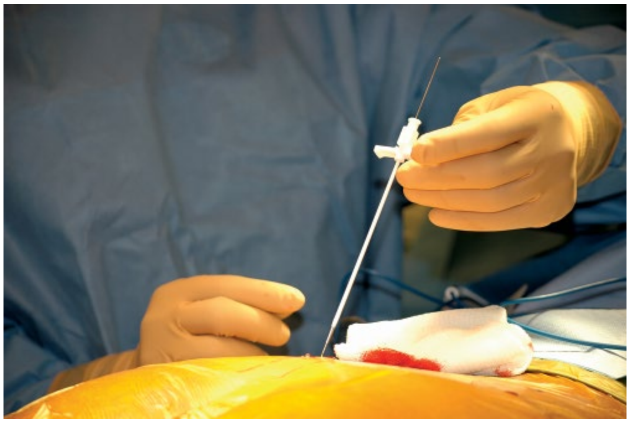

**Figure 166.4** Permanent lead placement. The lead introducer is inserted over the guidewire.

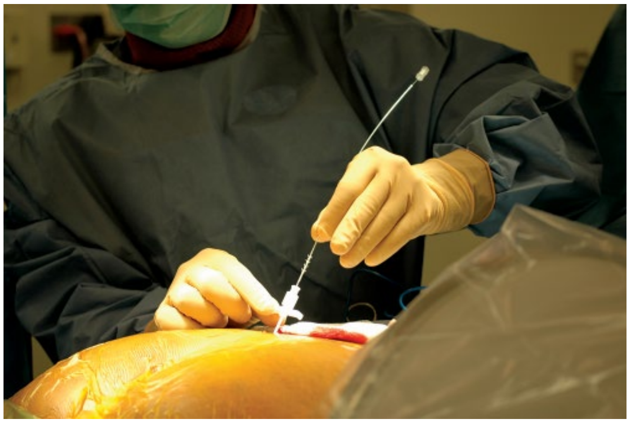

**Figure 166.5** Tined lead placement. The tined lead is inserted into the lead introducer sheath.

for observation for motor responses. In a similar fashion as described above for the PNE procedure, the S3 foramen is identified and an insulated foramen needle is placed in both foramens. Once the needles have been placed, with confirmation via fluoroscopy, and the sensory and motor responses obtained, a decision is made to use the best responses. The needle's stylet is removed, a guidewire is inserted, a scalpel is used to incise the skin along the wire, and the tract is dilated over the guidewire under fluoroscopic guidance using an introducer (Figure 166.4). Radiopaque markings on the introducer (one at the dilator tip and one at the introducer sheath tip) allow for appropriate positioning of the device within the S3 foramen. The sheath from the dilating apparatus is then left in; the tined lead (so called as it has tines that hold it in place) is inserted (Figure 166.5), and its position is optimized by again checking the neural responses. The sheath is then removed, and the tines are activated to hold the lead in place.

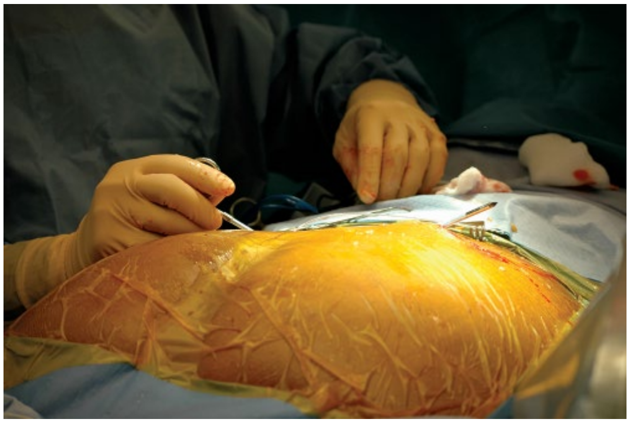

**Figure 166.6** With the bladed tunneling device the permanent lead is tunneled subcutaneously to the medial aspect of the lateral buttock incision (location of the eventual implantable pulse generator (IPG) site). Redundant lead wire and connection covers are buried in the subcutaneous pocket. Another tunnel is then created to externalize the connection further laterally to exit superolaterally to the IPG site to prevent infection.

A 3 cm skin incision is made in the contralateral upper buttocks, and a small subcutaneous pocket is created, which will be the future site of the IPG. The tined lead is now tunneled to the location of the eventual IPG, where it is connected to an externalizing wire, and then another tunnel is created to externalize the connection and to prevent infection (Figure 166.6). Redundant lead wire and connection covers are buried in the subcutaneous pocket previously developed, and the subcutaneous tissue and overlying skin are closed with absorbable sutures in two layers. If the patient reports more than 50% improvement in symptoms, a stage 2 procedure is performed, in which the external connection is removed and the IPG is placed (Figures 166.7 and 166.8). The IPG is programmed, and the patient is taught to set the unit at a comfortable setting at which the stimulation can be felt but is not painful. The patient is able to control the amplitude and to turn the unit on and off; the IPG is completely programmable using an external programmer. Thus, the various parameters can be adjusted on a routine basis as necessary to provide optimal stimulation and results.

Implantation of the IPG (stage 2) after a trial period with a quadripolar lead (stage 1) is sometimes referred to a two-stage procedure. When both the quadripolar permanent lead and IPG are implanted in the same operating room setting, generally after an office-based test stimulation, this is referred to as a complete or one-stage procedure.

Patients who have undergone successful test stimulation may be considered for implantation of the currently available neurostimulator, the InterStim® device (Medtronic, Inc., Minneapolis, MN, USA). The patient should understand fully the benefits and risks of the

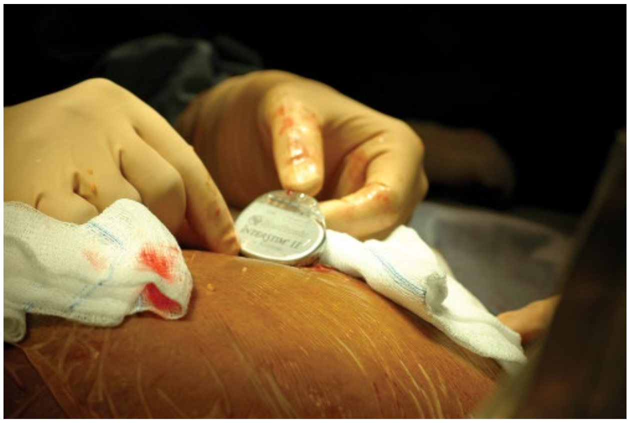

**Figure 166.7** Implantable pulse generator (IPG) implantation. During the second-stage procedure, the external connection is removed and the IPG is connected to the tined stimulation lead and placed in a subcutaneous pocket that is large enough to accommodate the IPG without any tension and with enough overlying tissue to prevent erosion. The overlying skin is closed with absorbable sutures.

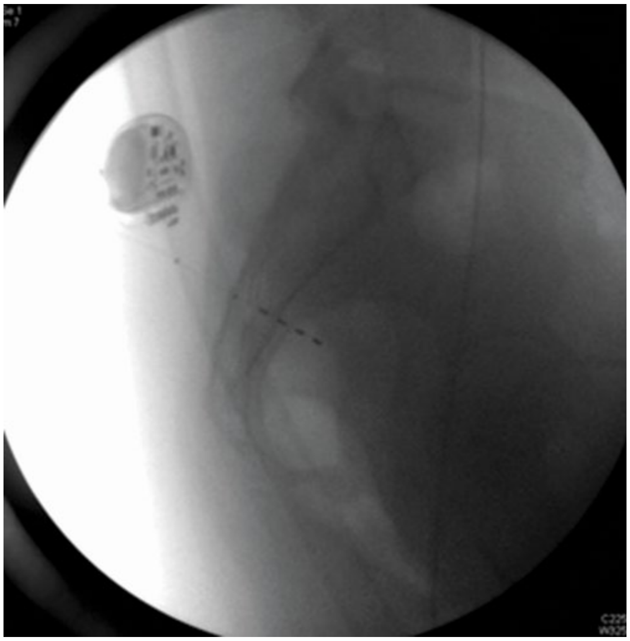

**Figure 166.8** Fluoroscopic image of tined lead placement, with implantable pulse generator contralateral upper buttock (lateral view). The lead is inserted until the first electrical contact point is straddling the ventral aspect of the S3 foramen.

procedure and that the battery life is limited to 2–5 years, depending on the settings. Patients who may become pregnant should consider alternative therapies, since the effect of neurostimulation on the fetus is unknown. Foreseeable need for MRI is also a relative contraindication to neurostimulator implantation (e.g. patients with multiple sclerosis).

**Table 166.1** Sacral nerve root motor and sensory responses to electrical stimulation.

| Nerve root | Pelvic floor | Lower extremity | Sensation |
|---|---|---|---|
| S2 | "Clamp" of anal sphincter | Leg/hip rotation, plantarflexion of entire foot, calf cramping | Sensations in base of penis/ vagina, and buttocks |
| S3 | "Bellows" response (levator muscles contraction) | Greater toe flexion | Pulling in rectum, extending forward to scrotum or labia |
| S4 | "Bellows" response | None | Pulling in rectum only |

## Sensory and motor neural responses

Intraoperative motor and sensory neural responses guide lead positioning during the test stimulation (Table 166.1). Sensory responses generally include a tingling, pulling, or vibratory sensation in the vagina and rectum in women and in the scrotum, phallus, and rectum in men. Motor responses include levator tightening (bellows response) and flexion of the big toe. Sometimes at S3, a plantarflexion of the entire foot is noted. In such cases, S4 may be the more appropriate foramen, as most patients are significantly bothered by such a foot response. An intraoperative motor response during the test procedure generally is considered to be more predictive of success after IPG implantation than a purely sensory response [34]. Although intraoperative motor responses are the primary neural responses used to locate the ideal site of electrode implantation, neuromodulation amplitude is usually applied at a level below that is needed to stimulate a motor response. The patient may use sensory perception to stimulation as an indicator of continued neuromodulation. Loss of sensory perception after implantation may herald a loss in benefit from neurostimulation.

## Permanent versus temporary lead test procedure

A major consideration for the clinician is whether to pursue an office-based test procedure, which, if successful, is followed by a "one-stage" implant of permanent lead and an IPG in the operating room. An alternative approach is the "two-stage" procedure, in which the patient has permanent quadripolar tined leads implanted in the operating room. The patient undergoes a trial period; if this is successful they then return to the operating room for tunneling of the leads and placement of an IPG.

Since the introduction of permanent quadripolar tined leads for test stimulation in 1997, multiple groups have published on the successful use of these leads. Today, most physicians in the United States perform a test procedure with these leads. One advantage of the quadripolar lead test procedure is that the same responses should be obtained once the external neurostimulator is replaced by the permanent IPG because the lead–nerve interface does not change. In theory, the tines should prevent lead migration and thereby allow a longer test period of up to two weeks.

A few studies have directly compared outcomes using temporary leads in the office compared with permanent tined lead placement in the operating room. In one recent nonrandomized study, Leong et al. [35] compared the patients' response rate to the PNE test and the first-stage tined lead placement test for SNS. They observed that in 69 patients with OAB when PNE was followed by stage 1 implantation, 47% had a positive response to PNE and 69% had a positive response to stage 1 implantation, which was statistically significant, suggesting that an additional 22% of patients may be salvaged with stage 1 implantation. A longer trial, up to two weeks, appears to increase eligibility for implantation, possibly because it takes some patients a longer time to adjust settings or otherwise achieve therapeutic benefit [36]. In practice, trial periods longer than two weeks are uncommon, primarily because of the potential for increased risk for infection. Furthermore, the manufacturer recommendation is not to exceed a two-week trial period.

Whether there is an advantage in performing a one-stage rather than a two-stage procedure has been evaluated. Everaert et al. [37] in a prospective trial randomized 41 patients who had a successful trial procedure with temporary leads to either direct IPG implantation (one-stage) or to undergo a test procedure with tined leads before implantation (two-stage). At 24 months of follow-up, patients who underwent a two-stage procedure had a lower rate of failure compared to the patients who had undergone a single-stage procedure (14% vs. 33%).

Overall, it seems that an office-based test procedure remains a reasonable option for most patients, and that a successful test procedure generally portends a good outcome after implantation. A test procedure with tined leads placed in the operating room may be more suitable for patients in whom the test procedure is equivocal, for patients who may require a longer test period to evaluate efficacy, and for patients in whom lead migration is suspected. Many experienced implanters, including the senior author, start with an office test stimulation in most patients.

## Percutaneous tibial nerve stimulation

The posterior tibial nerve is a mixed sensory–motor nerve, with axons from L4 to S3 spinal roots. It is thought that electrical stimuli of these nerve inhibits bladder activity, which then evokes a central inhibition of the micturition reflex pathway in the spinal cord and brain. McPherson first demonstrated in a cat model in 1966 that stimulation of cut ends of peripheral nerves, including the posterior tibial nerve, inhibited bladder contractions [38]. Almost two decades later in 1983, McGuire et al. applied electrical stimulation of hindquarter nerves to treat detrusor instability in spinal cord-injured nonhuman primates [39]. They later on went on to demonstrate its efficacy in humans with stimulation of the posterior tibial nerve [12]. PTNS was approved by the FDA in 2000 for OAB and has the advantage of lacking a permanent implant.

The current practice of PTNS treatment generally uses a 34-gauge needle electrode that is inserted approximately 5 cm cephalad to the medial malleolus and slightly posterior to the tibia. The needle is inserted at a 60° angle, and advanced to a depth of approximately 4 cm. A surface electrode is placed on the calcaneus of the ipsilateral foot. The electrode and needle are connected to a battery-powered stimulator, which is set at a current of 0.5–9.0 mA at 20 Hz, based on motor and sensory responses. Appropriate needle localization is verified by great toe plantarflexion or fanning of digits 2 through 5 in response to an initially higher amplitude stimulation. The patient generally undergoes treatment for 30 minutes weekly for 12 weeks. During this treatment period, patients complete voiding and pain diaries to ensure improvement of their symptoms. This is followed by treatments as needed based on patient symptoms. The procedure can be performed in the office without anesthesia and has minimal adverse effects. Currently, there is only one PTNS system commercially available, The Urgent® PC Neuromodulation System (Uroplasty Inc., Minnetonka, MN, USA).

### Percutaneous tibial nerve stimulation efficacy and outcomes

PTNS has shown good efficacy in the treatment of OAB symptoms with several studies demonstrating success rates of about 60–70% [40, 41]. In the Study of Urgent PC vs. Sham Effectiveness in Treatment of Overactive Bladder Symptoms (SUmiT) trial [41], 220 patients with OAB were randomized to receive either PTNS or a sham therapy. Compared with patients receiving sham therapy, patients who received PTNS had significant improvements in urinary frequency, urgency, urge incontinence episodes, and nocturia; 54.5% of patients receiving PTNS compared with 20.9% of patients receiving sham therapy reported moderate to marked improvements in global response assessment [41]. These findings were confirmed in a European study randomizing 35 women with medication refractory OAB to either PTNS or placebo (electrical stimulation of the gastrocnemius muscle). In that study, 71% of patients receiving PTNS reported improvement compared with 0% in the placebo group [40].

PTNS also has an effect equivalent or superior to anticholinergic medications but with a lower side-effects profile. In the Overactive Bladder Innovative Therapy trial, 100 patients were randomized to either 12 weeks of PTNS without pharmacotherapy or tolterodine extended release 4 mg. A global response assessment demonstrated significantly more patients reporting substantial improvement with PTNS compared with tolterodine (79.5% vs. 54.8%) [42]. However, both treatments led to similar objective improvements in terms of urinary frequency and urge incontinence episodes, leading the investigators to conclude that PTNS offered efficacy similar to that of tolterodine.

It is well known that both anticholinergics and sacral neuromodulation lose their efficacy when they are discontinued. However, an important advantage of PTNS is that it seems to provide a prolonged carryover effect with sustained symptom improvement even when the nerve is not being stimulated [43]. The Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation (STEP) study examined this carryover effect by enrolling patients who demonstrated clinical improvement after 12 weekly sessions. Study participants were prescribed a fixed-schedule 14-week tapering protocol followed by a personal treatment plan aimed at sustaining overactive bladder symptom improvement. Over a 36-month period, 77% of patients sustained moderate or marked improvement in all domains (nighttime voids, urge incontinence episodes, quality of life, $P < 0.0001$), requiring only an average of 1.1 treatments per month [44].

## Complications

Over the years, percutaneous test stimulations have been exceedingly safe, and complications at the preimplantation stage are rare. The main problem with temporary lead test procedures is lead migration reported at a rate of about 10–15%; however, this rate is lower when tined leads are used [19]. With placement of the IPG in the upper buttock region rather than the abdomen, significant decrease in IPG site pain has been recorded [19]. Infection rates have been reported to be between 5% and 10% [19, 45]. The overall revision rate reported in the literature is approximately 20–30% [19, 45–47].

According to published data in the literature, PTNS is safe and well tolerated. Complications of percutaneous tibial nerve stimulation are rarely reported. As with acupuncture, patients may experience a temporary discomfort during the initial needle placement as it travels through skin; however, there is minimal pain reported as the needle enters the deeper tissues. Nevertheless, future studies should continue to evaluate safety data of the technique.

## Cost considerations

Disadvantages of SNS include high initial treatment costs because of device costs, operating room and anesthesia costs for implantation. SNS must have excellent long-term efficacy to justify initial costs. Watanabe et al. estimated that the initial cost for SNS was US$22 226 but that is likely a significant underestimate [48]. An office-based test procedure is useful in identifying patients who are likely to fail implantation and since an office-based test procedure is significantly less expensive than an operating room procedure with permanent leads, it should help reduce cost. In the randomized trial by Everaert et al. [37], costs per patient were about €2000 higher for patients undergoing a two-stage procedure. The added benefit of a longer test period and of not implanting an IPG in patients who fail a test procedure with permanent leads may offset this cost difference somewhat. Cost-effectiveness modeling studies have been limited and generally compared neuromodulation to other entities such as botulinum toxin injection [49].

A major limitation of PTNS as a treatment option is the financial burden/time requirement for some patients and families who need to travel to the office weekly for stimulation. There is currently a significant amount of ongoing research examining home administration systems and micro implants which may improve patient access and treatment compliance while improving treatment costs. Although overall success rates may seem similar for PTNS and SNS, comparisons are quite difficult because the populations undergoing each of these treatment options is quite different. A recent cost-effectiveness study used estimated success rates as 67% for PTNS versus 55.4% for an SNS test stimulation. A slightly higher percentage (90% vs. 71%) remained on therapy with SNS versus PTNS after a successful initial treatment, but at a significantly higher cost (US$24 342 vs. US$4867) [50]. It is clear that appropriately randomized long-term studies are needed to better understand the cost-effectiveness of neuromodulation.

## Summary

Common voiding disorders including OAB, nonobstructive urinary retention, and pelvic pain affect millions of patients' quality of life with associated high economic costs. For patients with OAB, many treatment options are available. First-line treatment options remain pelvic floor rehabilitation and behavioral therapies and second-line options would be anticholinergic and other medications. Although antimuscarinic drugs can reduce voiding symptoms, many patients do not tolerate the side-effects, and some do not experience sufficient relief. More invasive treatment modalities such as surgery are indicated in patients who are refractory to medical management and have persistent urinary morbidity. Modulation of bladder reflex pathways with office-based procedures, such as SNS and PTNS, have proven to be efficacious. Since their approval for OAB symptoms, these treatment modalities have grown in popularity, with multiple case series and randomized controlled trials demonstrating adequate safety and efficacy. PTNS has the benefit of being an office-based procedure with relatively low cost, while SNS has the advantage of permanent implantation with constant electrical stimulation, avoiding the need for weekly or monthly office visits.

Given the relatively high cost of the SNS procedure, patient selection remains a challenge for the clinician. Factors predicting a response to SNS for OAB symptoms are not well known. Physicians must depend on their clinical acumen and a test procedure to identify appropriate candidates for IPG implantation. Whether office-based percutaneous test stimulation is initially carried out or whether the tined quadripolar lead is initially placed remains at the discretion/experience of the clinician and patient preference. The office-based procedure is inexpensive and provides the patient and physician with valuable information to make an informed decision about proceeding further. The advantages of the permanent lead include decreased lead migration and a longer test period of up to two weeks. Furthermore, with the permanent lead, the patient will have the exact same sensory and motor responses during the test phase as the permanent implant as the lead remains unchanged. However, permanent leads require placement under monitored anesthesia care, have an increased cost, and will require two procedures in the operating room even if unsuccessful. With the continued evolution of the procedure, complication and revision rates are gradually decreasing.

As ongoing research provides insight into the mechanism of action of neuromodulation, expanding indications for its usage are likely to be found. Efforts now turn to developing even smaller devices with rechargeable batteries with the goals of making the procedure less invasive. Hopefully, these improvements will not come at increased cost to an already expensive healthcare system. Therefore, further innovation to provide better access to care and improved cost-effectiveness is needed for SNS and PTNS to endure as a treatment option for voiding disorders.

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